

# DETERMINANTS AND CHALLENGES OF PERSONALIZED OBESITY TREATMENTS

**A D O P T**  
**CORE MEASURES**



National Institutes  
of Health

ACCUMULATING DATA TO OPTIMALLY PREDICT OBESITY TTREATMENT

**Paul MacLean, Alex Rothman, Holly Nicastro, Tanya Agurs-Collins,  
Katrina Serrano, Elise Rice, Susan Czajkowski, Catherine Loria.**

# **No conflicts to disclose.**

## **Funding Support**

- NIH R01 DK038088 (exercise and weight regain)**
- NIH P01 HD038129 (obesity and lactation)**
- NIH P50 HD073063 (menopause and weight regain)**
- NIH R01 CA164166 (obesity and breast cancer)**
- Colorado Obesity Research Initiative**
- Colorado Nutrition Obesity Research Center**
- Colorado Comprehensive Cancer Center**

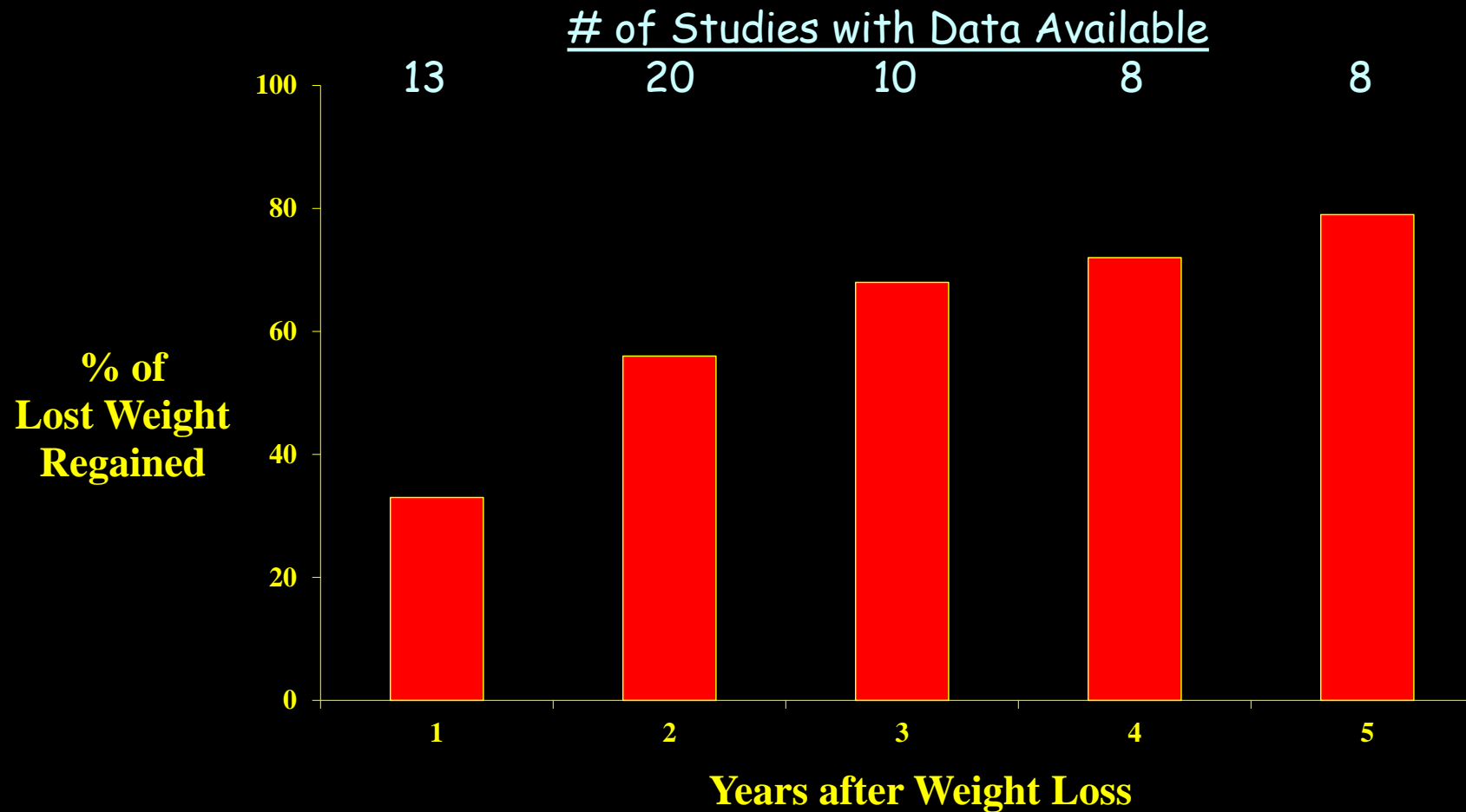
# The Problem of Obesity

- **High Incidence**
  - Over 2/3 of adults are overweight or obese
  - Does not discriminate by sex/race
- **Numerous Co-Morbidities**
  - \$100-\$150 billion/yr health care cost
- **Numerous Consequences**
  - Social stigmatization
  - Discrimination
  - Reduced quality of life



