

DESIGNING MORE EFFECTIVE BEHAVIORAL INTERVENTIONS: USING THE ORBIT MODEL FOR BEHAVIORAL INTERVENTION DEVELOPMENT

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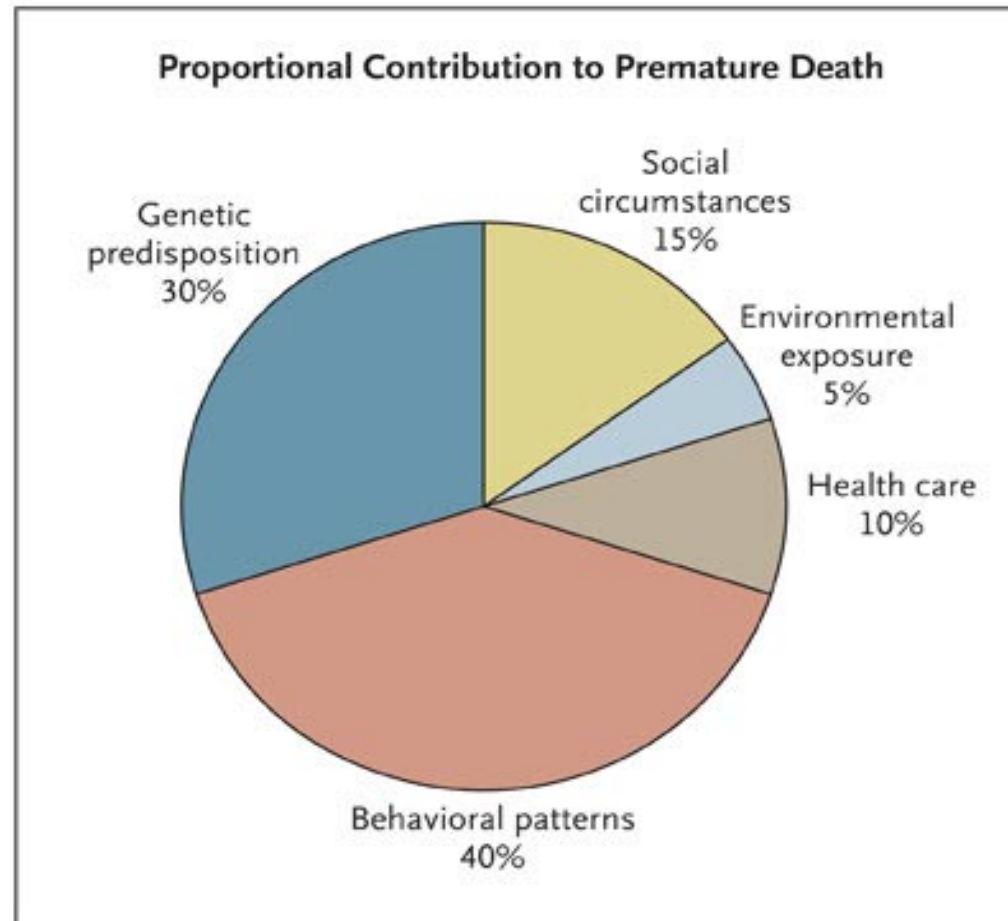
Chief, Health Behaviors Research Branch
Behavioral Research Program
Division of Cancer Control & Population Sciences
National Cancer Institute

International Behavioural Trials Network Meeting

May 20, 2016

Montreal, Quebec, Canada

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

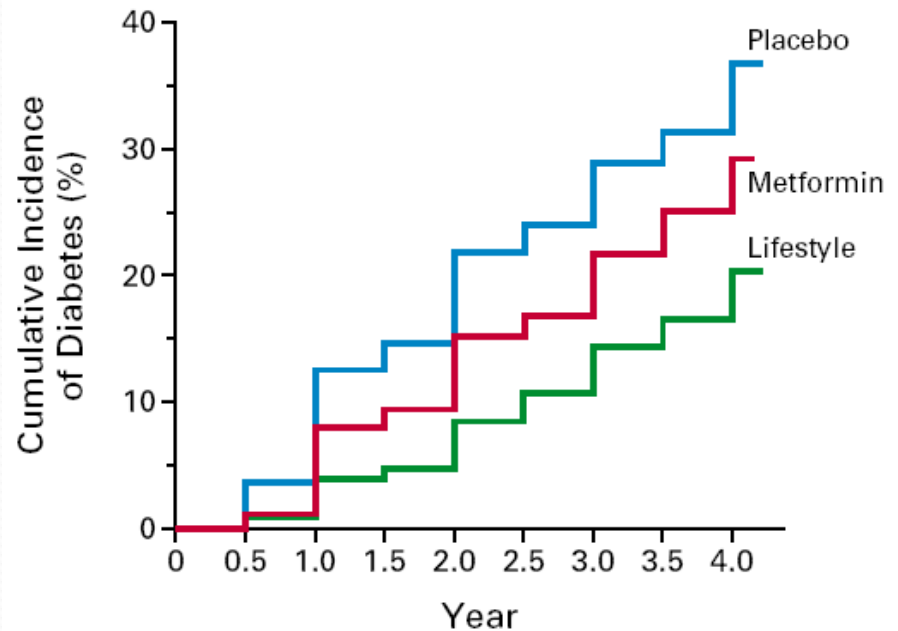
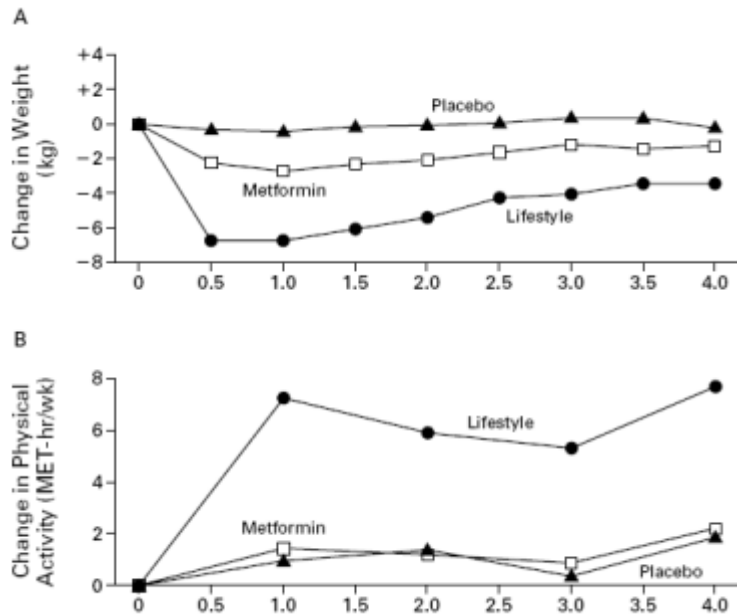


Estimates are that 50% of new cancer cases could be eliminated through engagement in healthy behaviors

- Smoking cessation
- Physical activity
- Healthy diets
- Weight management
- Regular screenings



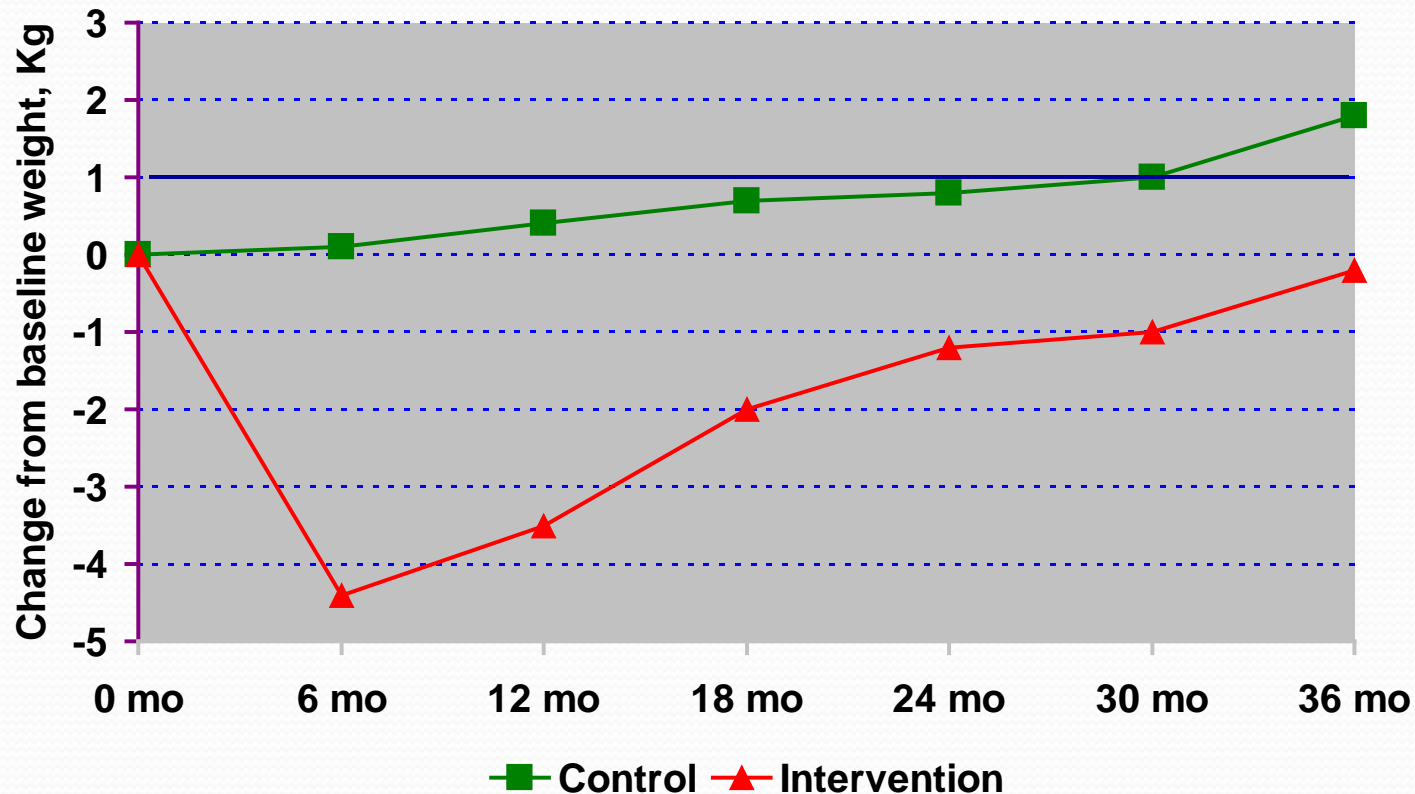
Improving health-related behaviors can have powerful effects on health ...



