May 16-18

Montreal, Canada

2024

CONFERENCE

10th Anniversary Edition

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international
behavioural
trials network

IBTN Workshop:
Using the ORBIT Model for Research on Complex Behavioral Interventions

Orbit
Obesity-Related Behavioral Intervention Trials

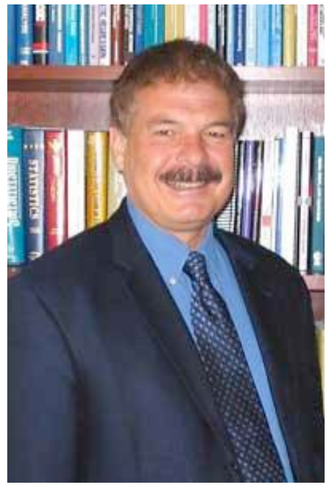
How Complex Interventions Fit Into the ORBIT Model

Susan M. Czajkowski, Ph.D.
National Cancer Institute
Bethesda, Maryland, USA

Early-Phase Research on Complex Interventions

Lynda H. Powell, Ph.D.
Rush University Medical Center
Chicago, Illinois, USA

Development and Testing of Stepped Care Algorithms



Kenneth E. Freedland, Ph.D.
Washington University in St. Louis
St. Louis, Missouri, USA

What is a Complex Intervention?

AN INTERVENTION THAT INVOLVES ONE OR MORE OF THE FOLLOWING:

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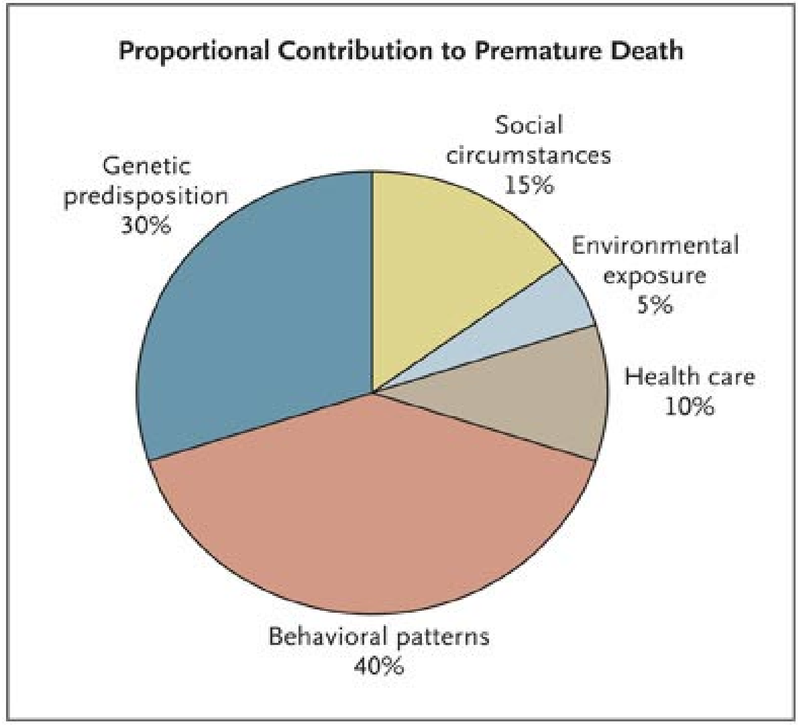
COMPLEX INTERVENTIONS ARE MOST LIKELY NEEDED TO INTERVENE ON COMPLEX OR DIFFICULT PROBLEMS AND PRODUCE A BENEFIT ON IMPORTANT HEALTH OUTCOMES

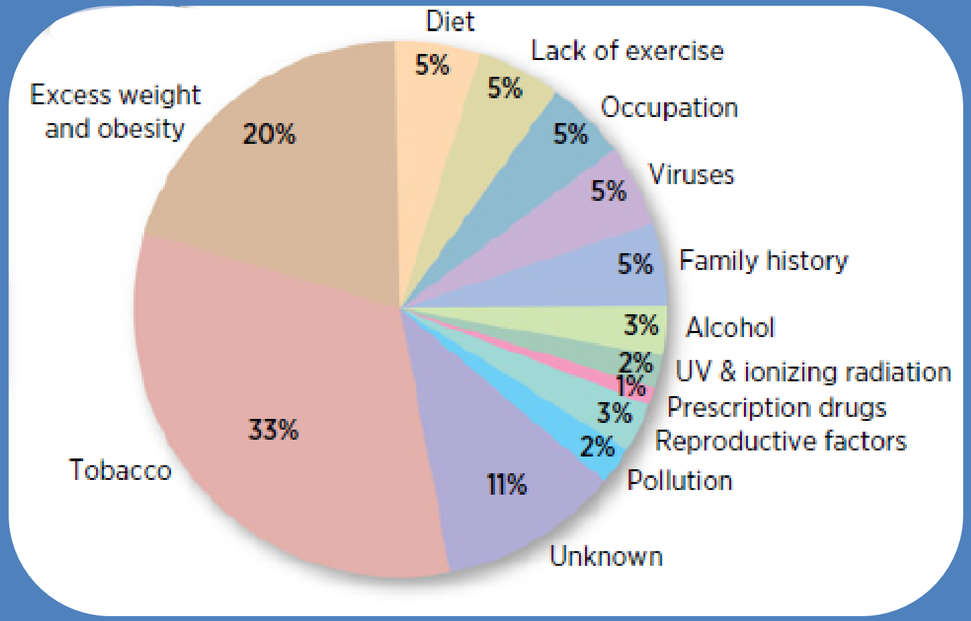
Behavioral Risk Factors are Major Contributors to Disease, Disability & Prrematurе Death

Changing unhealthy behaviors is the “single greatest opportunity to reduce premature deaths…”



Schroeder SA. N Engl J Med 2007;357:1221-1228

Up to 50% of Cancers May Be Preventable through Health Behavior Change



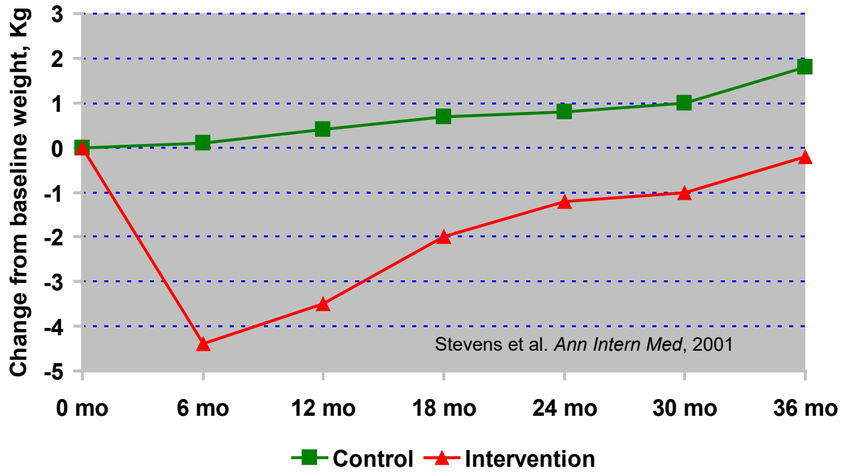
Lippman et al., Cancer Prev Res, 2018

There are many challenges to adopting & maintaining a healthy lifestyle, especially given our busy lives & environments that promote unhealthy habits

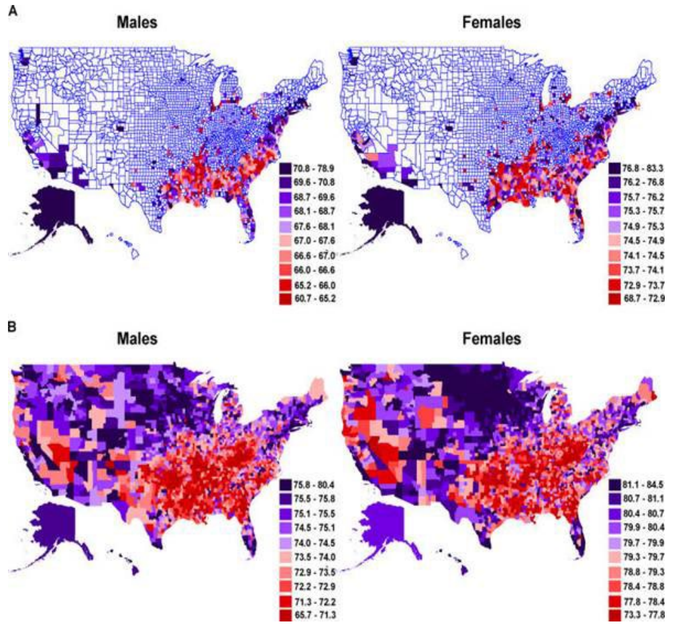
Even when behavior change is successful, maintenance of healthy behaviors across time is challenging

Trials of Hypertension Prevention II:

Weight loss over 36 months in 2382 overweight pre-hypertensives



Disparities exist in behavioral risk factors & health outcomes based on ethnicity, race & geographic location



(A) Life expectancy at birth for black males & females
(B) Life expectancy at birth for white males & females

