



Behavioral Treatment Development: A Framework for Progression

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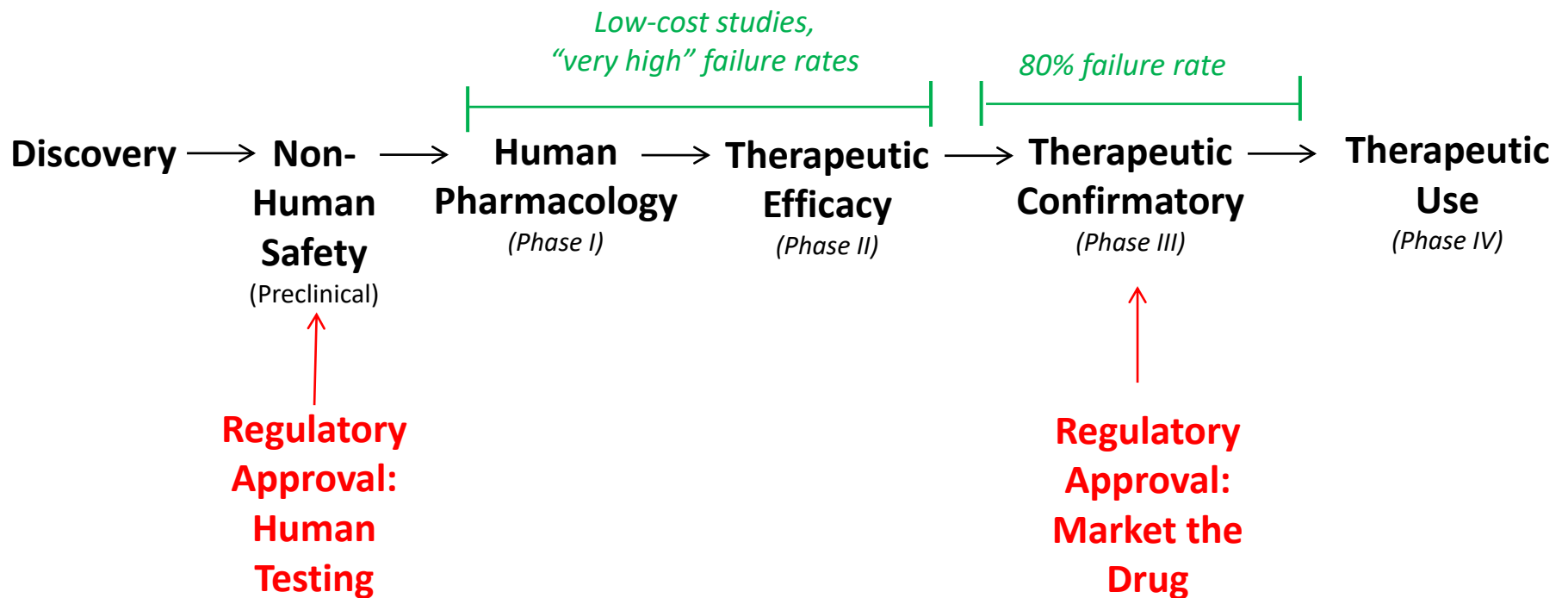
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International Behavioral Trials Network 2020 GLOBAL

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The Process of Drug Development