A 7% weight reduction and 2.5 hour per week activity increase led to a 58% reduction in the cumulative incidence of Type 2 diabetes in older insulin-resistant individuals (Diabetes Prevention Program Research Group, 2002).

But 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



The Challenge: *How can we design more effective health-related behavior change interventions?*

In biomedical research, a well-defined translational process exists that guides the development of new basic biological discoveries into efficacious therapies

Building better behavioral interventions depends on defining a similar process to accelerate the translation of basic behavioral science research into more effective behavioral interventions

The Translational Research Spectrum

T1 Translation

Basic science discoveries used to develop new treatments

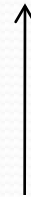
T2 Translation

Testing use of proven therapies in clinical practice & community settings

Bench

Bedside

Public Health



Basic Research
Discovery
Mechanisms
Associations

Efficacy Trials

The whole point of the research enterprise

....applied to health behavior change research

T1 Translation

Basic science discoveries used to develop new treatments

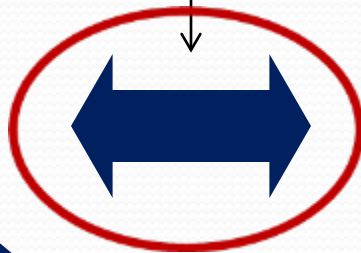
T2 Translation

Testing use of proven therapies in clinical practice & community settings

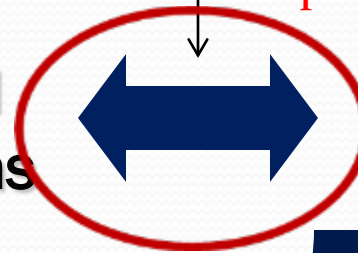
Intervention Development

Dissemination & Implementation

bBSSR



Behavioral Interventions



Public Health

Efficacy Trials

Basic Research
Discovery
Mechanisms
Associations

The whole point of the research enterprise



Many findings from basic behavioral & social sciences research are ripe for translation into intervention

- We are seeing a rapid expansion of knowledge in the basic behavioral & social sciences in a variety of fields:
 - Behavioral neuroscience
 - Communication science and social marketing
 - Executive functions (memory, planning, inhibitory control)
 - Affective, motivational and social processes
 - Choice & decision-making
 - The psychophysiology of stress
 - The dynamics of social systems
- New basic behavioral science discoveries are leading to important new insights about behavior & behavior change

Basic, interventional & clinical/community behavioral research: a continuum or parallel play?

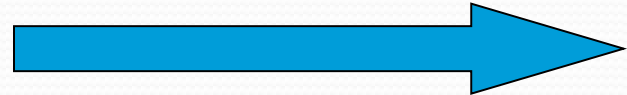
Basic behavioral & social science research

T1

Behavioral & psychosocial intervention studies

T2

Public health & community interventions



Challenges in Translation I behavioral science

- Findings from cutting-edge basic behavioral science discoveries are often underutilized in the design & testing of health behavior change interventions due to:
 - **no widely accepted framework** to describe behavioral translation I/behavioral intervention development (as is true for drug development research)
 - **lack of industry support** for health behavior intervention development (no equivalent to the pharmaceutical industry);
 - **few NIH funding opportunities**, no training opportunities, review groups not set up to review translation I/behavioral intervention development
 - **few incentives** to create & maintain interdisciplinary teams required to conduct translational research;
 - **lack of academic recognition** for bridging basic-clinical fields of study; and
 - **high-risk nature** of translational and intervention development research

Obesity Related Behavioral Intervention Trials (ORBIT) RFA program

- **Objective:** To translate findings from basic research on human behavior to develop more effective interventions to reduce obesity & improve obesity-related health behaviors
- **Mechanism:**
 - Trans-NIH U01 (Cooperative agreement)
 - Supported by NHLBI, NCI, NIDDK, NICHD, OBSSR
 - 7 ORBIT research sites & 1 Resource & Coordination Unit (RCU)
- Each research center supports interdisciplinary project teams of basic and applied biological, clinical, behavioral and social scientists who are developing novel obesity-related interventions through formative & experimental research, early phase trials & pilot studies

ORBIT Projects

- **SCALE: Small Changes and Lasting Effects** (NHLBI) Mary E. Charlson, M.D., Weill Medical College of Cornell University, NYC
- **Translating Habituation Research to Interventions for Pediatric Obesity** (NIDDK) Leonard H. Epstein, Ph.D., SUNY at Buffalo, NY
- **Novel Interventions to Reduce Stress-induced Non-homeostatic Eating** (NHLBI) Elissa Epel, Ph.D., Barbara Laraia, Ph.D., Nancy Adler, Ph.D., UCSF, CA
- **Increasing Sleep Duration: A Novel Approach to Weight Control** (NCI) Rena Wing, Ph.D., Miriam Hospital, Providence, R.I
- **Habitual & Neurocognitive Processes in Adolescent Obesity Prevention** (NHLBI & NICHD) Kim Daniel Reynolds, Ph.D., Claremont Graduate University, CA
- **Developing an Intervention to Prevent Visceral Fat in Premenopausal Women** (NHLBI) Lynda Powell, Ph.D., Rush University Medical Center, Chicago, IL
- **Interventionist Procedures for Adherence to Weight Loss Recommendations in Black Adolescents** (NHLBI & NICHD) Sylvie Naar-King, Ph.D. & Kai-Lin Catherine Jen, Ph.D., Wayne State University, Detroit, MI
- **Resource and Coordination Unit** (RCU) (OBSSR) David Cella, Ph.D., Northwestern University, Chicago, IL
- **National Institutes of Health** S. Czajkowski (NHLBI/NCI), J. Boyington, S. Arteaga, P. Kaufmann, C. Stoney, M. Stylianou (NHLBI); F. Perna, L. Nebeling (NCI); C. Hunter (NIDDK); D. Olster, W. Smith (OBSSR); L. Haverkos, L. Esposito (NICHD)



Translating Ideas into Interventions: The Process of Developing Behavioral Interventions

NIH-sponsored Workshop December 6-7, 2010

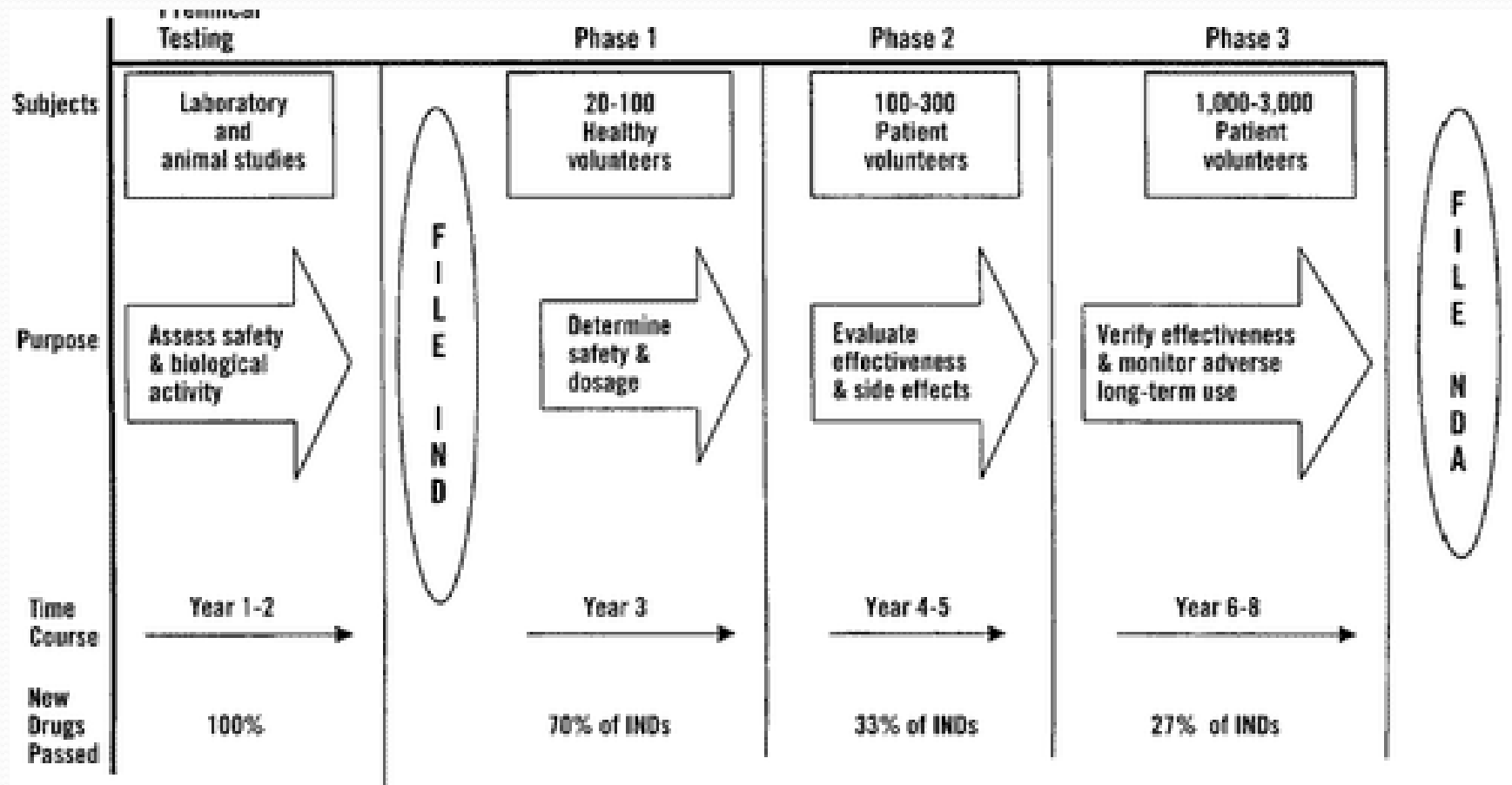
- *What **model or framework** can we use to guide the behavioral intervention development process?*
- *Which **study designs & methods** are most appropriate for the development of behavioral interventions?*
- *How do we create environments that **foster creativity** & encourage the development of innovative behavioral interventions?*



Why do we need a framework to guide behavioral intervention development?