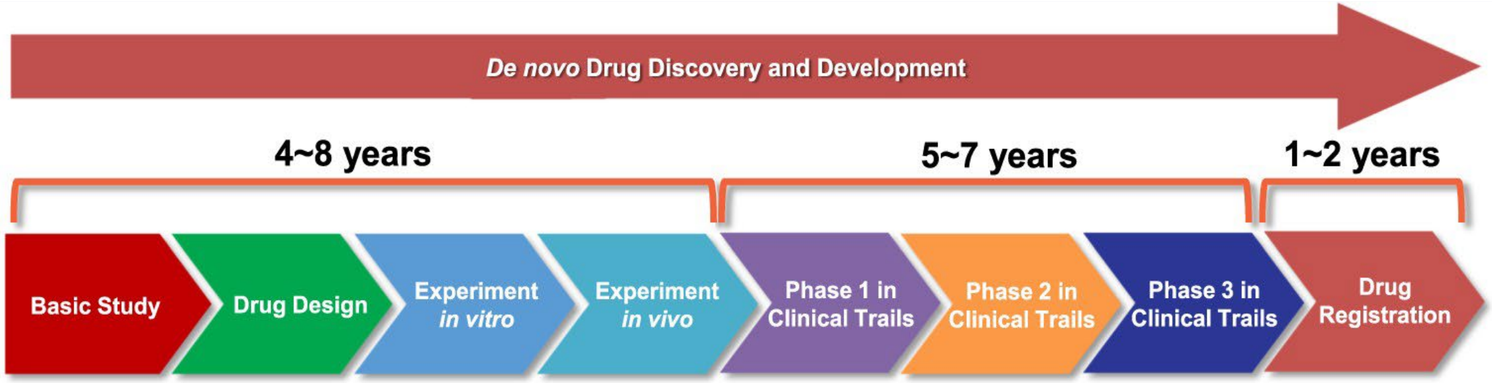
Murray, *PLoS*, 2008

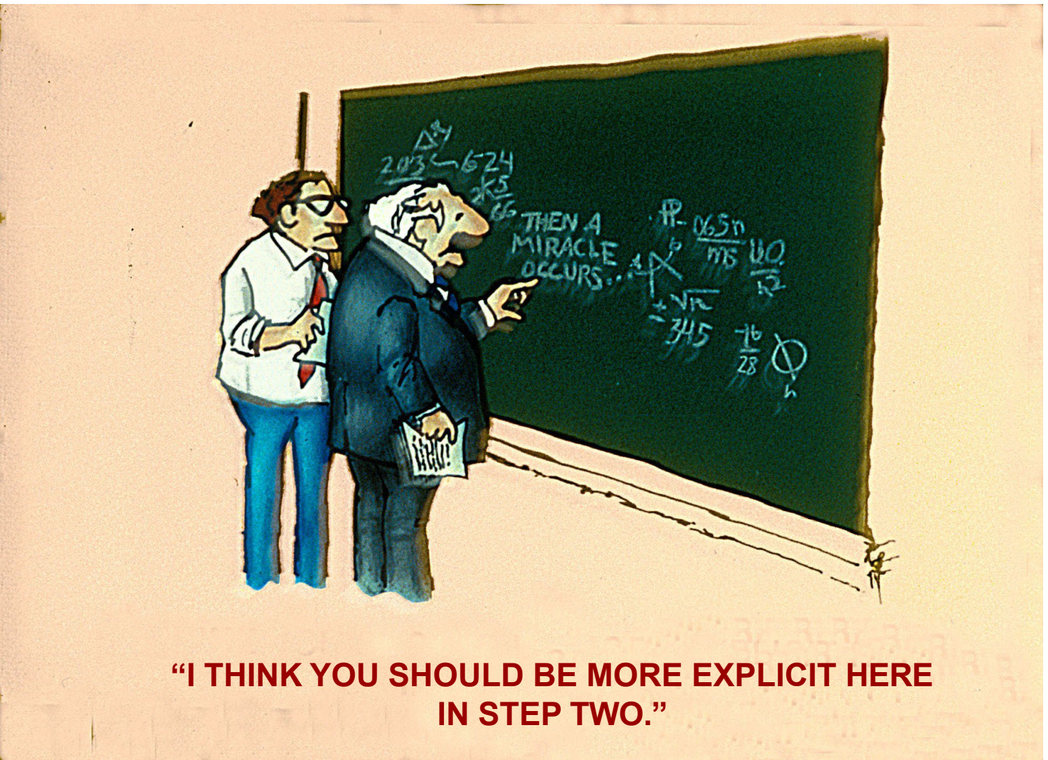
Engaging in a healthy lifestyle is the exception, not the rule

- Only 7.7% of US adults practice a combination of 5 healthy behaviors: not smoking, ≥ 5 fruits & vegetables/day, adherence to recommended amounts of physical activity, sleep, and alcohol use (Adams et al., 2013)
- Over 78 million U.S. adults and about 12.5 million (16.9%) children and adolescents are obese (Ogden et al., CDC, 2012)
- By 2030, it is estimated that half of all adults (115 million adults) in the United States will be obese (Wang et al, Lancet, 2011)

Developing and Testing Interventions for Chronic Diseases

The drug development process





"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."

Behavioral intervention development: The ISLAGIATT principle*

*It Seemed Like A Good Idea At The Time

What's the Problem?

- Lack of industry support
- No regulatory requirements
- Institutional, cultural & systemic barriers
  - High-risk nature of translational & intervention development research
  - Institutional incentives favor short-term not long-term progressive programs of research
  - Behavioral development frameworks/models not widely known or used

What's the Result?

WE PRODUCE MANY OBSERVATIONAL STUDIES

Strong Evidence that Behavior Is Associated with Health Problems

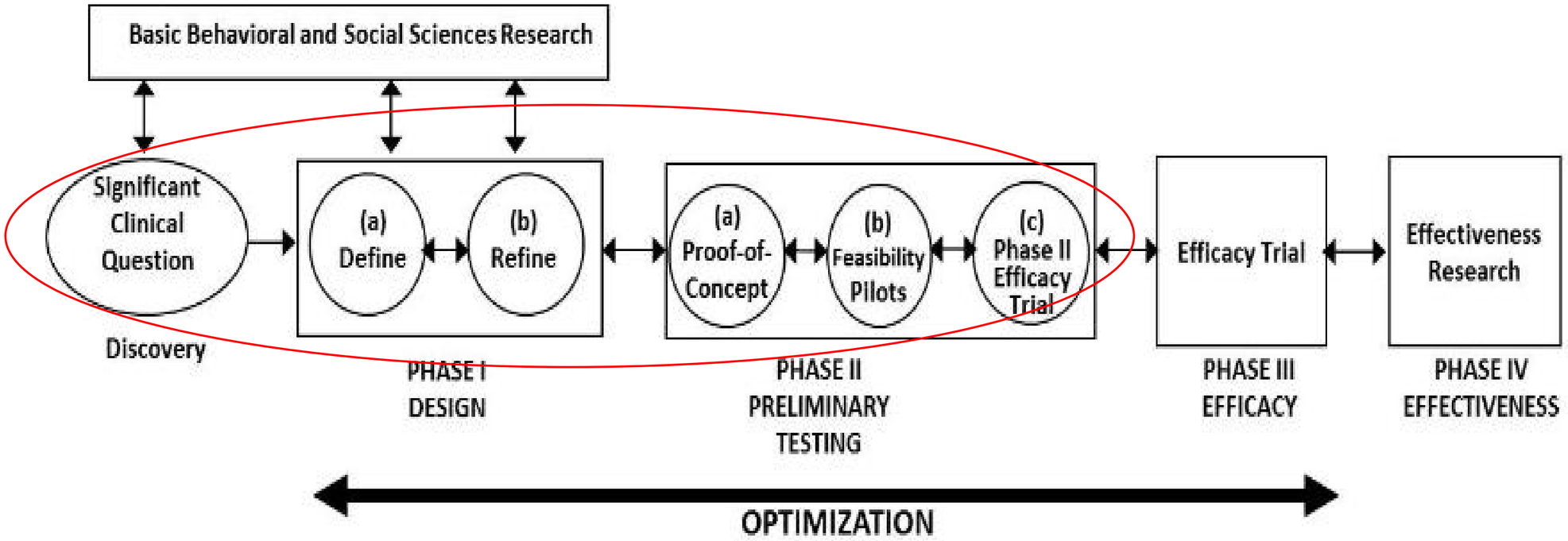
OUR INTERVENTION STUDIES

Focus on Demonstrating Statistically Significant but NOT Clinically Significant Effects

Produce Weak Evidence that Behavioral Interventions Can Improve Health

The ORBIT Model

Progressive Early Treatment Development



Czajkowski, Powell et al., *Health Psychology,* 2015
Powell, Freedland, Kaufmann, *Behavioral Clinical Trials,* Springer, 2021

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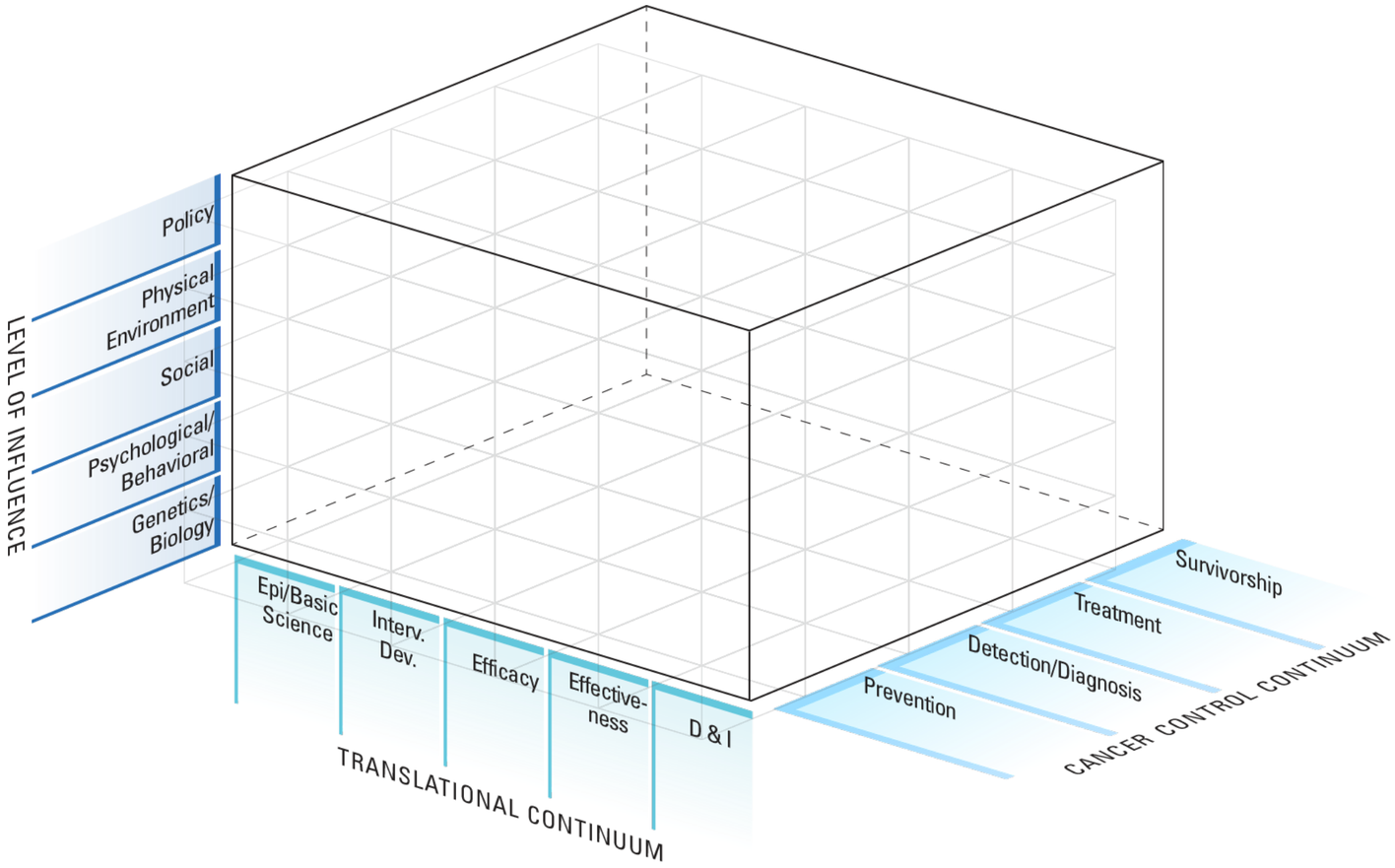
COMPLEX INTERVENTIONS ARE MOST LIKELY NEEDED TO INTERVENE ON COMPLEX OR DIFFICULT PROBLEMS AND PRODUCE A BENEFIT ON IMPORTANT HEALTH OUTCOMES