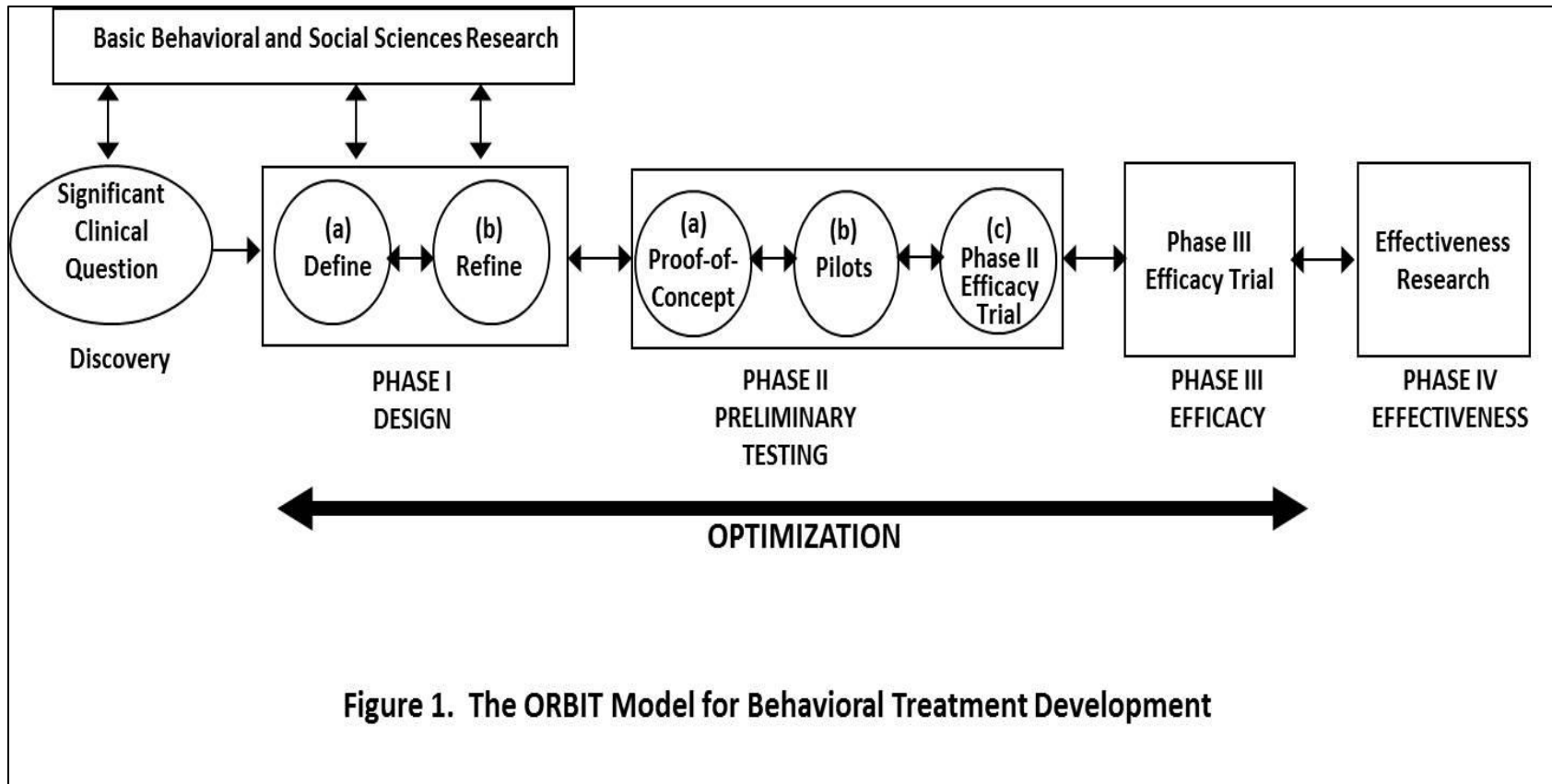


The ORBIT Model

For Behavioral Treatment Development



Why do we need a framework?



Why do we need a framework?

We Are Stuck

Limited Progression



Which is better?

Does treatment improve:
behavior, biomarkers?