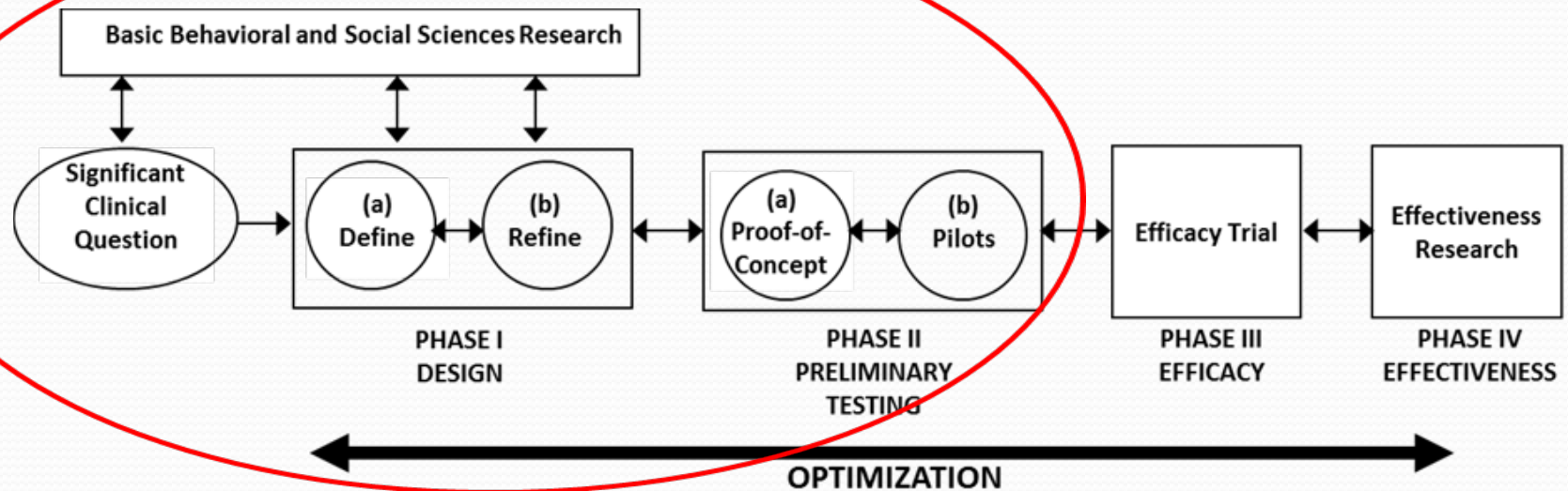
- The drug development model, while not without flaws, has resulted in the creation & testing of many life-saving and life-extending treatments
- Use of a framework and identification of well-defined and appropriate methods in behavioral intervention development research can:
 - Accelerate the flow & development of new, innovative approaches to changing behavior from basic studies of human behavior to efficacious interventions
 - Encourage the development of behavioral interventions that are well-characterized, appropriately tested & optimized prior to testing in larger, more expensive Phase III trials – ultimately leading to better, more powerful behavioral interventions
 - Identify “failures” earlier in the process, allowing for refinement of interventions and reducing premature testing of “weak” behavioral interventions in Phase III trials

The drug development process



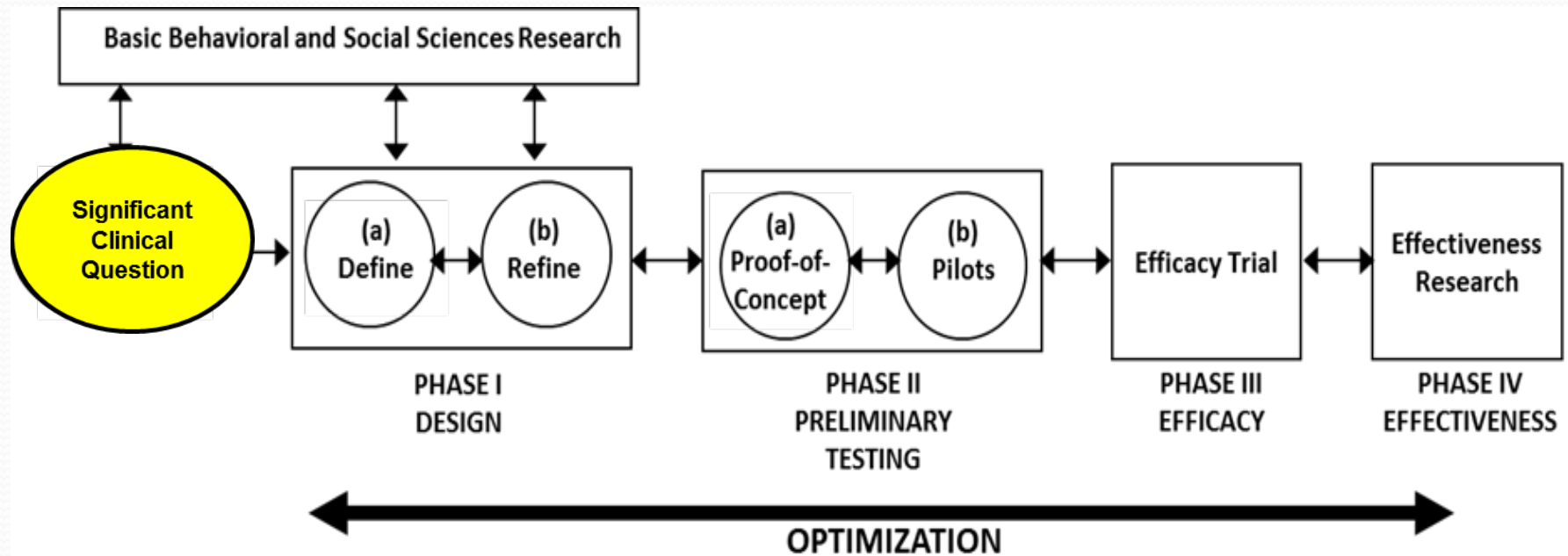
Model/framework	Primary focus	Level of detail	Translational Phases Included	Consistent w/ drug development process?
ORBIT model	2-phase model for developing behavioral interventions w/ a focus on preventing & treating chronic physical diseases	--IDs clinically significant target(s), cutpoints, milestones --provides examples of methods, bi-directional --ID'ing mechanisms of action not essential	Focuses on pre-efficacy phases (Phases I & II)	Yes – uses similar phases, terminology
Greenwald & Cullen (1985)	5-stage model to guide cancer control research	--does not include ID of clinically significant targets, cutpoints, milestones --does not define all steps needed, designs/methods	Includes all phases from hypothesis development (Phase I) through D & I (Phase V) research	Yes – uses similar phases, terminology
Flay, 1986	8-phase framework for development of health promotion programs	--does not include ID of clinically significant targets, cutpoints, milestones --does not describe designs/methods --not bi-directional	Includes all phases from basic research (Phase I) through Demonstration studies (Phase VIII)	Uses similar terms (eg “phases”), but different meaning (e.g., Phase V = efficacy trials)
Rounsaville et al. (2001); Onken et al. (2014) Stage Model	3-stage model, updated in 2014 to include 5-stages, w/ a focus on developing psychological treatments for mental health, substance use/abuse disorders	--does not include ID of clinically significant targets & cutpoints --does include milestones, methods, bi-directionality --emphasis on ID'ing mechanisms in each stage	Includes all phases from basic research (Stage 0) to D & I (Stage V)	No – “stages” not “phases” with different meanings (e.g., “Stage I” = intervention development, “Stage II” = efficacy testing)
Medical Research Council (MRC), 2008	Proposes a 4-phase cyclical framework for developing & evaluating complex interventions	--does not include ID of clinically significant targets, cutpoints, milestones, all steps in intervention development --does include example methods.	Includes all phases from intervention development through Implementation	No – not consistent w/ biomedical model (e.g., 3 rd phase – “Evaluation” – assesses effectiveness & cost-effectiveness)

The ORBIT Model for Behavioral Intervention Development



Czajkowski, Powell, Adler, Naar-King, Reynolds, Hunter, Laraia, et al., *Health Psychology*, 2015 Oct; 34(10): 971-982.

The ORBIT Model for Behavioral Intervention Development



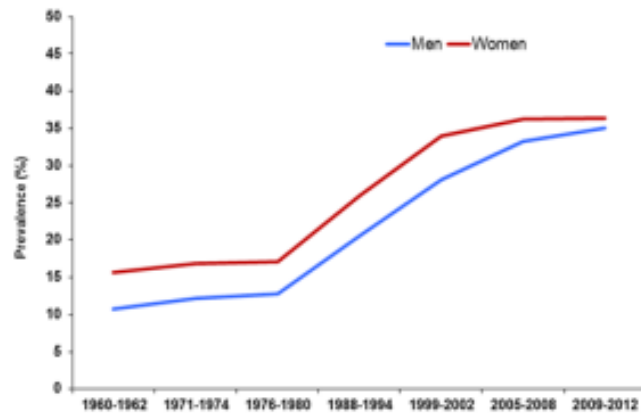
SIGNIFICANT CLINICAL QUESTION

Begin with a health issue that poses a significant problem

- A disease that is increasing in numbers, severity, exclusively affects or is increasing in a subgroup
- A health problem for which no treatment exists, or treatment is not very effective (could be optimized)
- Requires a new approach to improve outcomes
- Involves a novel risk factor or new approach to treatment

Improving Obesity-Related Behaviors: A Significant Clinical & Public Health Problem

Trends in Obesity* Prevalence by Sex, Adults 20 to 74 Years, US, 1960-2012



*Obesity=body mass index ≥ 30 kg/m² Note: Estimates are age adjusted to 2000 US standard population.
Source: National Health and Nutrition Examination Survey, National Center for Health Statistics, Centers for Disease Control and Prevention.