A Multi-level, Translational Framework for Understanding and Improving Cancer-related Health Behaviors



https://cancercontrol.cancer.gov/brp/hbrb/strategy.html

The ORBIT model can be used as part of multilevel frameworks: Integrating the ORBIT model with Policy-focused Research

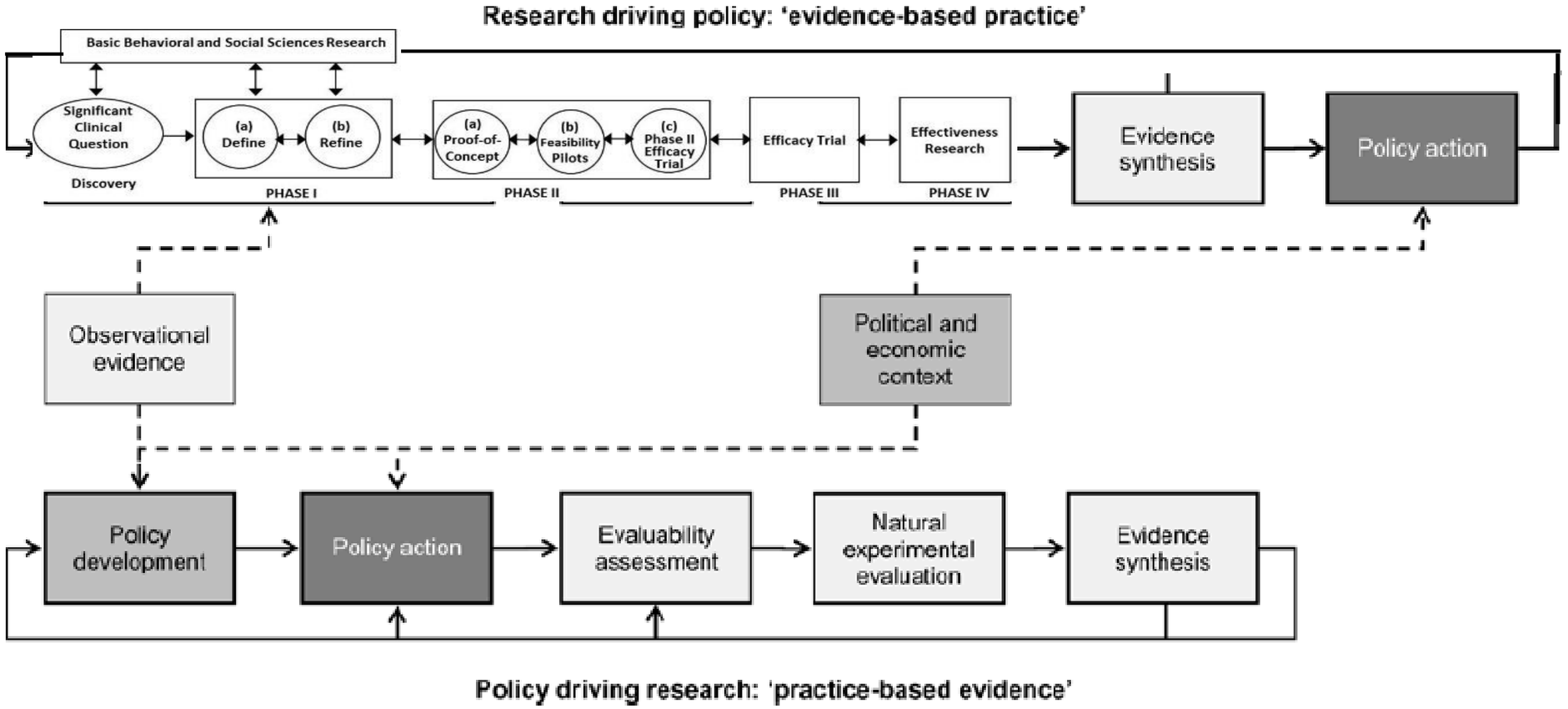


Figure 1 Two complementary modes of evidence generation.

Ogilvie et al., 2019

Obesity-related Policy, Systems, and Environmental Research in the US

June 4-5, 2024

Join this virtual workshop on June 4–5 to delve into policy, systems, and environmental strategies for preventing childhood obesity. Featuring experts from leading research and academic institutions, this event aims to advance equity in obesity prevention.

Learn more and register today: https://shorturl.at/hDEWX

NCCOR
National Collaborative on Childhood Obesity Research

Accelerating Progress to Reduce Childhood Obesity

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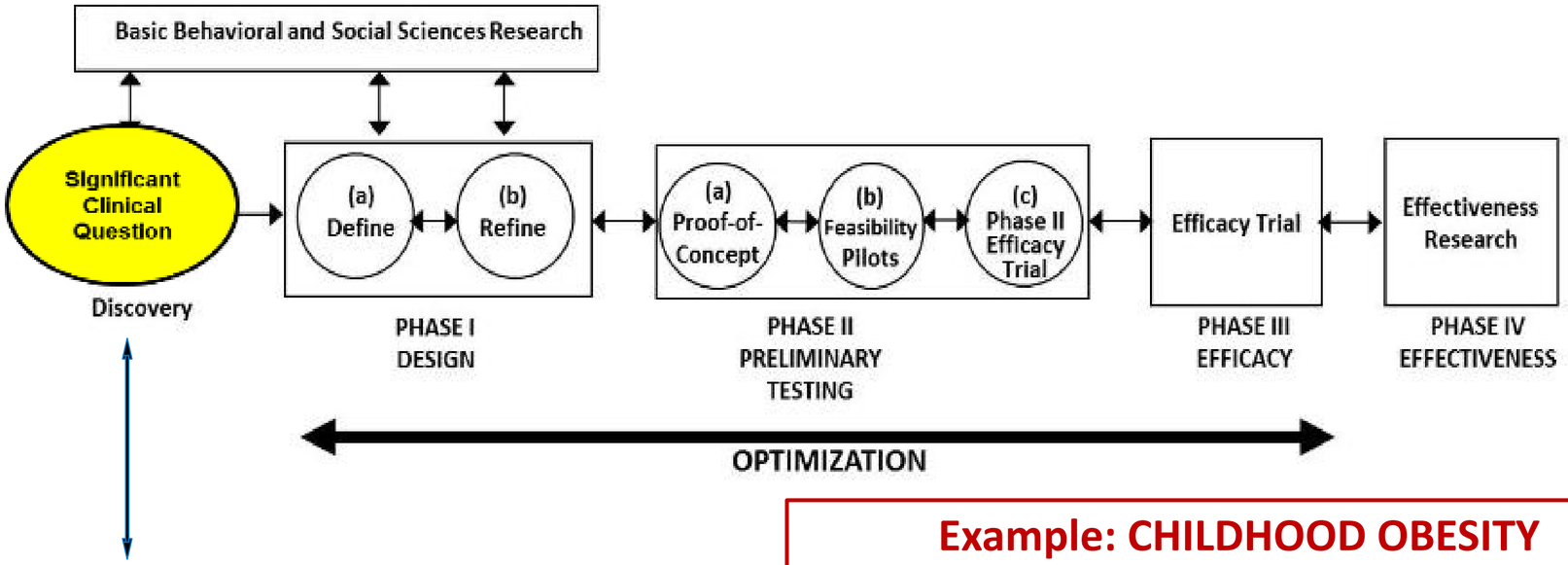
DISCOVERY: Significant Clinical Question



BEGIN WITH THE END

Significant health problem is:

--highly prevalent

--highly prevalent in a subgroup

Current treatment is

--not very effective

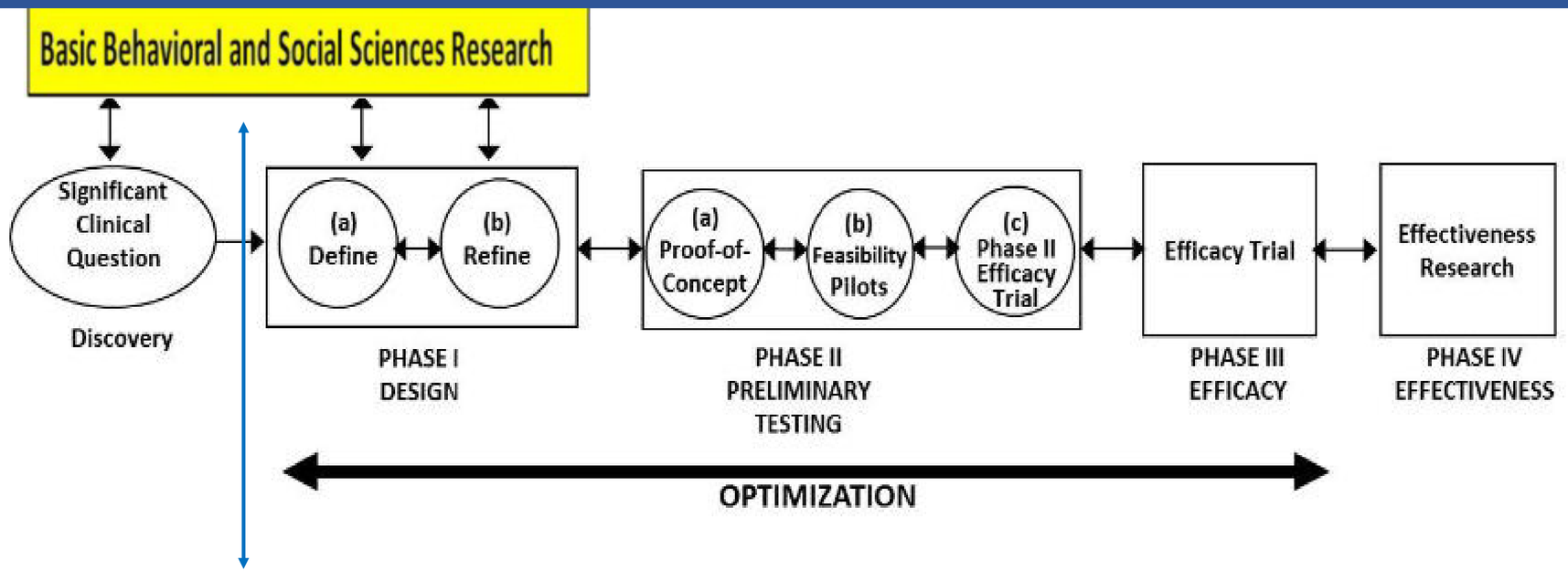
--not adhered to

Example: CHILDHOOD OBESITY

- 2/3 of U.S. adults & 1/3 of children are either overweight or obese
- Overweight & obesity in childhood are linked to chronic diseases – heart disease, cancer, diabetes
- Obesity often affects multiple family members – children, siblings & their parents
- We need more effective approaches to addressing obesity in children & their families

DISCOVERY: Basic Behavioral and Social Science

Orbit
Obesity-Related Behavioral Intervention Trials



MECHANISMS

Fundamental principles of behavior based on classical and operant conditioning:

- – Cue-based learning & habit formation -
- - Food is a powerful reinforcer
- – Habituation – the reduced responding to repeated stimuli – occurs across a variety of types of stimuli, including food

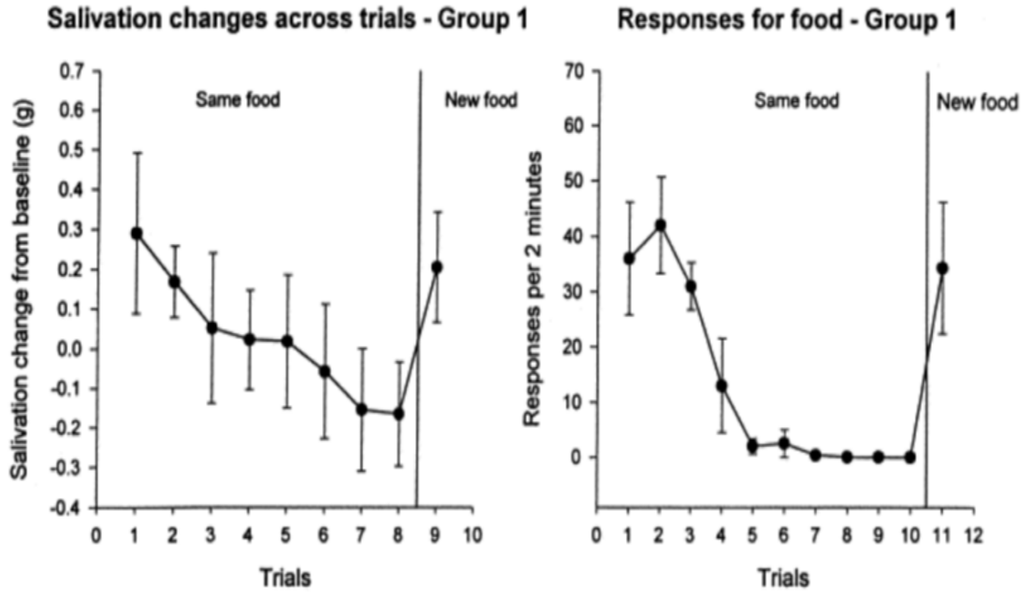
Example
CHILDHOOD OBESITY

--What role might learning theory principles, such as habituation, play in eating behavior & weight loss?

Harnessing habituation, via reducing dietary variety, to enhance obesity treatment

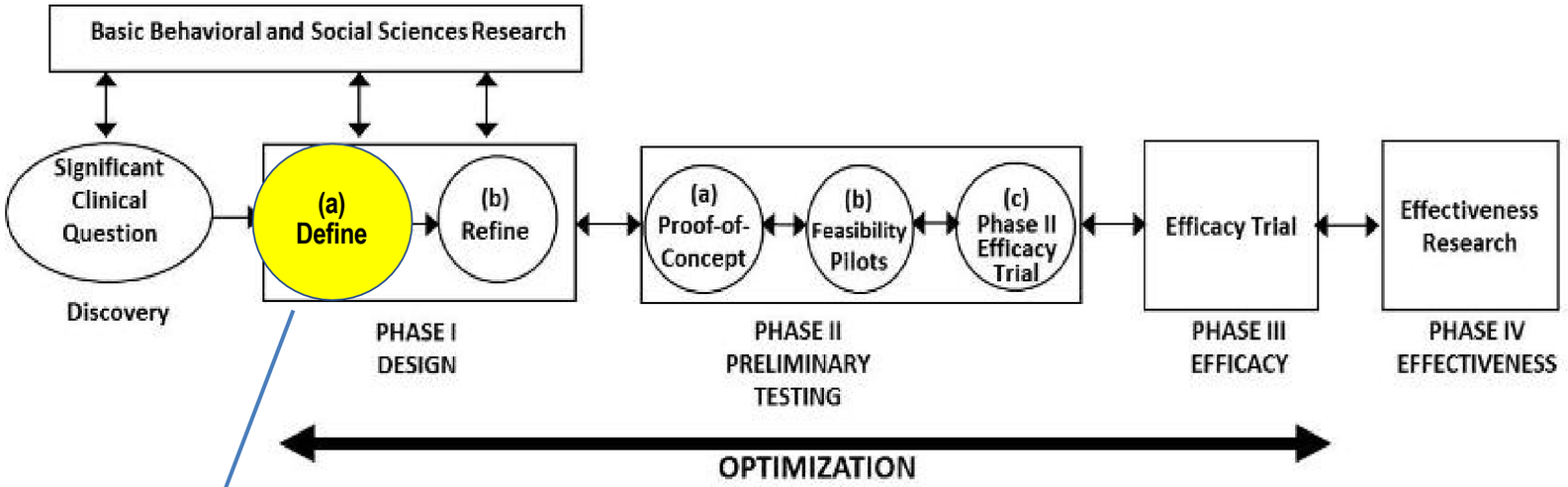
PI: Leonard Epstein, Ph.D., University at Buffalo

- **For treatment of obesity, the goal of all dietary prescriptions is to reduce energy intake**
- **Habituation theory -- repeated presentation of a stimulus influences responding to the stimulus (behaviorally, physiologically)**
  - **Repeated presentations of the same food over time should reduce responsivity, decrease the length of an eating occasion, enhance satiation & reduce food intake**
- **Can a limited dietary variety prescription be developed that harnesses the effects of habituation on satiation & can it be implemented within an intervention?**



Epstein et al, *Appetite,* 2003

DESIGN: Define



DEFINE
Basic Elements

--Candidate Components
--Hypothesized Pathway
--Clinically Significant Targets

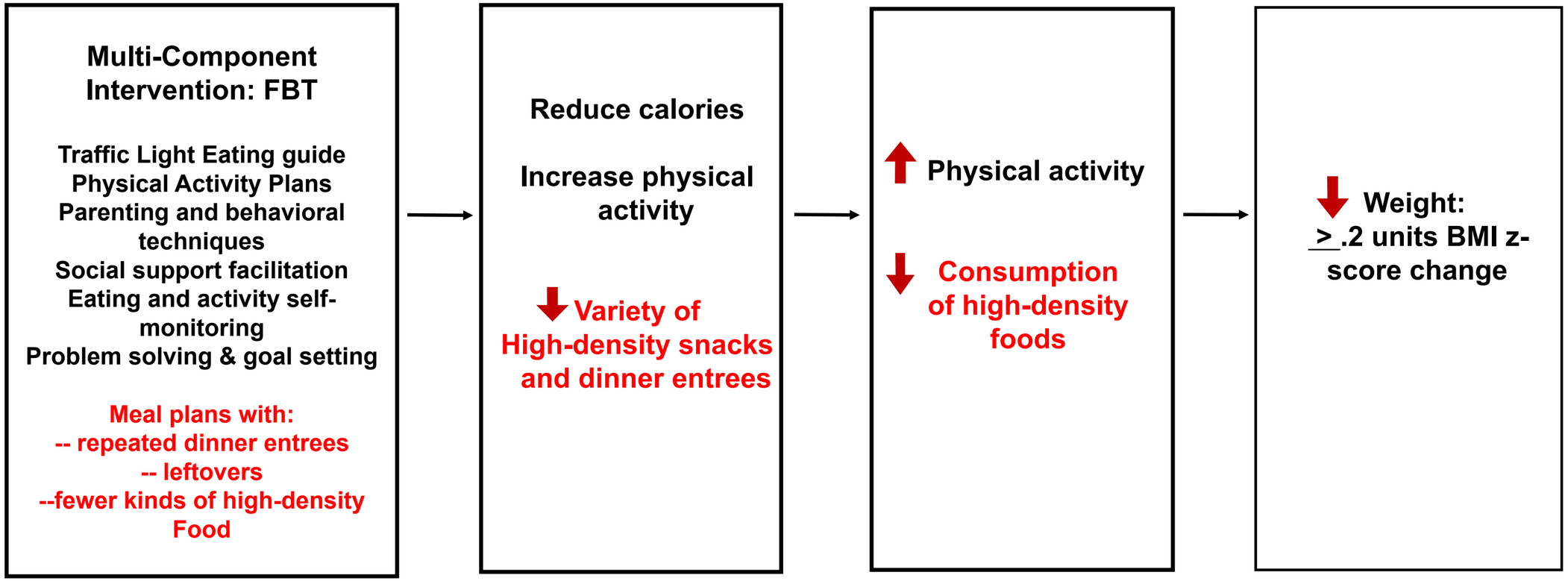
Example
CHILDHOOD OBESITY

Multiple Components: Family-based Treatment (FBT) supplemented with family meal plans that repeat dinner entrees, include leftovers, reduce variety of high-density foods