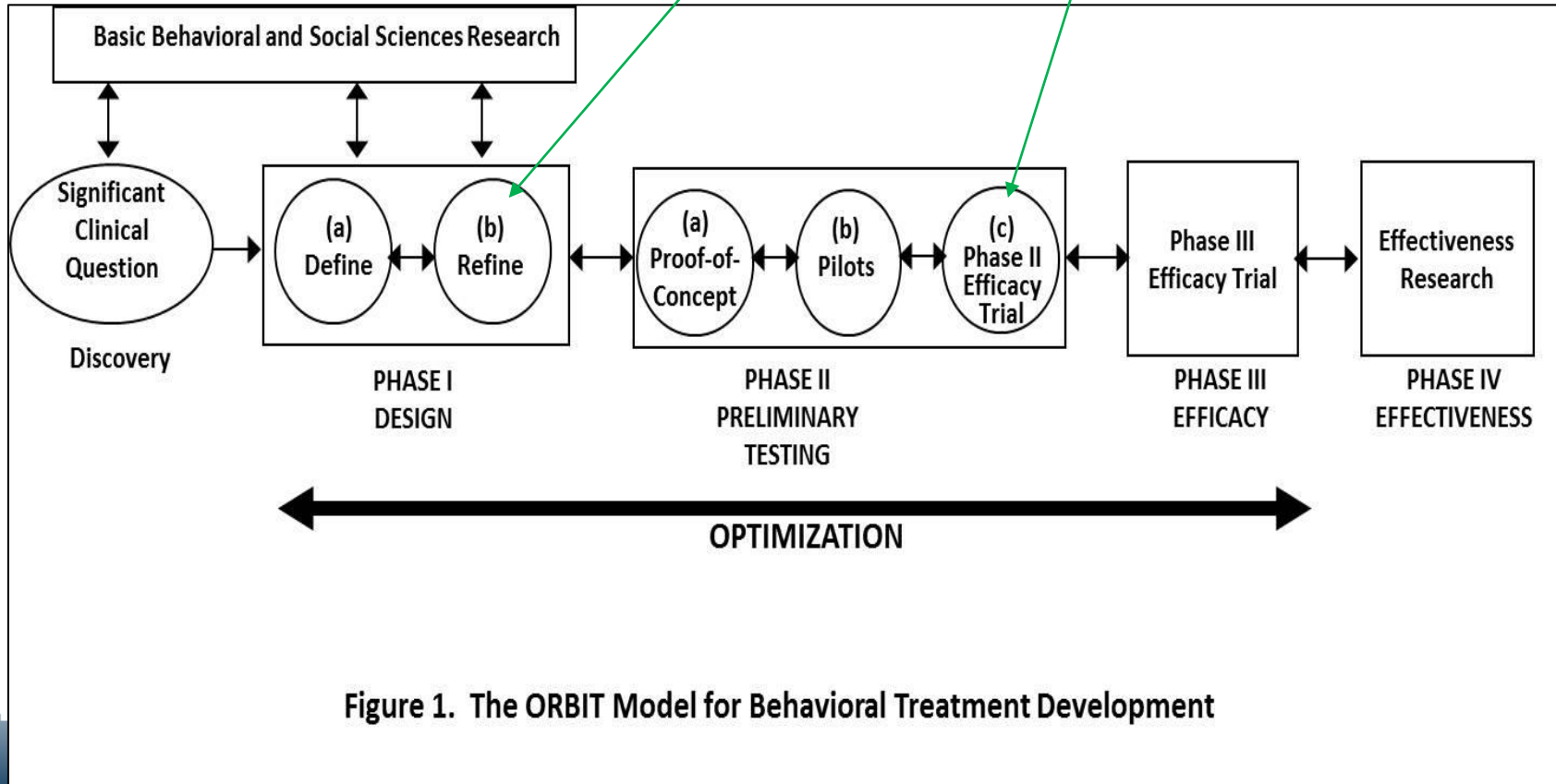


Figure 1. The ORBIT Model for Behavioral Treatment Development

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 have a framework?

We Are Stuck Irrelevance



“Phase III efficacy trial is the highest quality of evidence for a new treatment.”

(Institute of Medicine, 2011)

COUNTRY

GUIDELINES GROUP

International

GRADE Working Group

United Kingdom

Centre for Evidence-Based Medicine

Scotland

Scottish Intercollegiate Guideline Network

New Zealand

New Zealand Guidelines Group

Canada

Canadian Hypertension Education Program

United States

Institute for Clinical Systems Improvement
American Family Physicians
US Preventive Services Task Force
American College of 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
American Academy of Neurology

(Institute of Medicine, 2011)