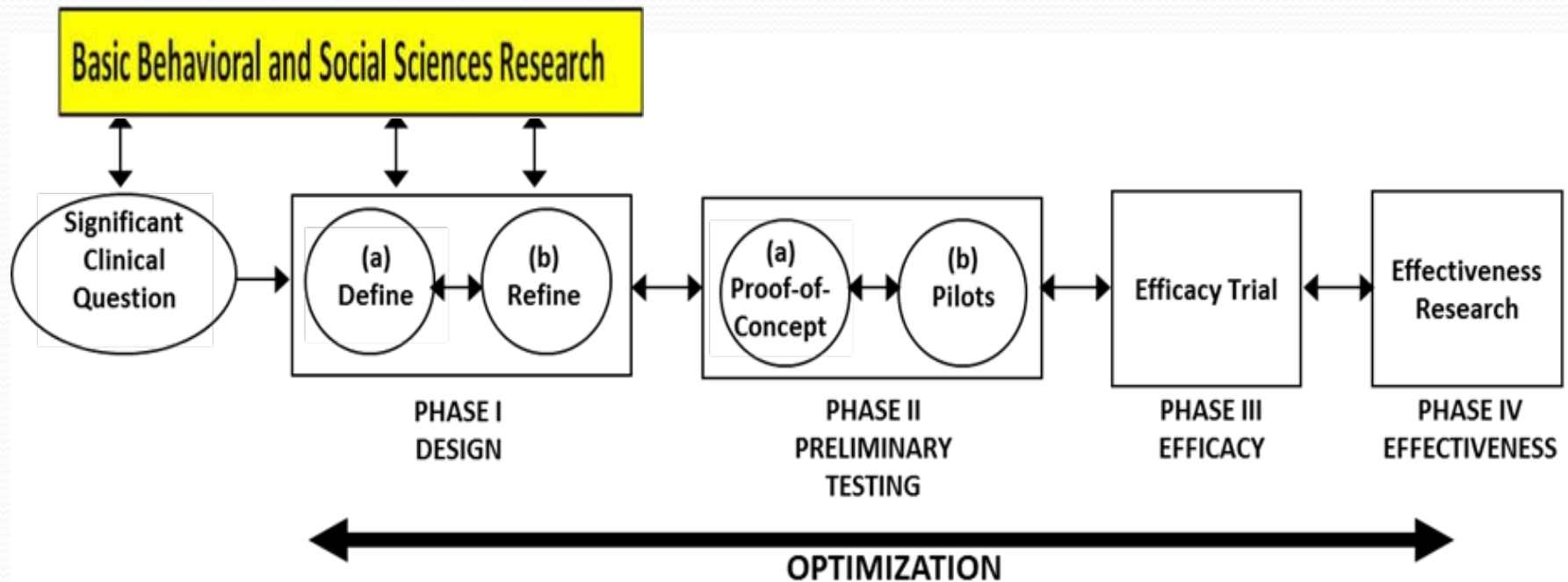
In the U.S., obesity has risen at an epidemic rate over the past several decades

2/3 of U.S. adults & 1/3 of children are either overweight or obese

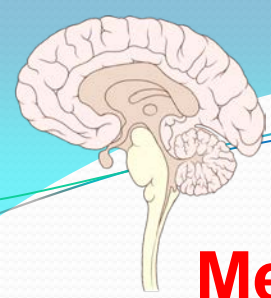
Overweight & obesity increases risk for cancer & other chronic conditions such as diabetes, heart disease, stroke



The ORBIT Model for Behavioral Intervention Development



Neuroscience & Eating Behavior



Mesolimbic Reward Pathway

- The “pleasure center”
Sex, Food, Drugs,
Gambling
- Impulsivity/Immediate Gratification
- Overrides the homeostatic energy system e.g. “*Always room for dessert!*”

Prefrontal Cortex: Executive Function

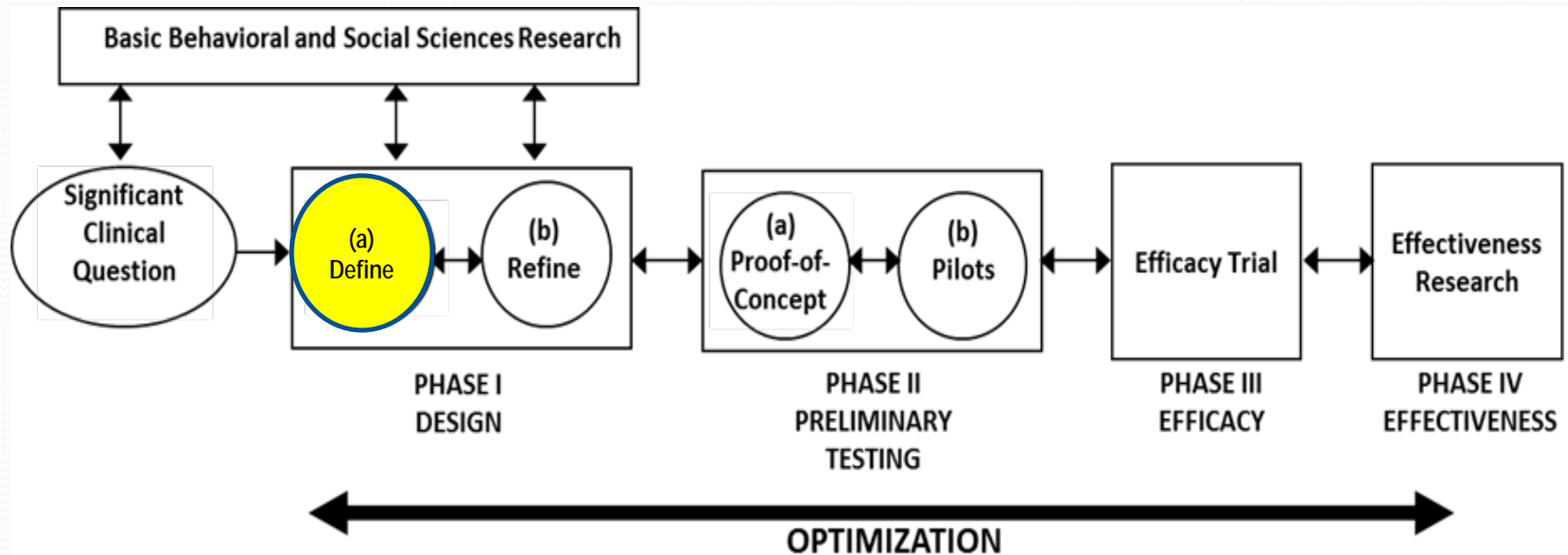
The “CEO” of your brain

- High-level decision-making
- Planning
- Self-Monitoring
- Pursuing goals
- Delaying gratification
- Behavioral inhibition

Implications for Weight Loss Interventions:

- **Avoid Triggering the Limbic Reward Circuit:** Remove temptations from the home
- **Enhance Executive Function:** Training in Inhibitory Control, Self-Management Skills, Planning

The ORBIT Model for Behavioral Intervention Development



Phases of Behavioral Treatment Development: ORBIT Model

Phase I: Design

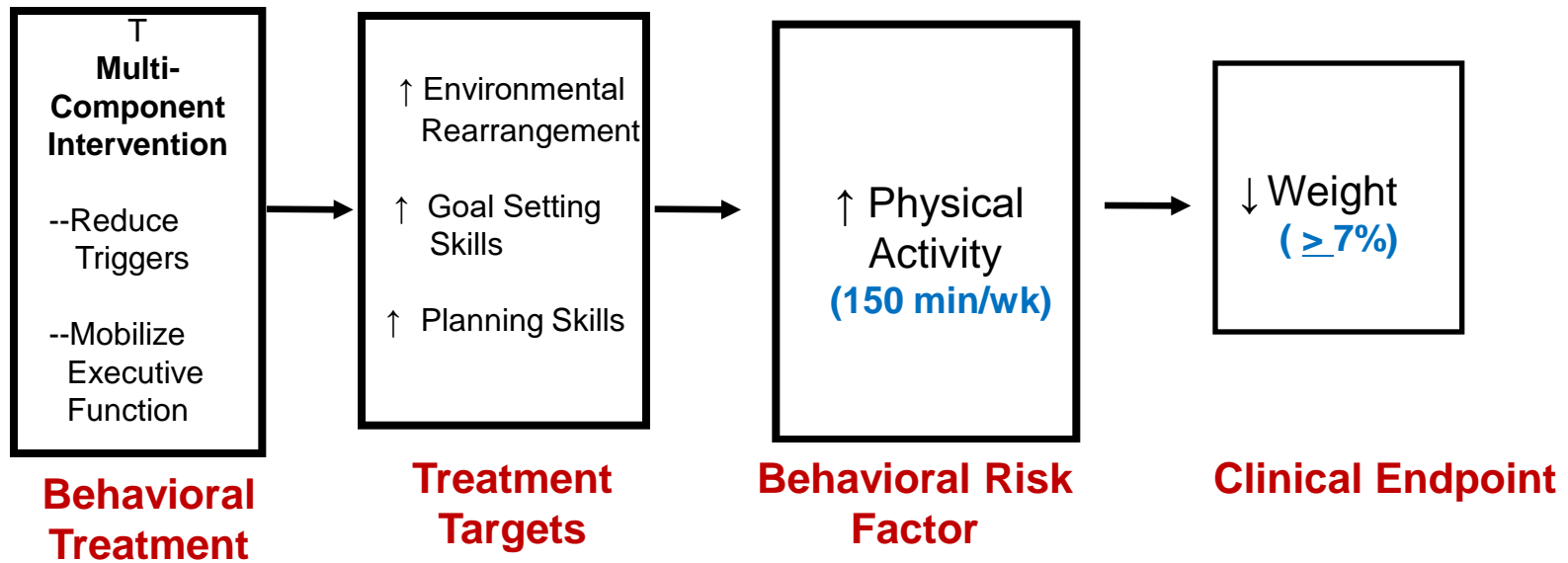
Phase Ia -- **Define** the scientific foundation & basic treatment elements

- Identify behavioral risk factor target & clinically significant milestones
- Provide basic behavioral & social science research basis for treatment components & targets
- Identify candidate intervention components
- Describe pathways through which treatment can affect outcomes

Study Designs & Methods:

- Laboratory & field experiments to identify behavioral & biological mechanisms of action
- Observational studies to identify key intervention targets & points of “entry”
- Qualitative & mixed methods research to assess acceptability of proposed approach to end-users – “user-centered” research