Pathway: ↓Variety → ↓ Consumption → ↑Weight Loss

Clinically Significant Target: The USPSTF defines clinically important weight loss in children as a change in BMI z-score by ≥0.2 units

Phase 1a: Define
Hypothesized Pathway, Intervention Targets & Components



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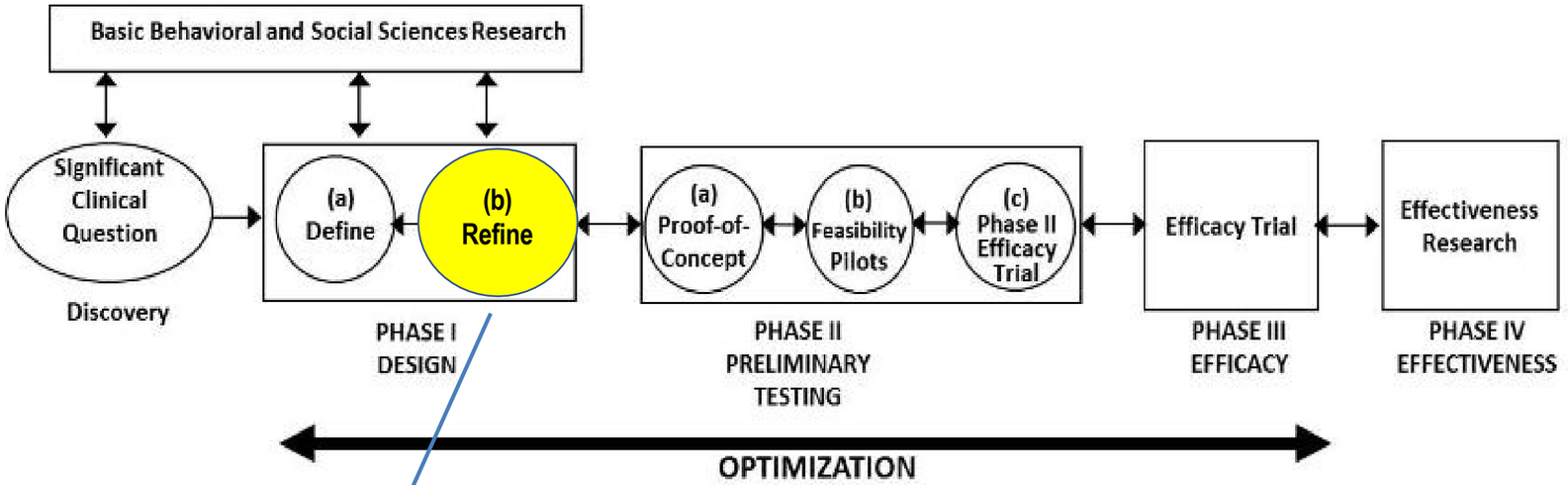
DESIGN: Refine



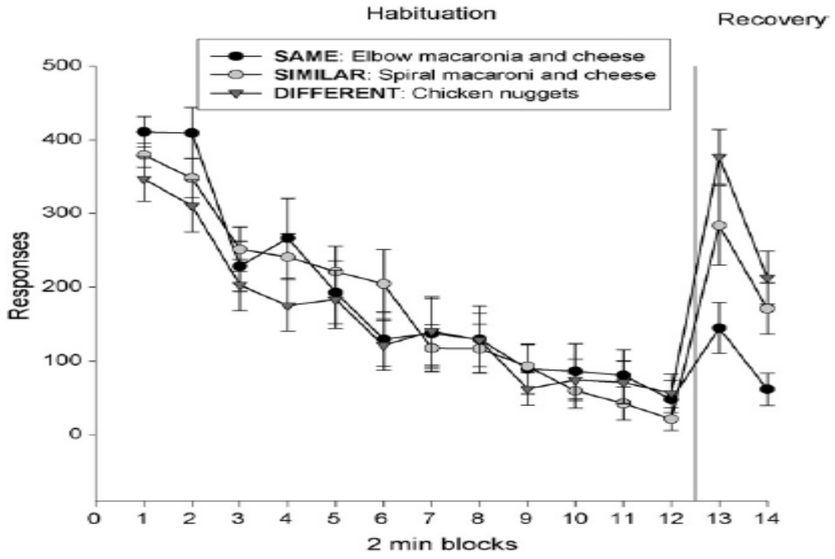
REFINE
For Strength and Efficiency

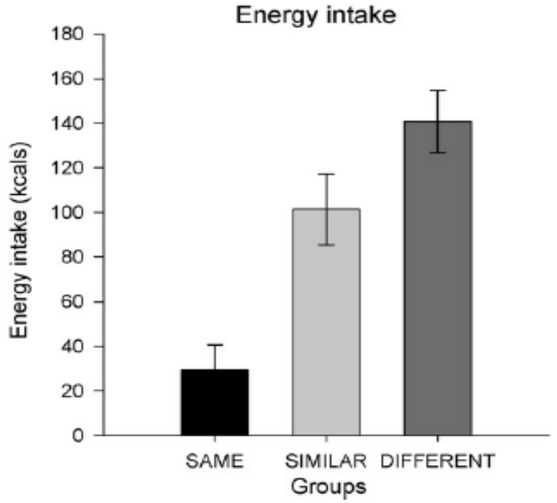
--Active Components?
--Optimum Duration, Dose, Delivery Mode, Frequency?

Example
CHILDHOOD OBESITY

--Focus group: feasibility, acceptability of meal plans that reduce variety
--Factorial design: Test effects of different ways of reducing variety in meals
--Experimental & Small N studies: How different do foods need to be to elicit response recovery (reducing habituation effects)?

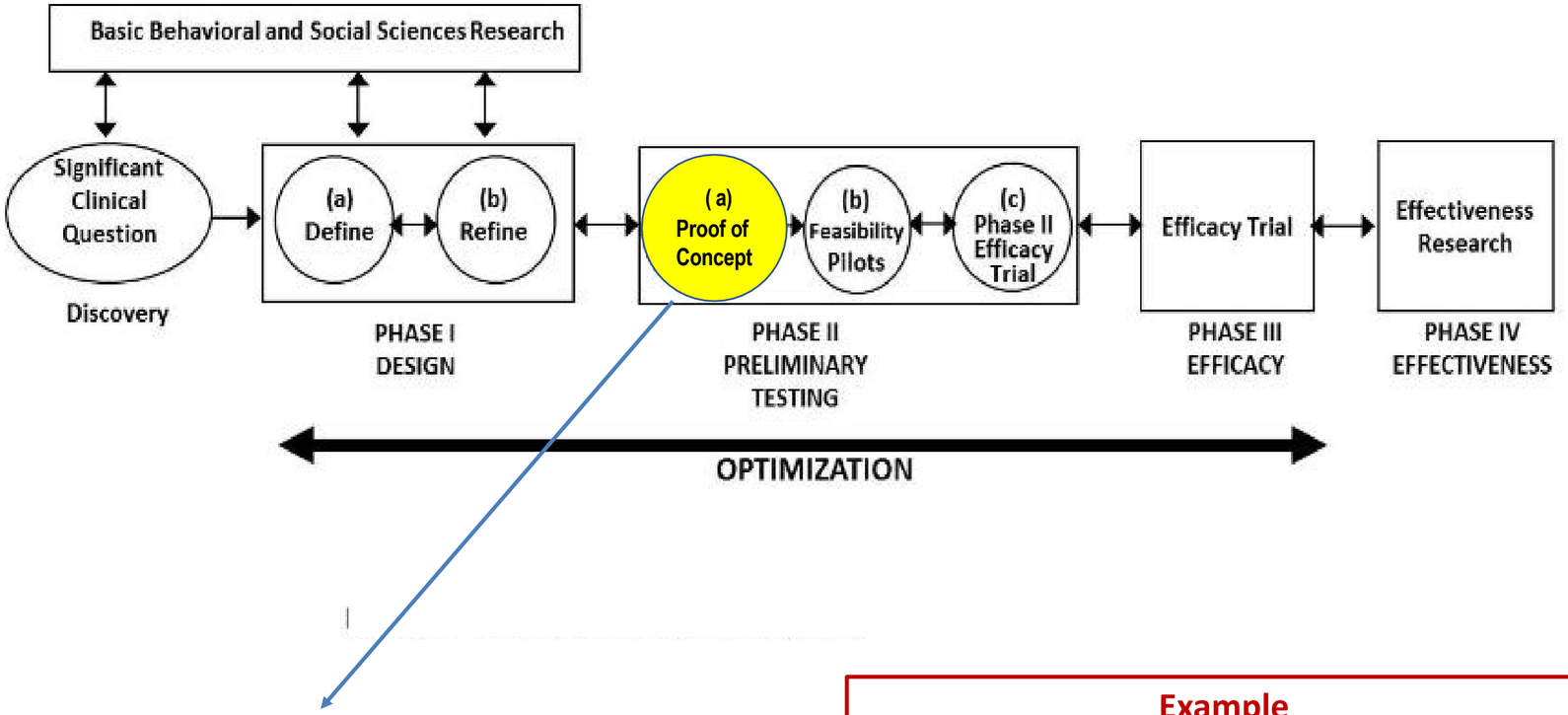
Habituation & Food Intake:
Phase Ib: Refining intervention content





Epstein et al, 2010

PRELIMINARY TESTING: Proof of Concept



PROOF OF CONCEPT

--Plausible Clinical Signal?