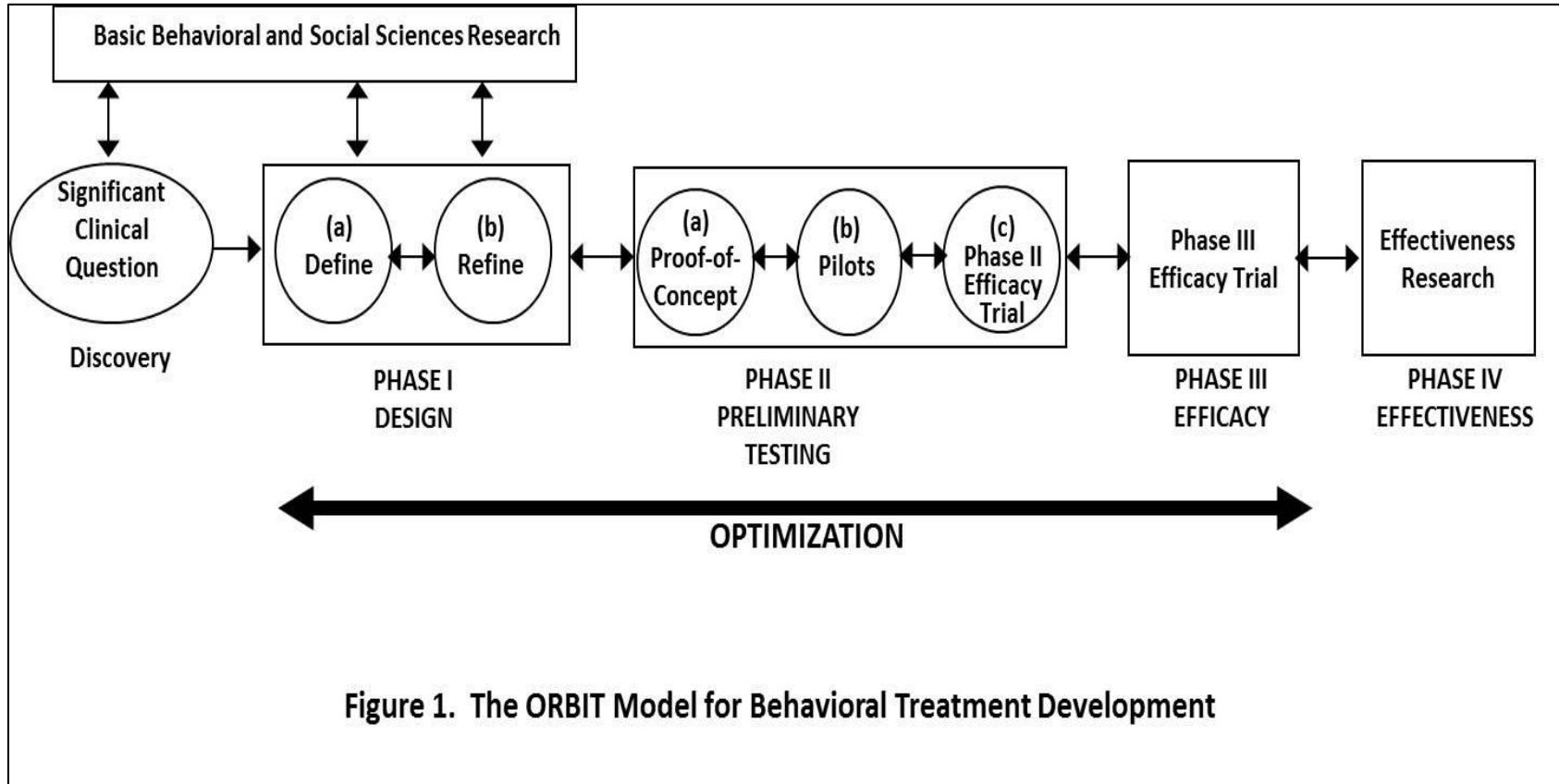
@ibtnetwork

#ibt2020

Behavioral Treatment Development



PROGRESSIVE QUESTIONS AND DESIGNS



DEFINE

“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

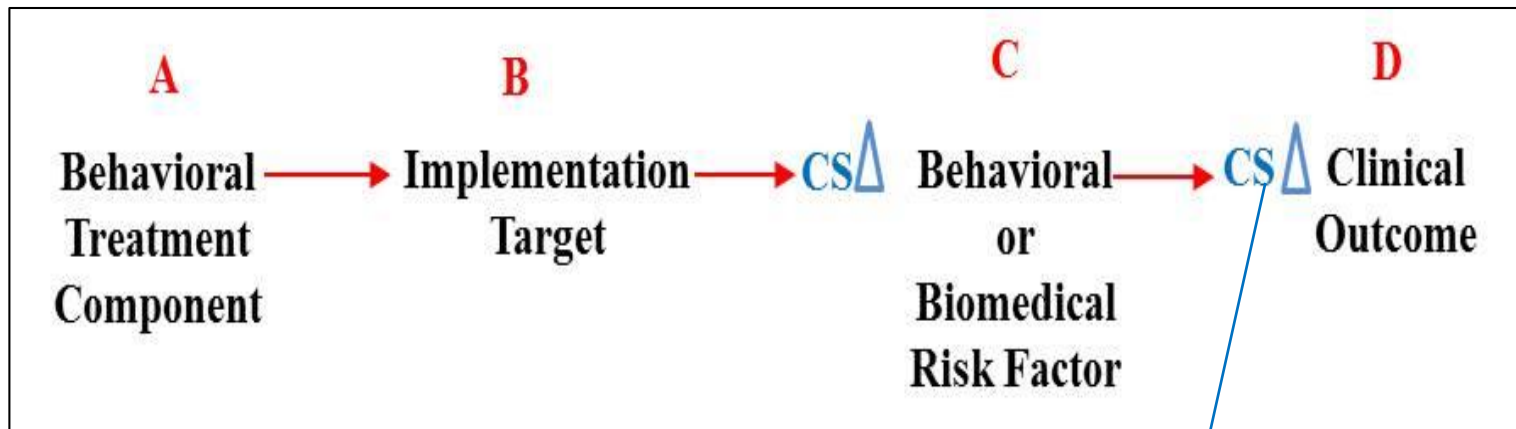