Phase 1a: Define Hypothesized Pathway



Habitual & Neurocognitive Processes in Adolescent Obesity Prevention

PI: Kim Reynolds, Claremont Graduate University

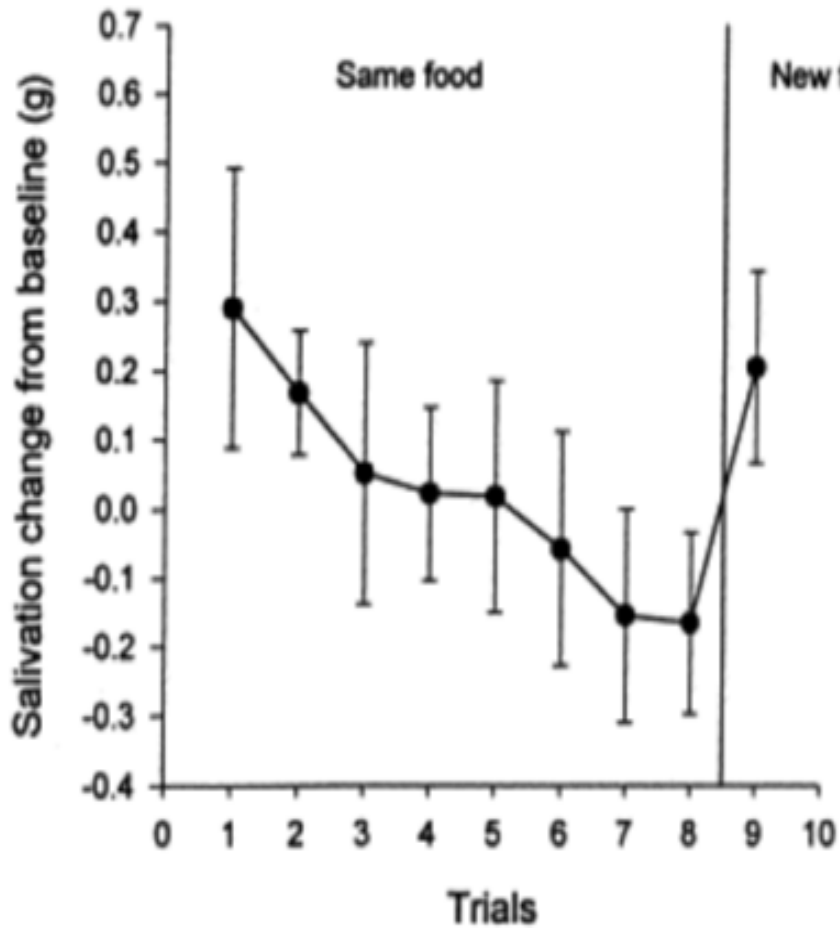
- Unhealthy dietary habits may be initiated by a cue that is linked to the eating behaviors in memory
 - Aim of the intervention was identify & disrupt these unhealthy cue-behavior links and create new and stronger links for healthy alternatives
- In Phase Ia, Ecological Momentary Assessment (EMA) was used to identify physical, social, and intrapersonal cues that were associated with the consumption of sweetened beverages and sweet and salty snacks in 158 low-income adolescents
- Answered brief surveys via PDA's about their eating behaviors (location, social environment, mood, stress, and food cravings, drink, snack, and meal time items consumed) over 7 days -- each time they ate or drank something, when randomly prompted by the PDA, and once each evening
- Identification of these cue-food links allowed development of an intervention designed to substitute a different behavior when the relevant food "cue" was encountered

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

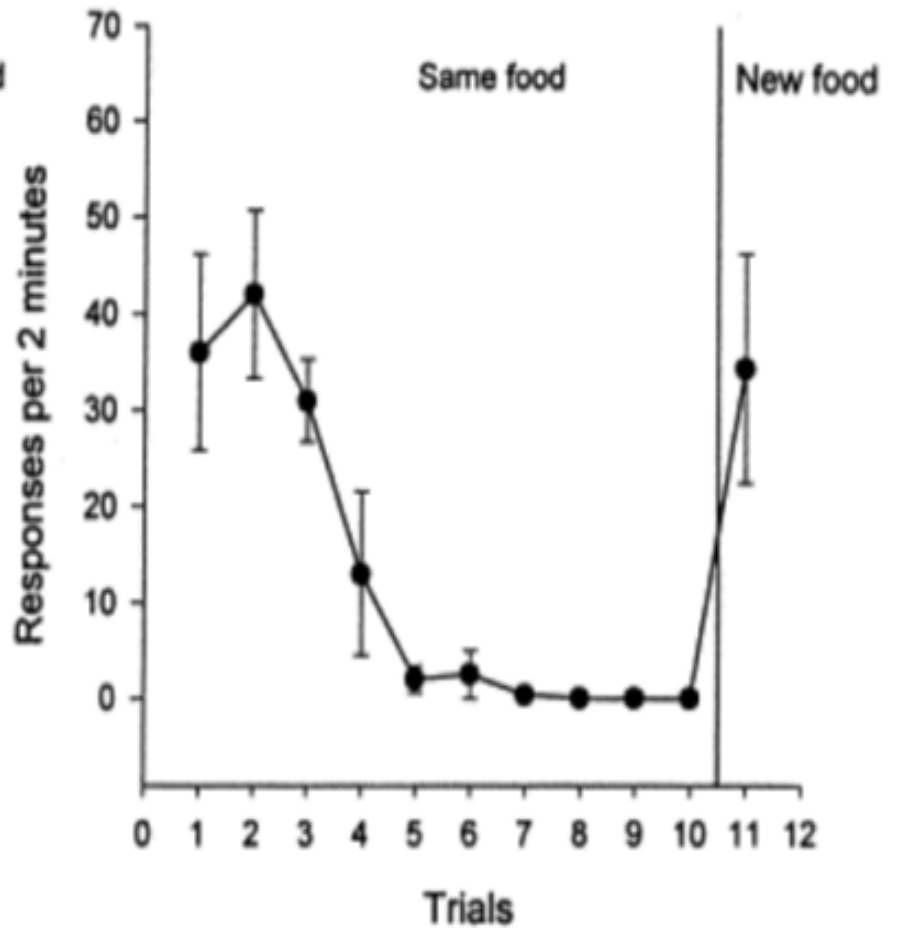
PI: Leonard Epstein, Ph.D., University at Buffalo

- For treatment of obesity, the goal of all dietary prescriptions is to reduce energy intake
 - Energy-dense, non-nutrient-dense foods are commonly targeted for reduction
 - Adherence to reduced energy intake is challenging & novel approaches that enhance satiation during treatment of obesity are needed
- Habituation theory -- repeated presentation of a stimulus influences responding to the stimulus
 - Eating involves the repeated presentation of food stimuli (visual, olfactory, and gustatory stimuli), both within and across eating occasions
 - Habituation is demonstrated by a reduction in physiological and behavioral responses to repeated presentation of a stimulus
 - Hastening the rate of reduction should decrease the length of an eating occasion (enhancing satiation), reducing food intake
- ***Can a limited dietary variety prescription be developed that harnesses the effects of habituation on satiation and can be implemented within an intervention?***

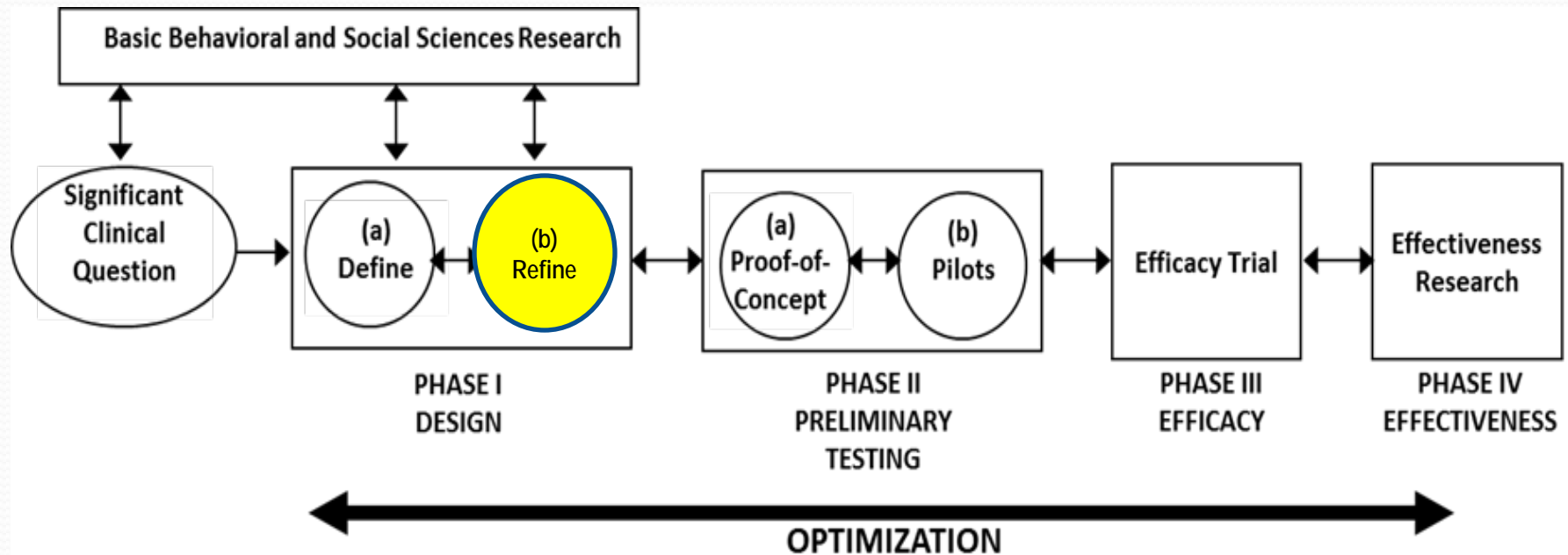
Salivation changes across trials - Group 1