--Go/NoGo Decision

Example
CHILDHOOD OBESITY

--Small N, single arm study
--Clinically significant target:
--Adults: 3-5% weight loss in adults
--Children: BMI z-score change ≥ 0.2 units

Phase 2a: Proof-of-Concept

Enhancing Lifestyles in the Metabolic Syndrome (ELM))

Single Question:

Plausible health benefit?

Clinically significant target and success rate

Internal Validity?

No control for:

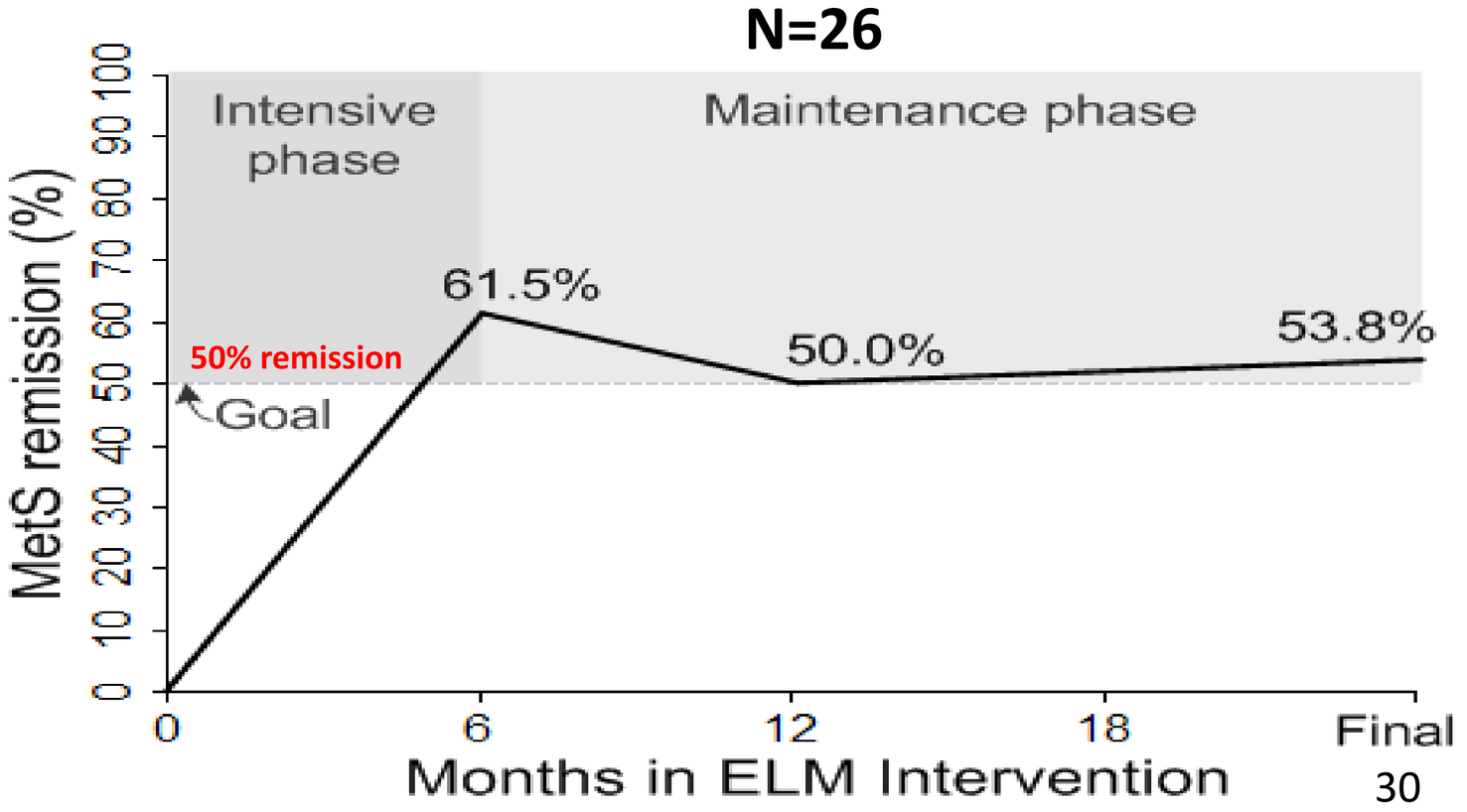
attention

passage of time

chance

Representative?

Accessible sample



Powell et al., 2018

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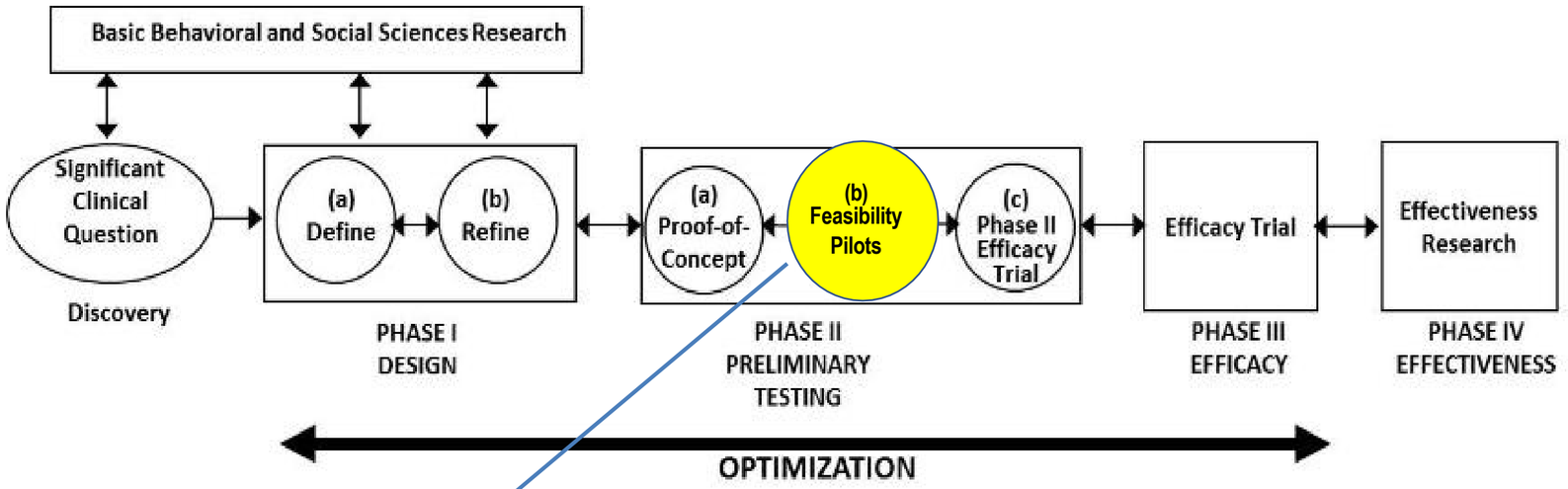
PRELIMINARY TESTING: Feasibility Pilots



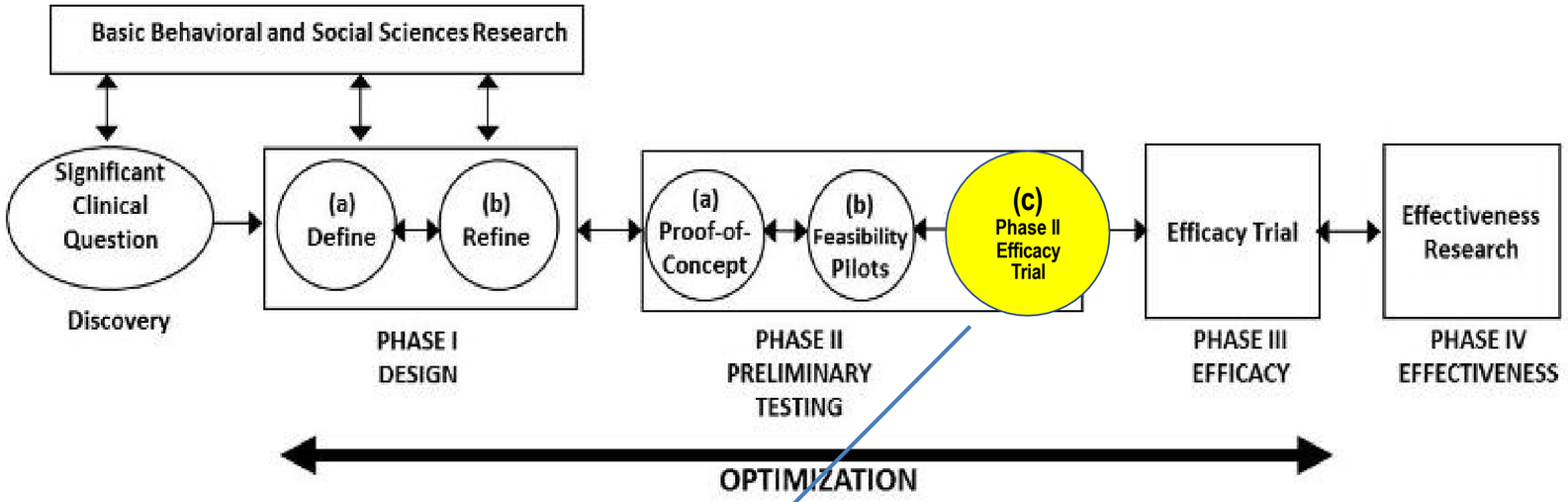
PILOT//FEASIBILITY STUDY

Preparation for clinical trial
- **--Recruit and retain?**
- **--Implement the trial protocol?**

