Behavioral Treatment Development: A Framework for Progression

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The Process of Drug Development

Discovery → Non-Human Safety (Preclinical) → Human Pharmacology (Phase I) → Therapeutic Efficacy (Phase II) → Therapeutic Confirmatory (Phase III) → Therapeutic Use (Phase IV)

Low-cost studies, “very high” failure rates

80% failure rate

Regulatory Approval: Human Testing

Regulatory Approval: Market the Drug
Why do we need a framework?

Figure 1. The ORBIT Model for Behavioral Treatment Development

Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, 2020
Why do we need a framework?

We Are Stuck
Limited Progression

Which is better?
Does treatment improve: behavior, biomarkers?

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**Figure 1. The ORBIT Model for Behavioral Treatment Development**

Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, 2020
Why do we need a framework?

We Are Stuck

Fragmentation

Basic science experiments
Studies of mechanisms
Optimization studies
Interventions on risk factors
Phase III Efficacy trials
Effectiveness trials
Dissemination studies
Implementation studies
Why do we need a framework?

We Are Stuck

Many Failures

Strong and consistent associations between healthy living reduced risk for chronic diseases.

Suboptimal evidence that behavioral interventions can reduce risk for chronic diseases.

4 out of 5 Phase III behavioral efficacy trials are null trials.

Failure rate in behavioral treatment development studies is unknown because of publication bias.

Only 7% of Americans live a healthy lifestyle.
Why do we need a framework?

We Are Stuck

False Successes

“P-values do not tell us whether a treatment improves health. . . . Retire statistical significance.” (American Statistical Society, 2011)
Why do we a framework?  
We Are Stuck  
Irrelevance

“Phase III efficacy trial is the highest quality of evidence for a new treatment.”
(Institute of Medicine, 2011)

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(Institute of Medicine, 2011)
Behavioral Treatment Development

PROGRESSIVE QUESTIONS AND DESIGNS

Figure 1. The ORBIT Model for Behavioral Treatment Development

Czajkowski, Powell et al., 2015;
Powell, Freedland, Kaufmann, 2020
“A new treatment is born into a hostile environment. It must be kept alive in infancy. It needs to mature until it reaches a point at which it can be brought into contact with the abundance of problems that could undermine it. Scientists should protect early development; not contribute to premature death.”

Feyerabend, 1965

**DEFINE**

**TINKERING**

**DEFINITION**

Attempt to repair or improve something in a casual way.

**USAGE**

He tinkered endlessly with the car.

**SYNONYMS**

adjust, fix, mend, play with, fiddle with, fool with, take apart
DEFINE

HYPOTHESIZED PATHWAY

A: Behavioral Treatment Component → B: Implementation Target → C: Behavioral or Biomedical Risk Factor → D: Clinical Outcome

CSΔ = clinically significant change

= “stick your neck out”
DEFINE

CLINICAL SIGNIFICANCE

@ibtnnetwork  #ibtn2020
DEFINE CHILDHOOD OBESITY

Conceptual Model

Hypothesized Pathway

Two-Components

Plan Ahead for Physical Activity

Reduce Eating Triggers

Planned for Physical Activity Most Days/Week (Weekly recall)

Presence of triggers in home (Random home visit)

↑ Physical Activity (120 min/wk)

↓ Weight (≥7%)

Treatment

Implementation Targets

Behavioral Risk Factor

Clinical Endpoint
Behavioral Treatment Development

WELCOME FAILURE

Figure 1. The ORBIT Model for Behavioral Treatment Development

Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, 2020
“Welcome failure as the opportunity for growth.”
(Popper, 1954)

“Failure provides the seedbed for innovation.” (mantra of Silicon Valley)

“An expert is one who has made all of the mistakes which can be made in a narrow field.” (Niels Bohr, 1922)

“The odds are 1 in 5 of having a positive result from a Phase III drug or behavioral efficacy trial.”
(Gordon 2013; Kaplan 2015; Irvin 2016)

“The only reason to have a hypothesis is to try to disprove it.
(Elizabeth Barrett-Connor, 1935-2019)

“It takes 6.8 years and $1.3 billion to bring a drug to market because of extremely high failure rates that are increasing over time and most common in drugs for chronic diseases.”
(Tufts Center for the Study of Drug Development Research, 2015)
Behavioral Treatment Development

PROOF-OF-CONCEPT

Basic Behavioral and Social Sciences Research

Significant Clinical Question

Discovery

PHASE I DESIGN

(a) Define

(b) Refine

PHASE II PRELIMINARY TESTING

(a) Proof-of-Concept

(b) Pilots

(c) Phase II Efficacy Trial

PHASE III EFFICACY

Effectiveness Research

PHASE IV EFFECTIVENESS

OPTIMIZATION

Figure 1. The ORBIT Model for Behavioral Treatment Development

Czajkowski, Powell et al., 2015; Powell, Freedland, Kaufmann, 2020
PROOF-OF-CONCEPT

Goal: Assess plausibility that a treatment can improve health

Rationale:
Low cost of failures
Basis for decision to move forward for more rigorous testing
or backward for refinement

Features:
Quasi-experimental “treatment only” design
Clinically significant milestone for success
No statistics
No sample size calculation
Small N
Accessible sample

A comparator is useless when a behavioral treatment is too weak to warrant any comparison.
PROOF OF CONCEPT

N=4

70% adherence (clinically significant treatment target)

Mosnaim, 2008
PROOF-OF-CONCEPT

N=26

Powell et al, 2018
SUMMARY

Frameworks are aimed at narrowing the gap between discovery and implementation.

Frameworks can provide:

--Guidance on where study fits in a progressive set of questions and designs

--Courage to “stick your neck out” with quantified milestones for success.

--Support for growth mindset: persistence in the face of failure.

TREATMENT DEVELOPMENT IS TEAM SCIENCE

You do not need to build the entire house.

You do need to see: the house as the goal; the variety of artisans needed to build it.