Responses for food - Group 1



The ORBIT Model for Behavioral Intervention Development



Phases of Behavioral Treatment Development: ORBIT Model

Phase I: Design

Phase Ib – **Refine** the intervention for strength & efficiency

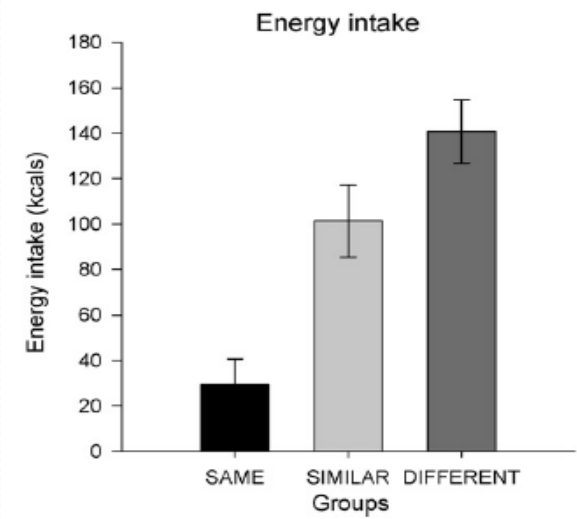
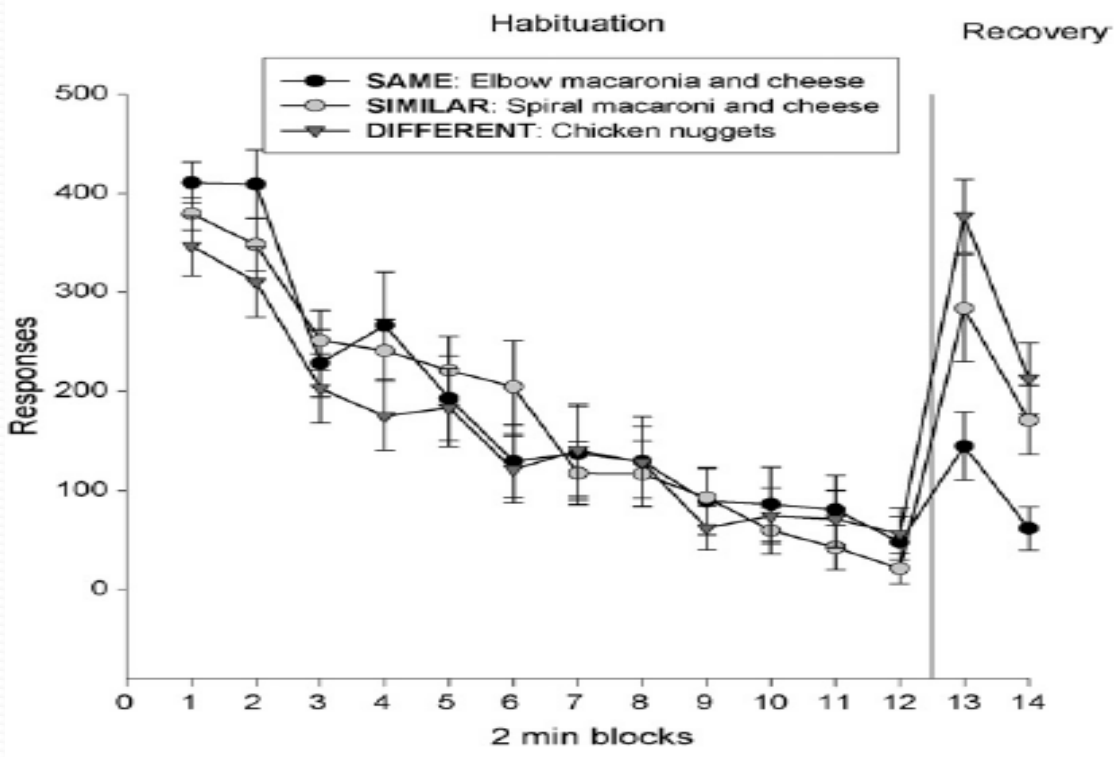
- Identify essential treatment components
- Determine aspects of delivery (mode, frequency, duration, dose, intensity)
- Determine need for tailoring (e.g., for subgroups)

Study Designs & Methods:

- Small-N, case series &/or experimental studies that test effects of varying an intervention's content, timing, frequency, duration, intensity & mode of delivery ("dose-finding") and describe dose-response relationships
- Novel methods for developing, testing & refining behavioral interventions such as Multiphase Optimization Strategy (MOST) & adaptive treatment (SMART) designs

Habituation & Food Intake: Phase Ib: Refining intervention content





Epstein et al, 2010

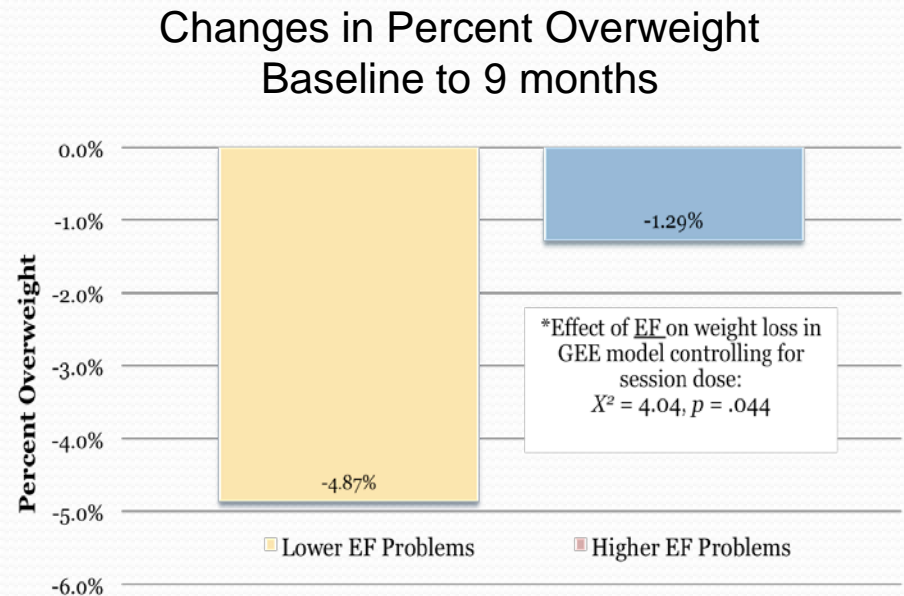
Habituation & Food Intake: Phase Ib: Refining intervention content



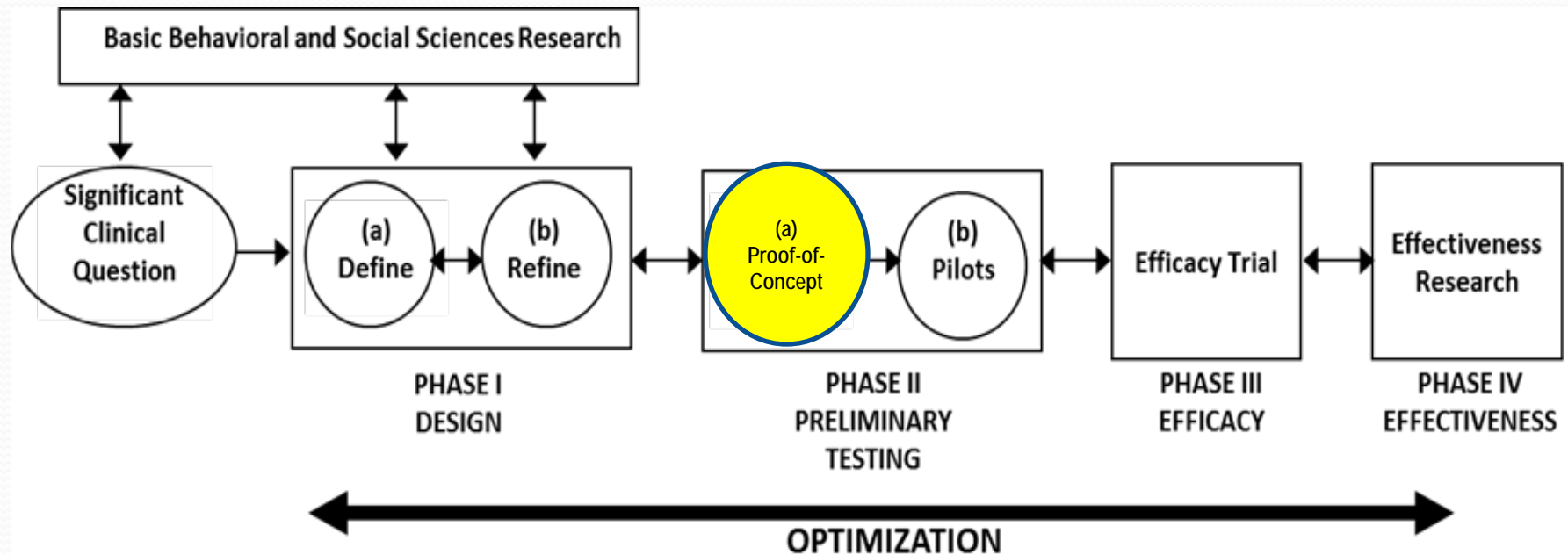
Fit Families – Potentiating Obesity Interventions for African American Adolescents

PIs: Sylvie Naar, K-L Catherine Jen, Wayne State University

- African American Adolescents ages 12-16 with BMI \geq 95 percentile & primary caregiver
- Examined potential moderators of weight loss treatment effects
- Better executive functioning (EF) was associated with more weight loss
- Suggests tailoring of weight loss interventions to address EF problems may enhance outcomes