TINKERING

- 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

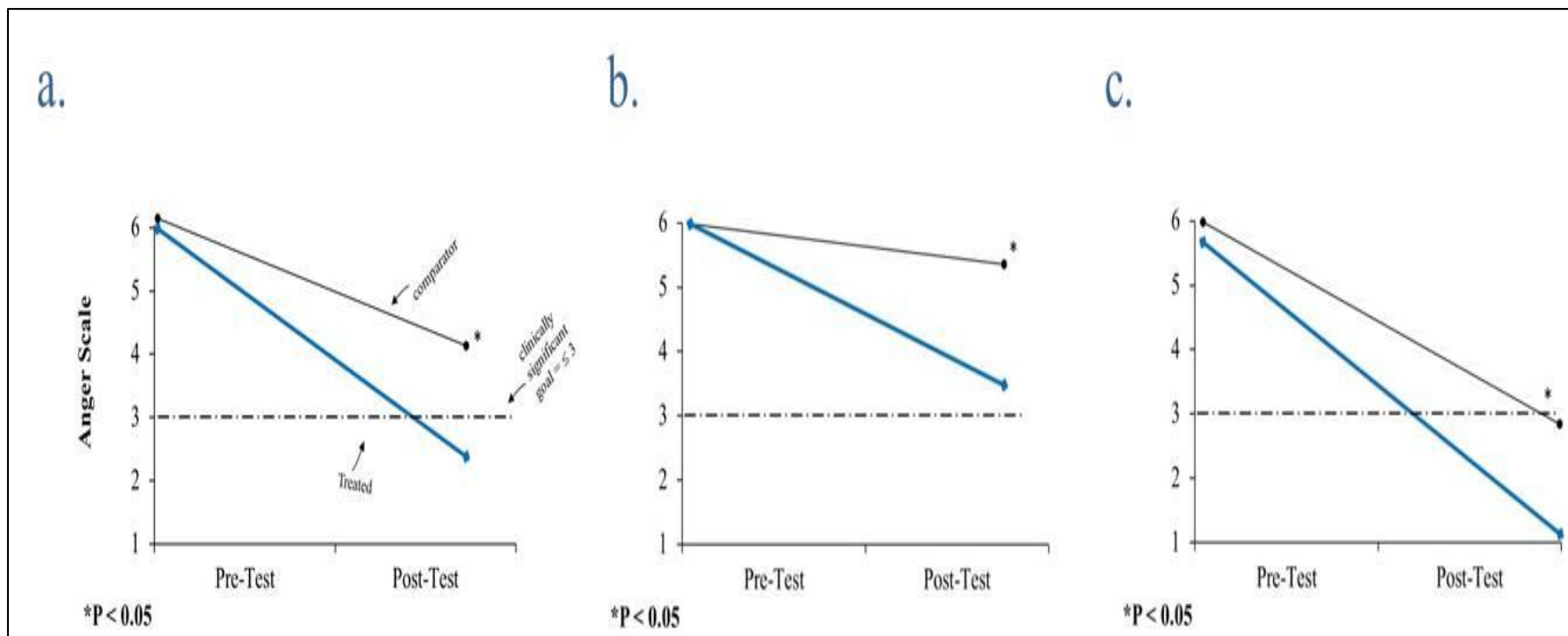


HYPOTHESIZED PATHWAY



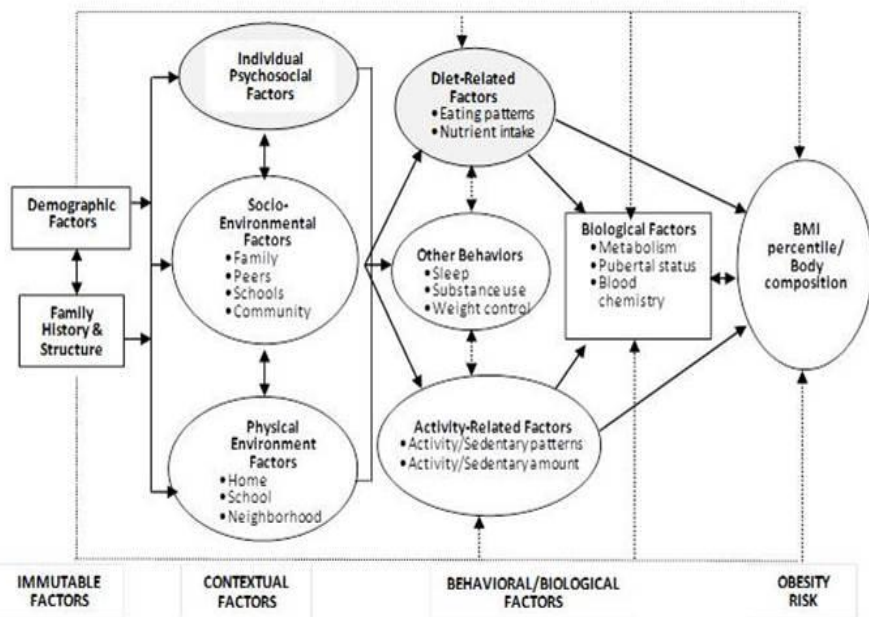
CS Δ = clinically significant change
= “stick your neck out”