Example
CHILDHOOD OBESITY

Can you successfully conduct a randomized trial?
- **--Can you recruit the required number of families who agree to adopt the specified meal plan?**
- **-- What's the control/comparison group?**
- **-- Drop-out rate from trial**

PRELIMINARY TESTING: *Phase II* Efficacy



***PHASE II* EFFICACY**

Statistical and clinical benefit on a behavioral risk factor, relative to a comparator

Example
CHILDHOOD OBESITY

--Fully powered randomized design
--Impact of reduced variety dietary intervention relative to a comparator

Phase IIc: Limiting dietary variety in family-based treatment (Epstein et al, 2015)

- 24 families, with a child ≥ 85th percentile BMI and aged 8 to 12 years

- Randomly assigned to 1 of 2 conditions:

  - Family-Based Treatment (FBT)
    - Traffic Light Diet (1000-1500 kcal/day, ≤ 2 servings/day of high-density foods)
    - Developed meal plans
    - ≥ 60 min/day of MVPA prescription

  - FBT+ Reduced Variety
  - Family-based treatment (identical to FBT)
    - Developed meal plans that repeated dinner entrees, included leftovers from the dinner entrees, reduced variety of high-density foods

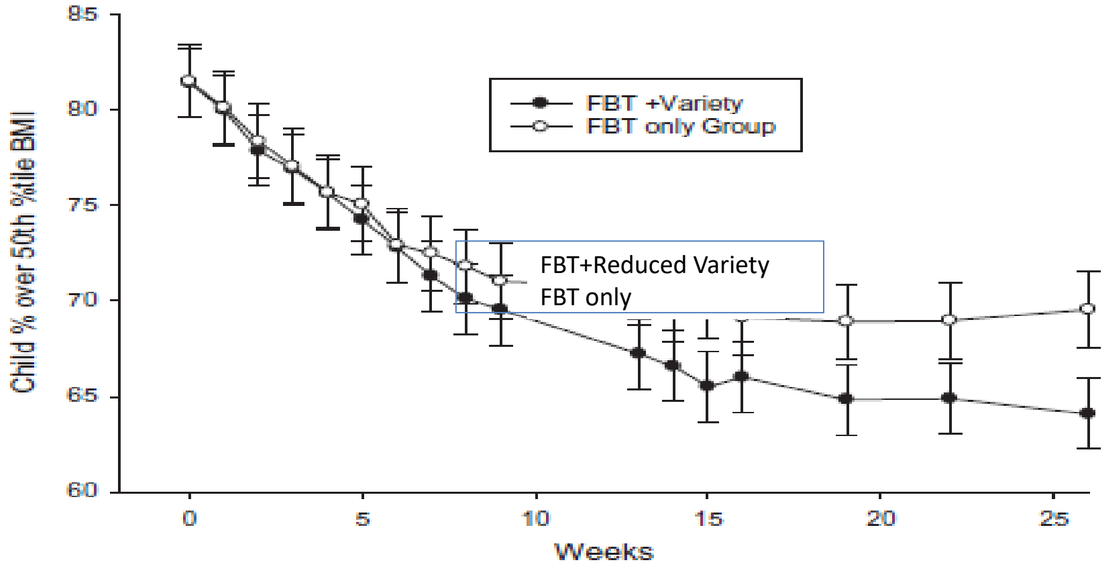
Outcomes

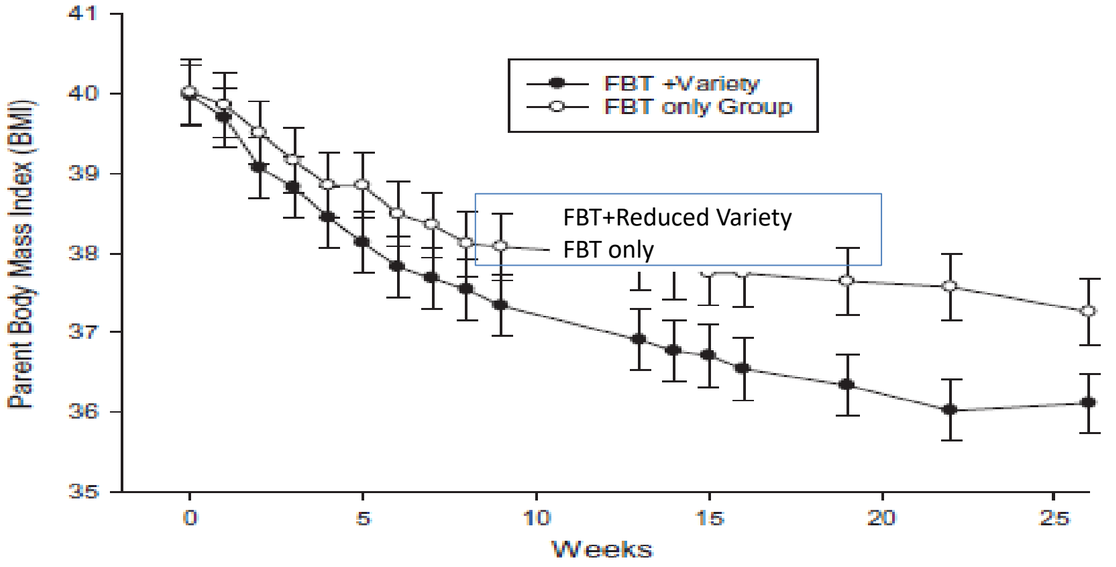
Child percent overweight:

- FBT+ Reduced Variety −15.4% vs. FBT only − 8.9%, p = 0.017

Variety of high-density foods consumed by family:

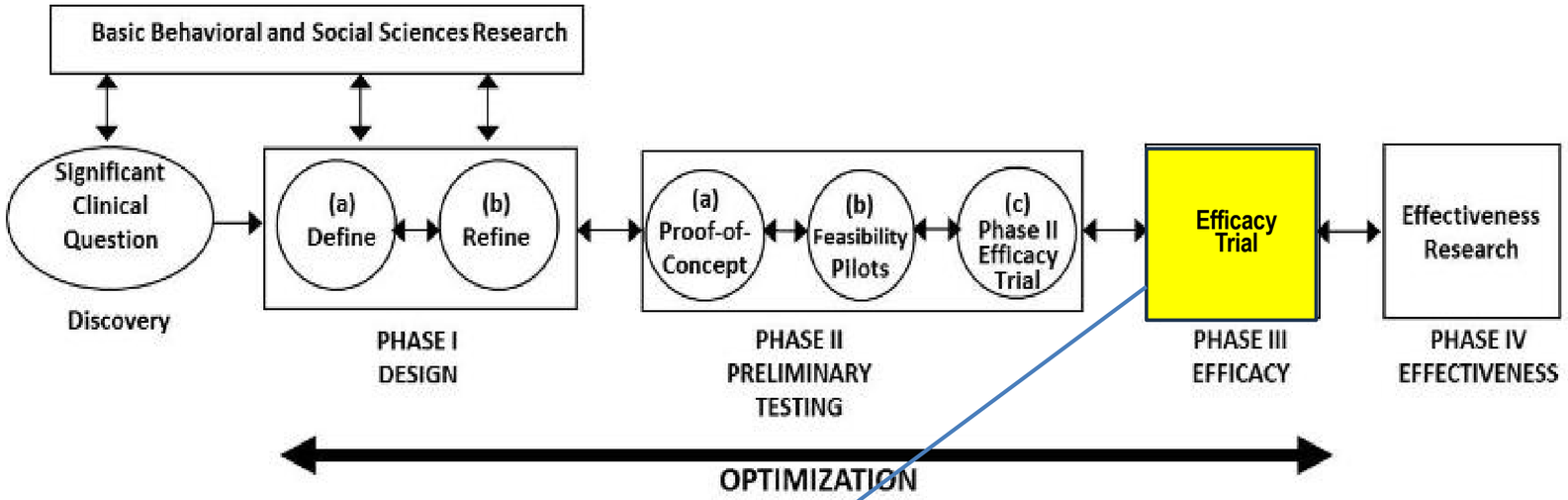
- FBT+Reduced Variety = 20.2 to 12.6 vs. FBT only = 19.7 to 16.8, p = 0.01





Adapted from Epstein et al, 2015

Phase III Efficacy



***PHASE III* EFFICACY**

Statistical and clinical benefit on a health problem, relative to a standard of care

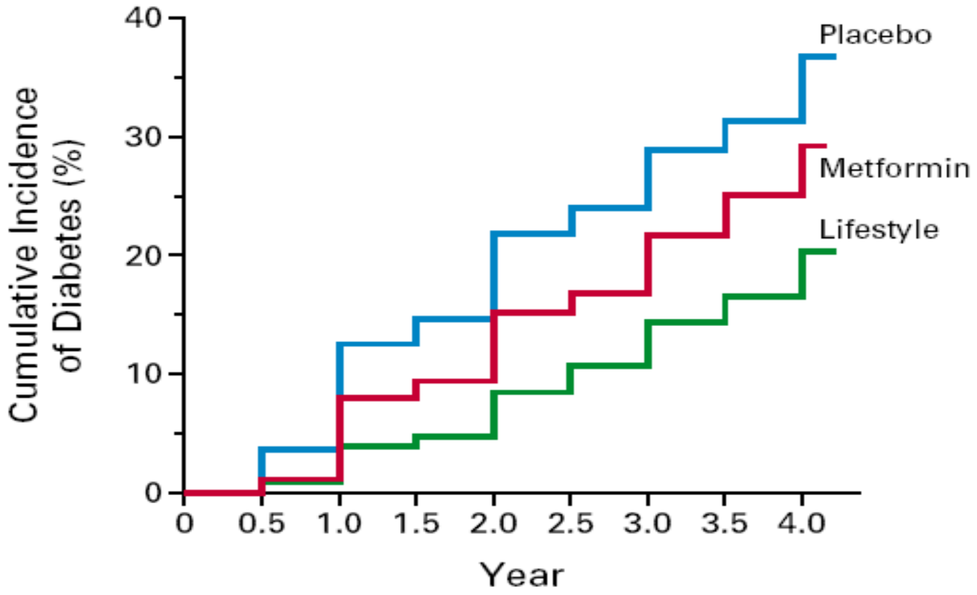
Example
CHILDHOOD OBESITY

--Fully powered randomized design
--Impact of combined reduced variety + Family-based obesity treatment on weight loss vs. usual care
--Larger, more diverse sample
--Longer follow-up (1-2 years)

"Why should I push toward a Phase III efficacy trial?"