The ORBIT Model for Behavioral Intervention Development



Phases of Behavioral Treatment Development: ORBIT Model

Phase II: Preliminary Testing

Phase IIa – ***Proof-of-Concept Studies***

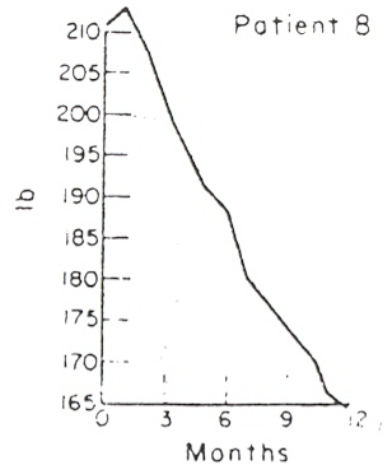
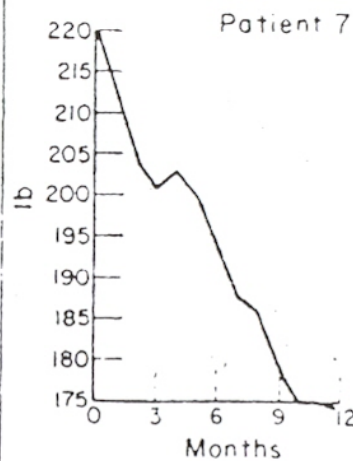
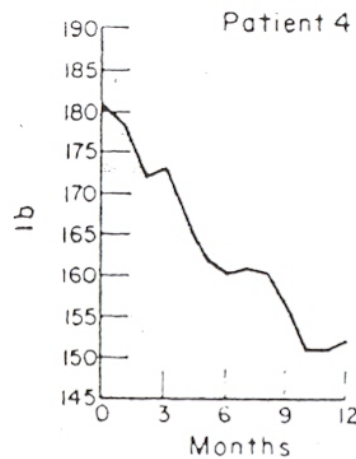
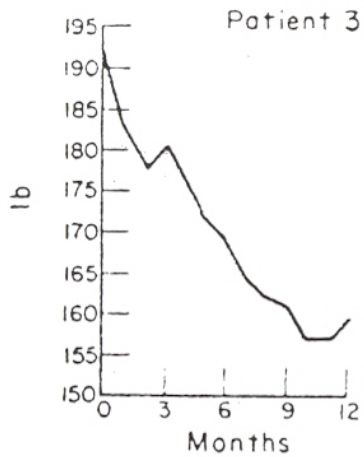
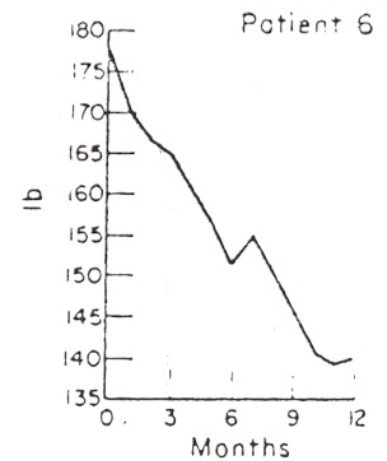
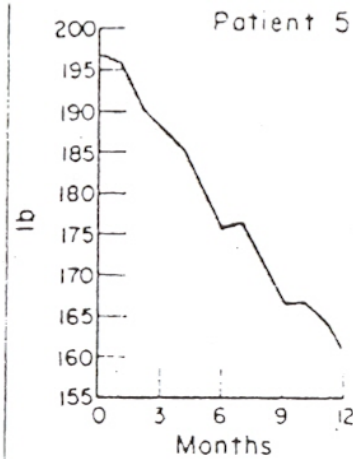
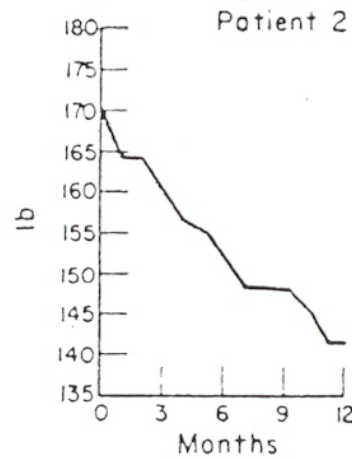
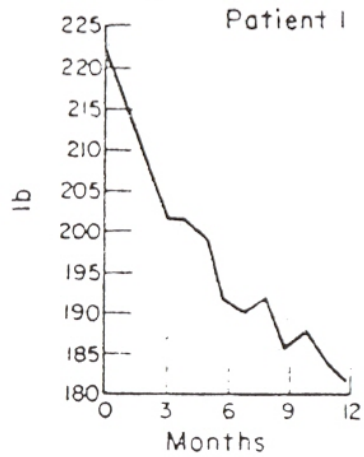
- Determine if the intervention can achieve a *clinically significant signal* on the relevant behavioral risk factor
- Inexpensive initial test of a fixed protocol

Study Designs & Methods

- Typically non-randomized
- No control group
- Small-N, single-case designs

Behavioral Control of Overeating

Stuart, R.B., 1967

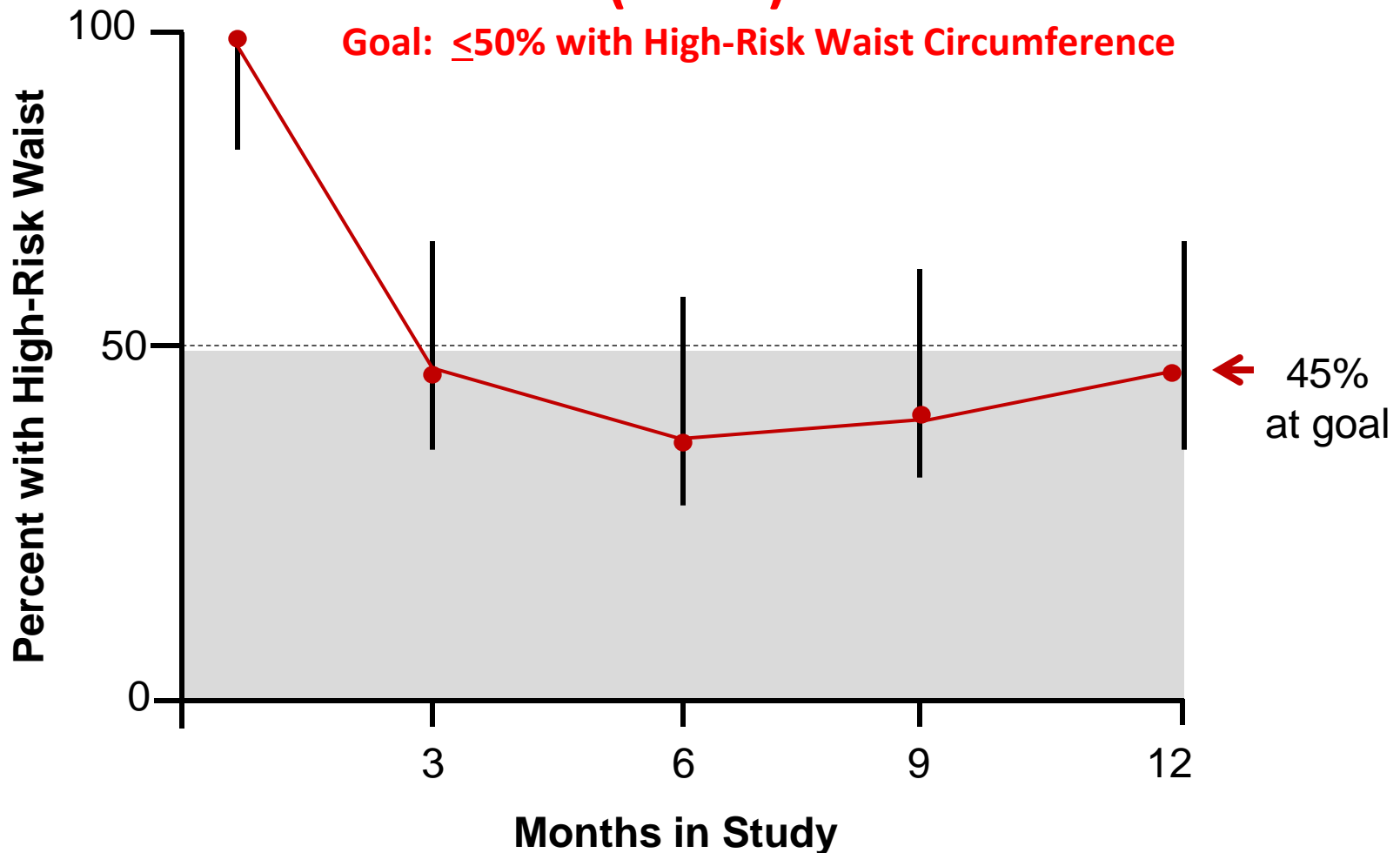


Phase 2a: Proof-of-Concept

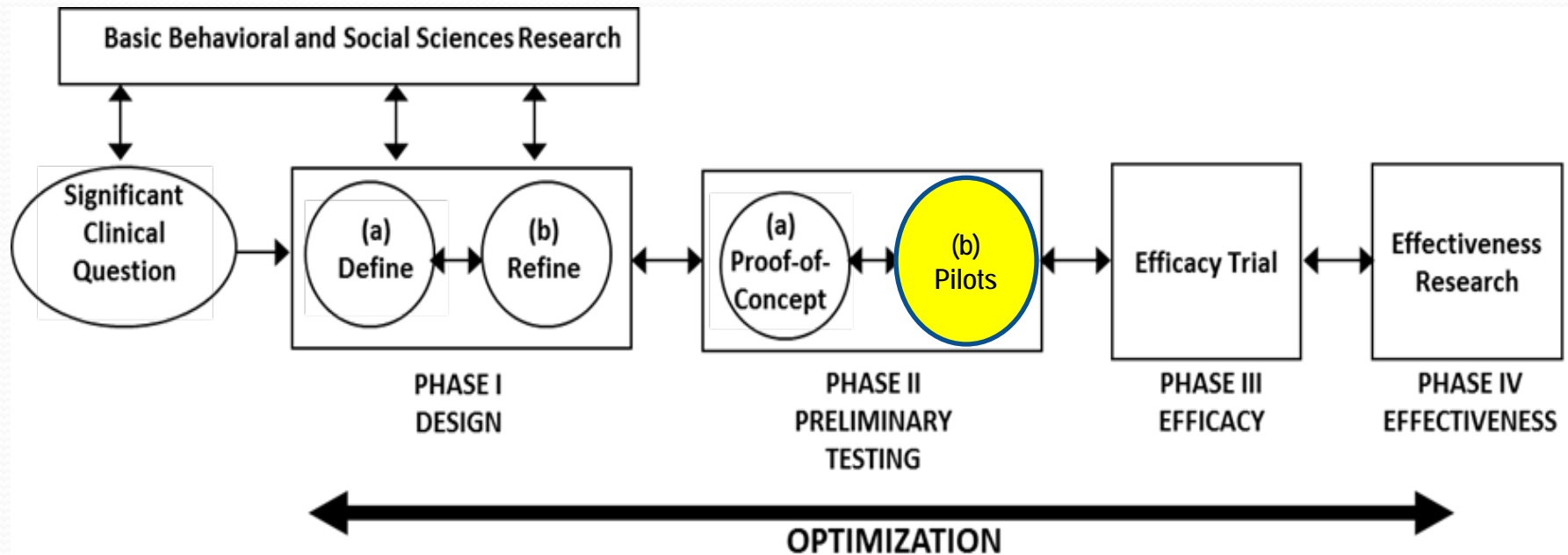
ELM

(N=29)