CLINICAL SIGNIFICANCE

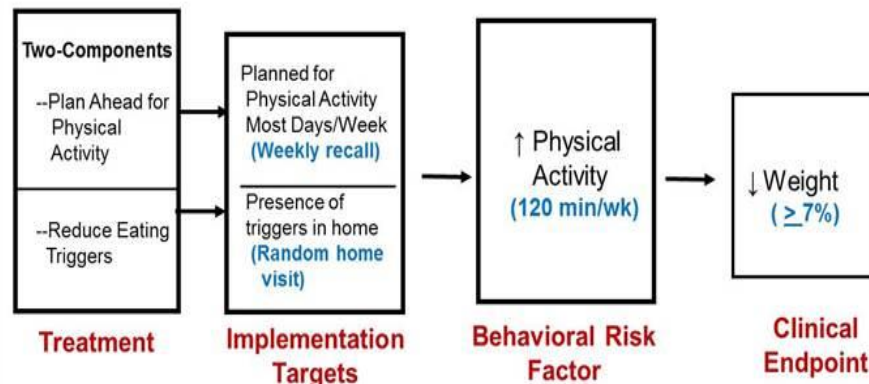


DEFINE CHILDHOOD OBESITY

Conceptual Model



Hypothesized Pathway



WELCOME FAILURE

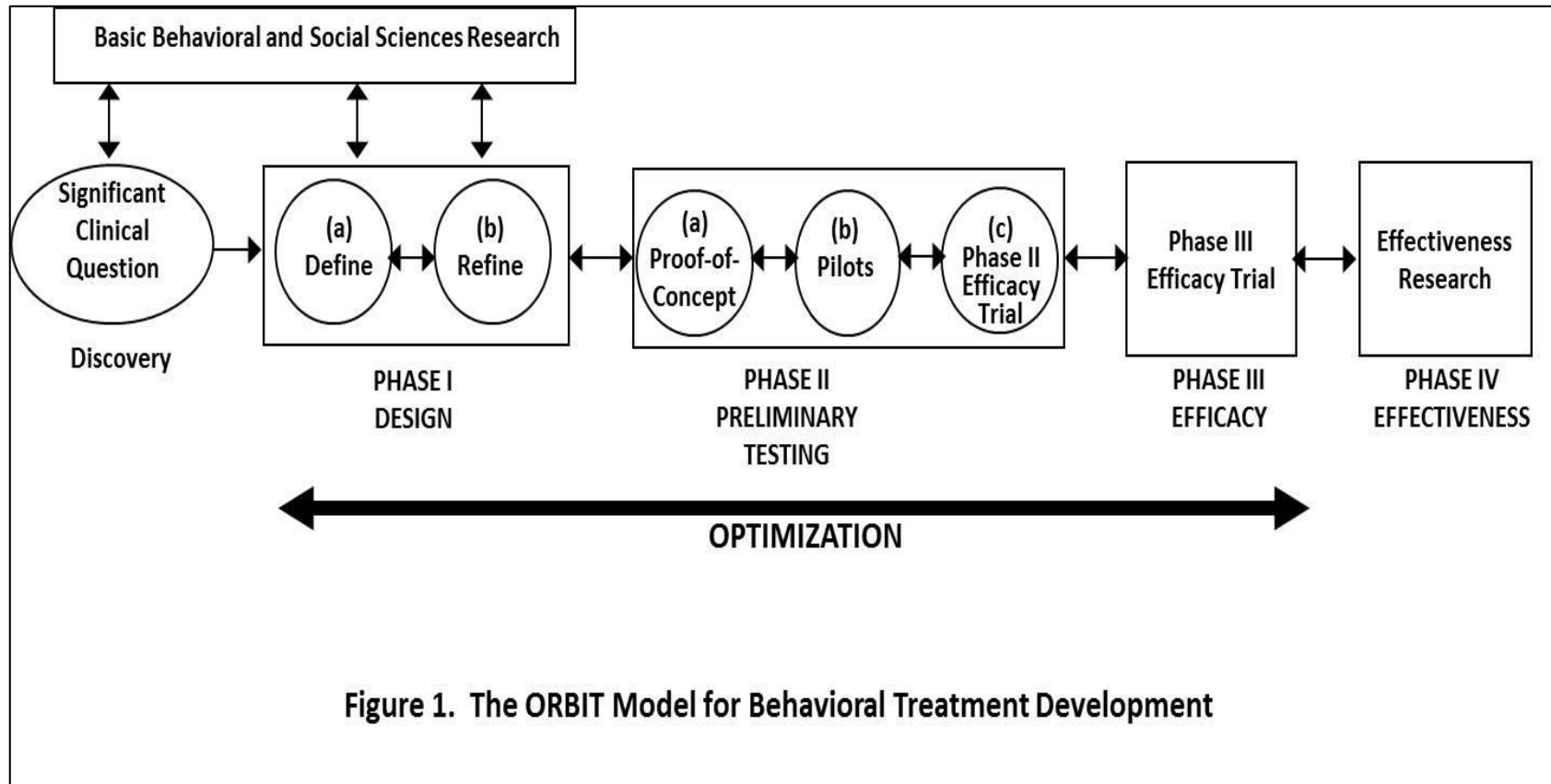


Figure 1. The ORBIT Model for Behavioral Treatment Development

WELCOME FAILURE

*“Welcome failure
as the opportunity for growth.”
(Popper, 1954)*



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“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