Orbit
Obesity-Related Behavioral Intervention Trials

Diabetes Prevention Program



Knowler et al, *NEJM* 2002

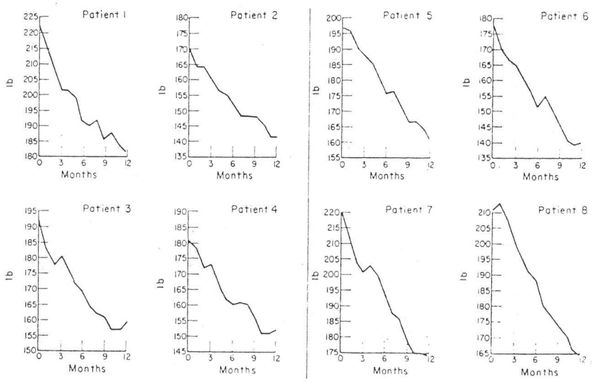
Implementation

Practice Guidelines that Prioritize *Phase III* Efficacy

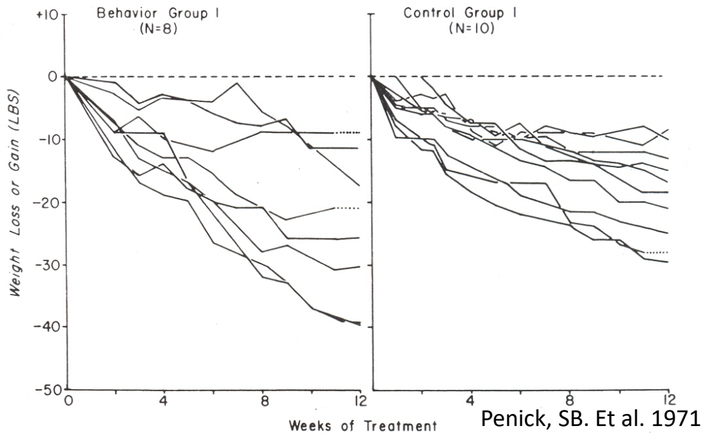
COUNTRY	RATING SYSTEM
INTERNATIONAL	GRADE
UNITED KINGDOM	Centre for Evidence-Based Medicine
SCOTLAND	Intercollegiate Guidelines Network
NEW ZEALAND	New Zealand Guidelines Group
CANADA	Canadian Hypertension Education Program
UNITED STATES	Minnesota Institute Clinical Systems Improvement
	American Family Physicians
	US Preventive Services Taskforce
	American College Cardiology/American Heart Association
	American Academy of Pediatrics
	American Academy of Neurology
	American College of Chest Physicians
	National Comprehensive Cancer Network
	Infectious Disease Society of America

30+ years of behavioral intervention development research leading to the DPP

Behavioral Control of Overeating



Stuart, R.B., 1967

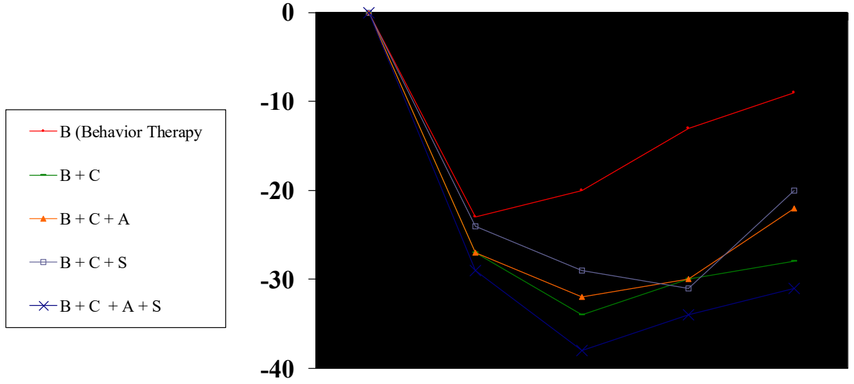


Penick, SB. Et al. 1971

Length of treatment

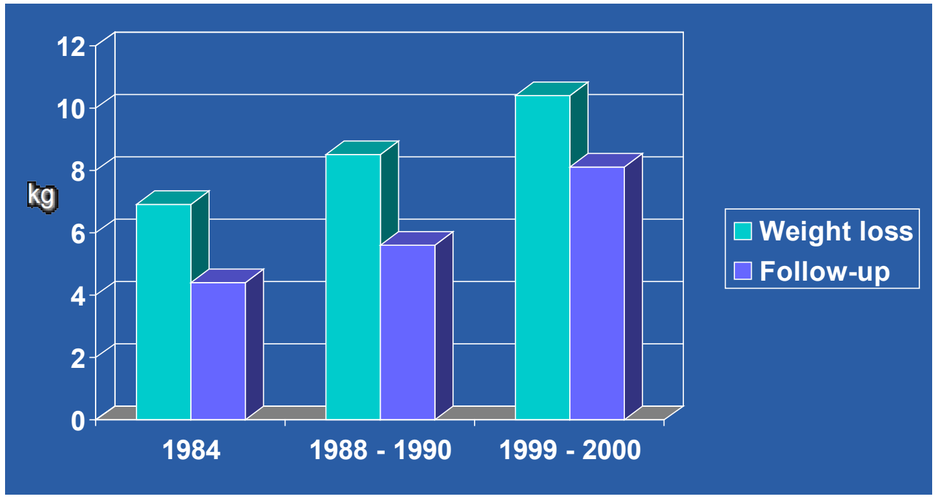
	1974	1978	1984
No. of studies included	15	17	15
Length of treatment (weeks)	8.4	10.5	13.2
Weight loss (kg)	3.8	4.2	6.9
Length of follow-up (weeks)	15.5	30.3	58.4
Loss at follow-up	4.0	4.1	4.4

Effects of Physical Activity on Long Term Weight Loss



Importance of Ongoing Treatment Contact

Study	Follow-up	Diet Only	Diet + Exercise
Pavlou	18 mo	-3	**-11**
Sikand	2 yr	-0.8	**-9.2**
Skendner	1 yr	-6.8	**-8.9**
	2 yr	+0.9	**-2.2**
Wadden	1 yr	-15.3	-13.5
	2 yr	-6.9	**-8.5**
Wing	1 yr	-3.8	**-7.9**
Wing	1 yr	-5.5	**-7.4**
	2 yr	-2.1	**-2.5**



Progress over time

SUMMARY: Core Elements

Orbit
Obesity-Related Behavioral Intervention Trials

❖ *Begins with the "end" in mind*

--Encourages push toward the *Phase III* efficacy trial to establish causality and implementation into practice.
--Discourages "*one and done*" interventions that fail to meet medical standards for implementation.

❖ *Progressive translational research*

--Encourages a progression of questions and research designs to answer them.

--Discourages "*one fell swoop*" studies that try to answer all questions in one trial and exclusive use of "*one size fits all*" randomized designs.

❖ *Emphasizes clinical significance in early-phase studies*

--Encourages early identification of clinically meaningful milestones to judge success of treatment.
--Discourages large samples powered for statistical significance during early treatment development.

❖ *Progressive but not prescriptive*

--Encourages identification of phase of research and rationale for skipping, combining.

--Discourages implementation without first showing efficacy.

❖ *Welcomes failure as the seedbed for success*

-- Encourages the mindset that failure is essential to ultimate success.
-- Discourages tendency to walk away from failure in defeat.

Health Psychology Special Issue:
From Ideas to Efficacy in Health Psychology

Leonard Epstein, Susan Czajkowski & Ken Freedland, Editors

Highlighting early-phase translational research in health psychology and behavioral medicine

Vol. 40, No. 12, December 2021

- Review and comparison of early-phase translational models.
- Description of novel methods in behavioral intervention development (e.g., N-of-1/single case designs, dose-finding designs).
- Empirical articles translating concepts from basic behavioral and social sciences research into health-related behavioral interventions.
- Commentary by Rena Wing on the translational journey leading to the Diabetes Prevention Program.

Orbit Institute

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ORBIT INSTITUTE: DEVELOPING BEHAVIORAL TREATMENTS TO IMPROVE HEALTH

MAY 7-10, 2024

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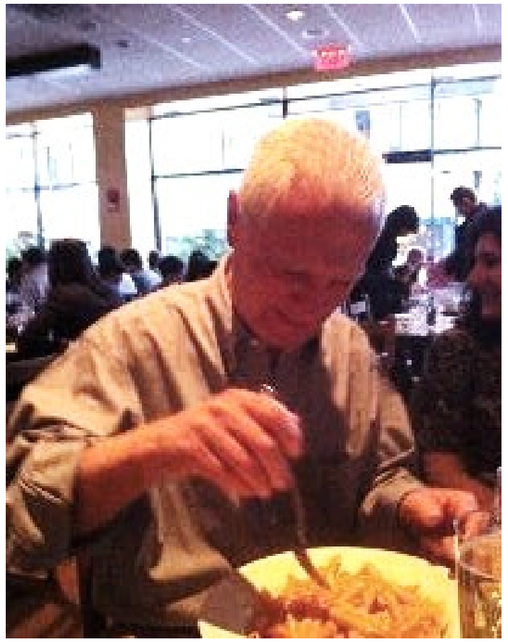
APPLICATION DEADLINE: **NOVEMBER 30, 2023**

Funded by the National Cancer Institute (1R25CA244065-01A1)



THANK YOU!
QUESTIONS?