Goal: $\leq 50\%$ with High-Risk Waist Circumference



The ORBIT Model for Behavioral Intervention Development



Phases of Behavioral Treatment Development: ORBIT Model

Phase II: Preliminary Testing

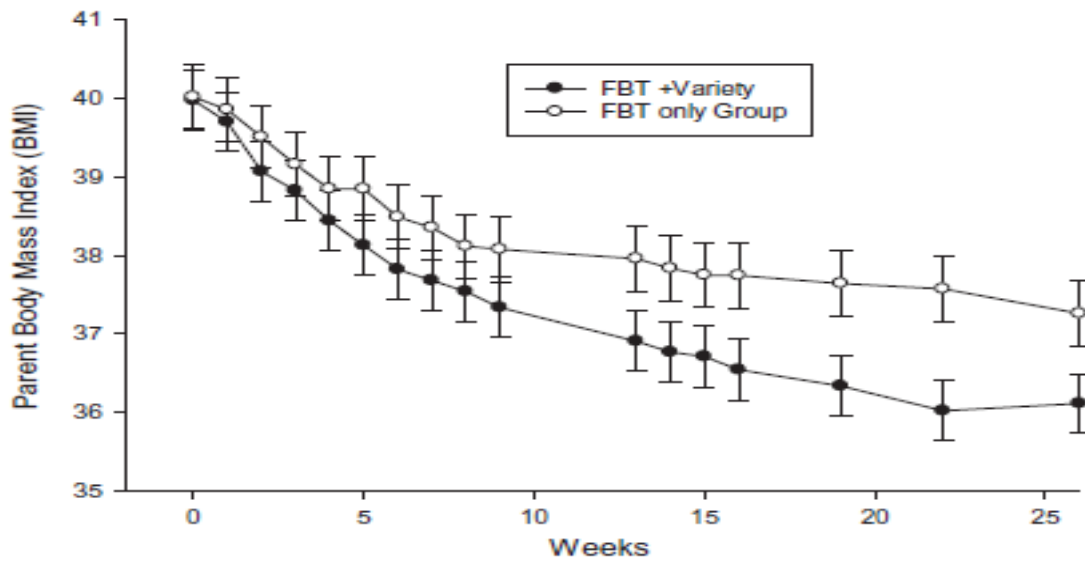
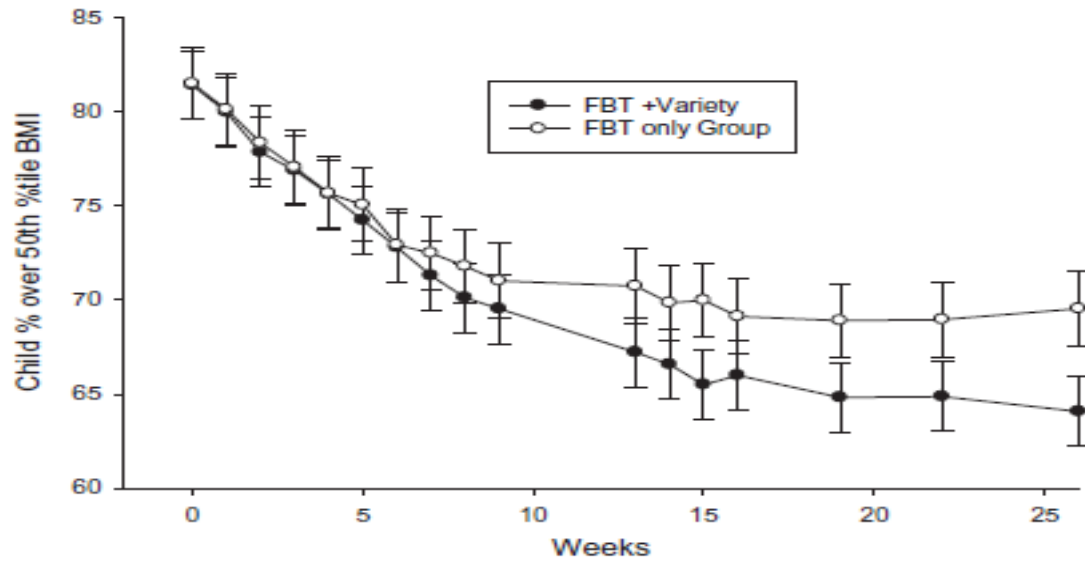
Phase IIb –

- **Pilot Testing** to determine:
 - whether the intervention's effects can be replicated in larger samples using a control condition
 - what is the appropriate control condition & how does it behave
- **Feasibility Pilot Testing** to determine:
 - whether the intervention is feasible & acceptable
 - Numbers available for screening & recruitment
 - Estimates of yield (screening to enrollment ratio), drop-out rate, crossovers, adherence to treatment
- **Study Designs & Methods:**
 - Randomized designs
 - Can include qualitative methods to understand patient experiences, acceptability, feasibility



Limiting dietary variety in family-based treatment: 6-month pilot study (Epstein et al, 2015)

- 24 families, with a child $\geq 85^{\text{th}}$ 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 RED foods)
 - Developed meal plans
 - ≥ 60 min/day of MVPA prescription
 - FBT+Variety
 - Family-based treatment (identical to FBT)
 - Identified two RED foods to consume during the intervention: one dinner entrée and one snack food
 - Developed meal plans that repeated dinner entrees and included leftovers from the dinner entrees and reduced variety of RED foods
- Outcomes:
 - Child percent overweight: FBT+Variety –15.4% vs. FBT – 8.9%, $p = 0.017$
 - Variety of RED foods consumed by family: FBT+Variety = 20.2 to 12.6 vs. FBT = 19.7 to 16.8, $p = 0.01$



ORBIT Behavioral Intervention Development Model: Key Features

- ▶ **Begin with the “end” in mind**
 - ▶ Process is guided by “significant clinical questions” from end users – patients, providers
- ▶ **Progression** from basic to more clinical/applied stages
 - ▶ **Pushes** toward the efficacy trial
- ▶ Each phase includes “**clinically meaningful” milestones**
 - ▶ Specify *a priori* criteria for moving to next phase of the intervention development process
 - ▶ Emphasis is on achieving “clinically significant” (not just statistically significant) change in behavioral targets
- ▶ **Flexibility** in terms of:
 - ▶ Number & types of studies within phases
 - ▶ Duration of each phase
 - ▶ Movement from one phase to the next (can “skip” a phase if necessary)
- ▶ Flow is **bi-directional**
 - ▶ Allows for “failure” & return to earlier phases as needed

ORBIT & behavioral intervention development: Lessons learned

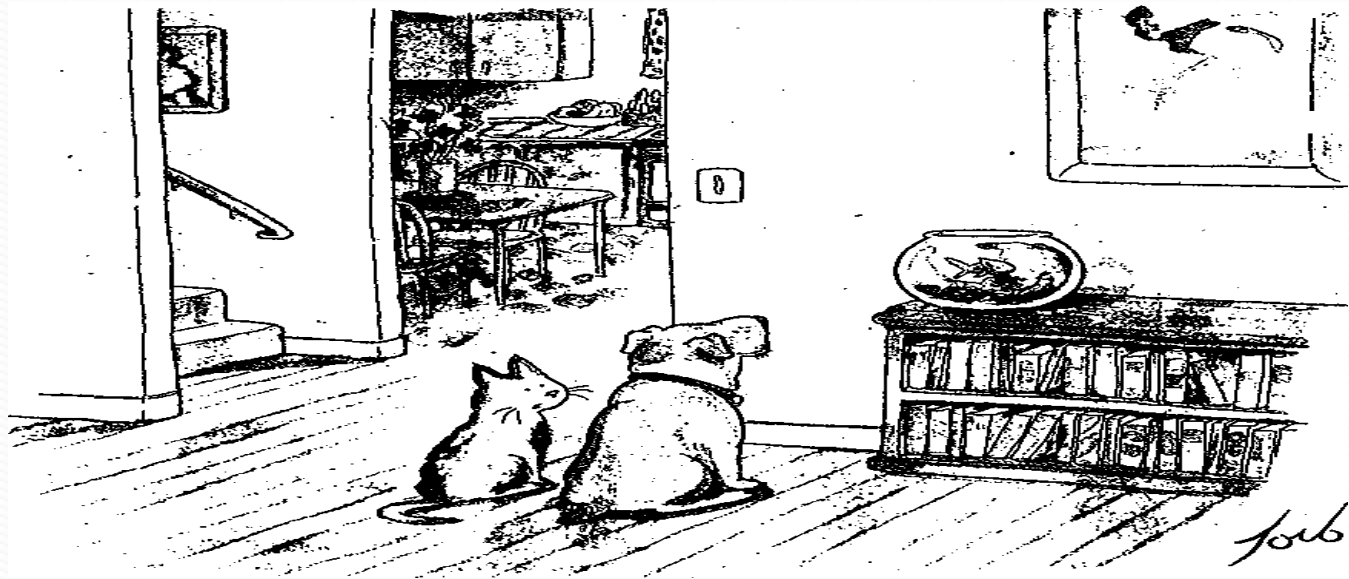
- **Reconceptualize & de-stigmatize “failure”** – it’s ok if you don’t find what you expect!
 - Often a “failure” to move forward to next phase is positive -- means an opportunity to refine ideas, drill down to better understand mechanism, try a different approach, revise theory, improve potency of intervention
 - There is value in the “fail early” philosophy behind early-phase translation/behavioral intervention development – promising ideas that do not meet preliminary efficacy goals do not go on to more expensive Phase III trials, saving time & cost



INCONCLUSIVE EXPERIMENT:
PAVLOV'S CAT

ORBIT & behavioral intervention development: Lessons learned

- ***The formation of cross-disciplinary teams is key*** – much is gained by involving diverse disciplines in the intervention development process & “vetting” ideas with other members of a research team, as well as with the larger network



"Look, I know you and I have had our differences, but can we at least agree that the goldfish is pointless?"



Thanks to all my colleagues
who participated in ORBIT
Questions?