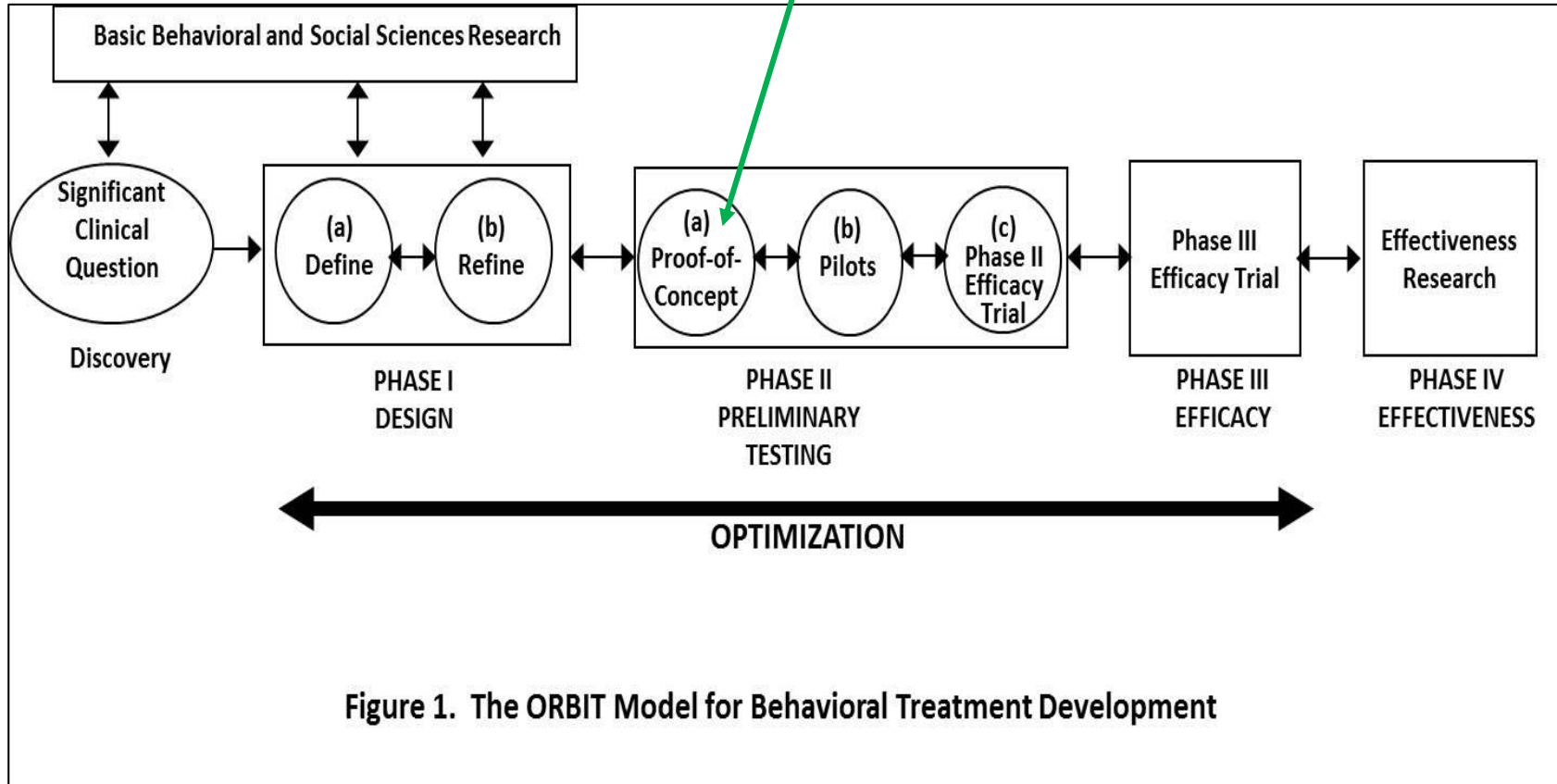


Figure 1. The ORBIT Model for Behavioral Treatment Development



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

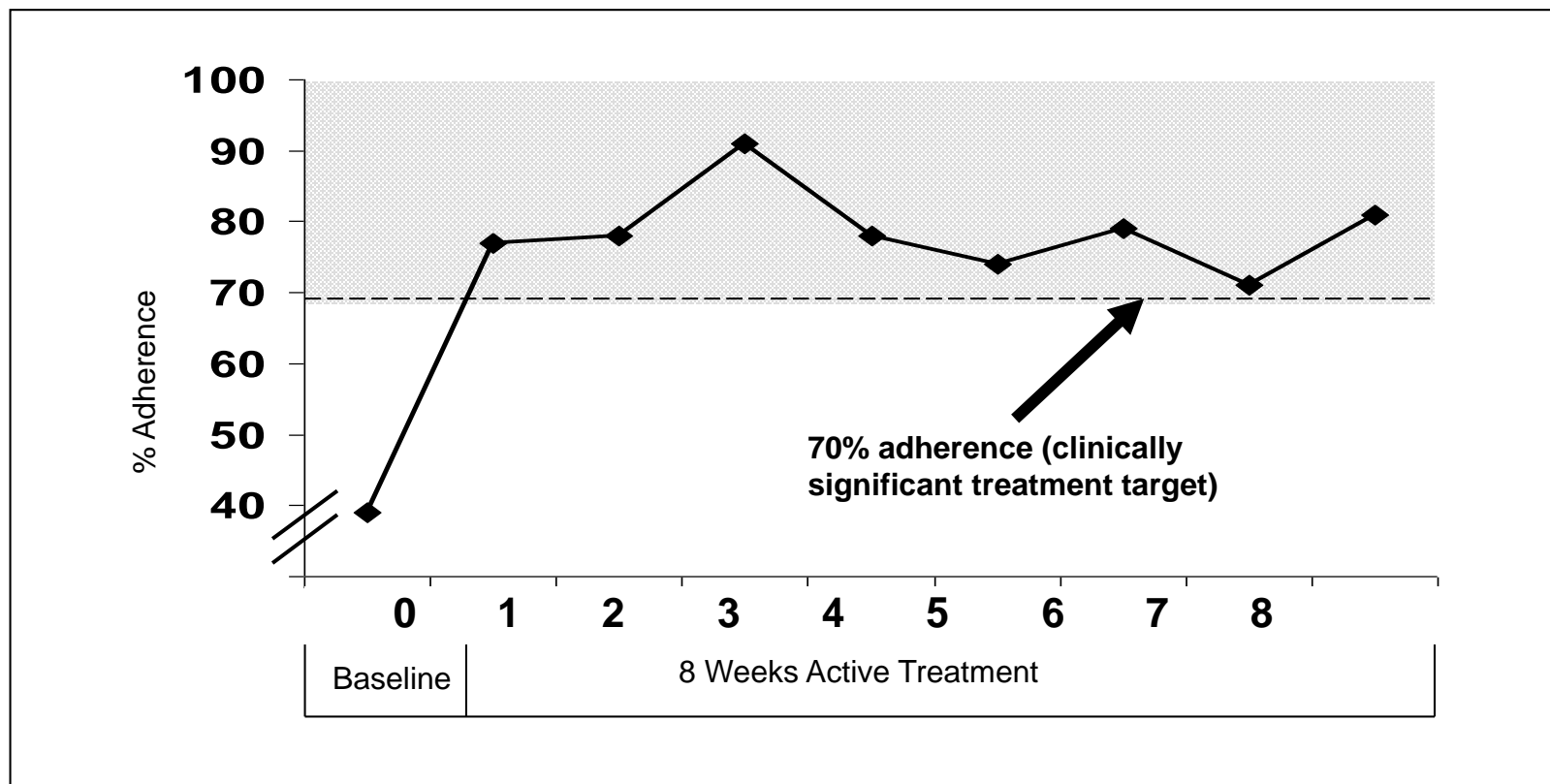
Accessible sample

**A comparator is
useless when a
behavioral
treatment is too
weak to warrant
any comparison.**

PROOF OF CONCEPT



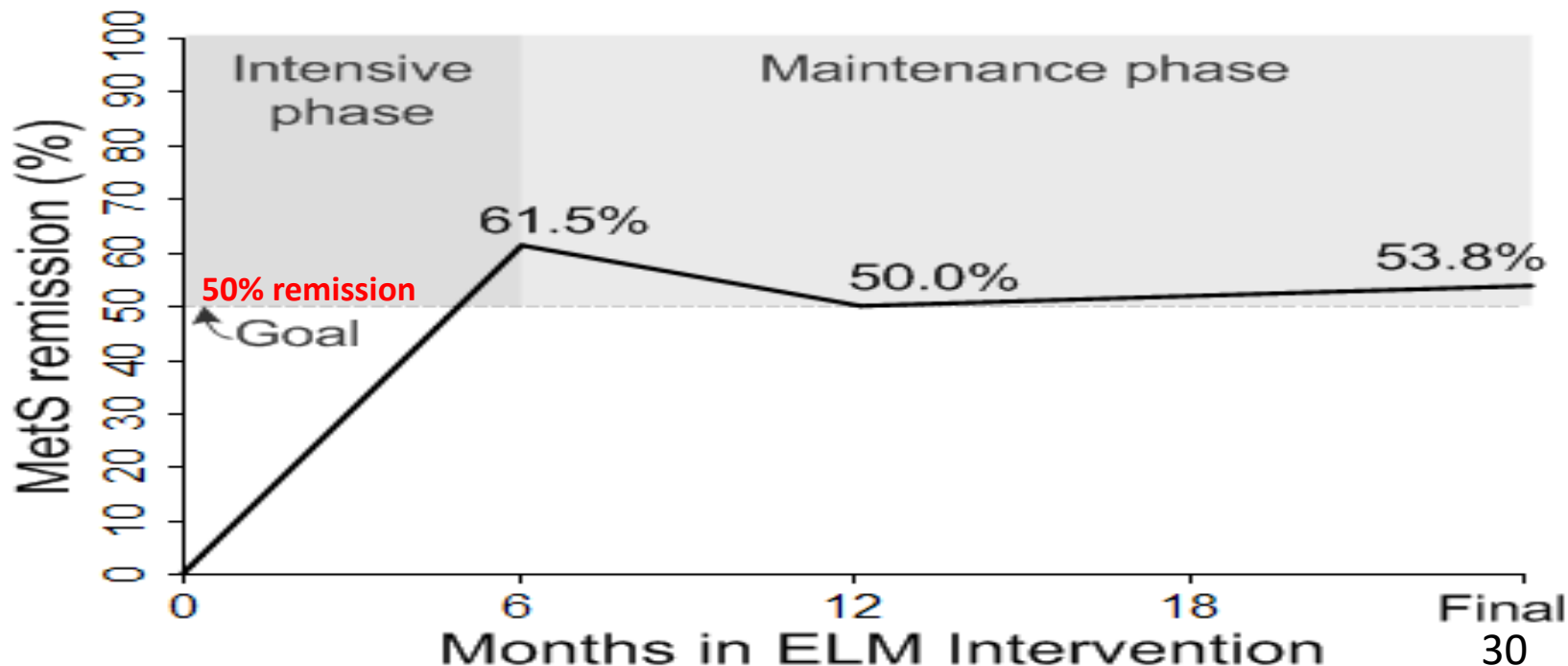
N=4



Mosnaim, 2008

PROOF-OF-CONCEPT

N=26



Powell et al, 2018



SUMMARY

ibtn
international
behavioural
trials network

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.