# Propensity to Regain Weight After Weight Loss

## Meta-Analysis of US Weight Loss Studies



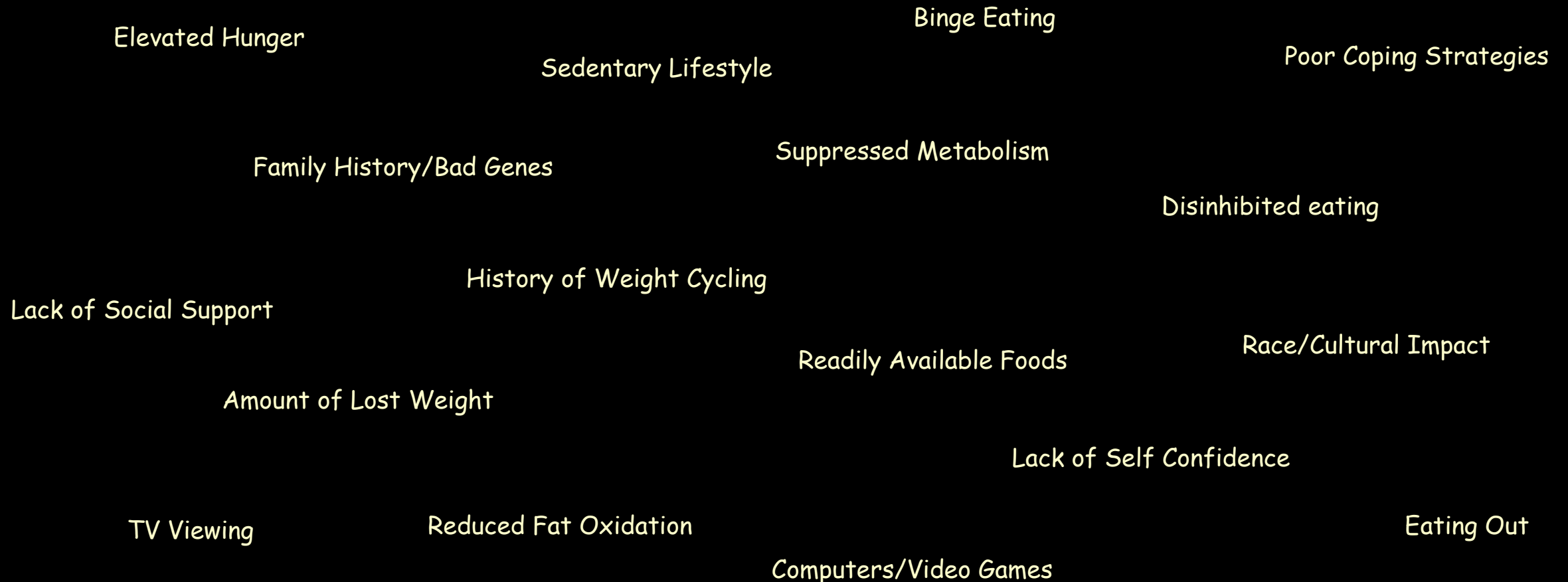
Adapted from Anderson et al, AJCN 2001

# Why Do We Regain?

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## FACTORS THAT HAVE BEEN LINKED TO WEIGHT REGAIN

*Elfhag and Rössner, 2005; Weiss et al., 2007; MacLean et al 2011*



# Overview

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- Pressures affecting body weight
- Barriers and challenges to weight loss and weight loss maintenance
- ADOPT Core Measures Project
  - One effort to pursue a personalized or targeted approach to obesity therapeutics

# NIH Working Group - 2014

## Innovative Research for Weight Loss Maintenance

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- Multiple Institutes Involved
  - NHLBI, NCI, NIDDK, NICHD
  - Led by Rena Wing and Paul MacLean
- Broad Range of Expertise
  - Behavioral psychologists, physiologists, neuroscientists, dietician/nutrition experts, epidemiologists, mathematical modelers, basic/clinical researchers
  - Terry Davidson, Leonard Epstein, Bret Goodpaster, Kevin Hall, Barry Levin, Michael Perri, Barbara Rolls, Michael Rosenbaum, Alexander Rothman, Donna Ryan



# Framing the Discussion

## *Pressures Affecting Body Weight*

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### Biology

genetic and epigenetic predisposition

metabolic homeostasis

### Environment

food composition and availability

need for exercise

promotion of activity

comfortable technology

climate and weather

social and cultural expectations

### Behavior

fast food vs gardening

stairs vs elevator

TV vs outside play

daily run vs daily nap

car vs bike

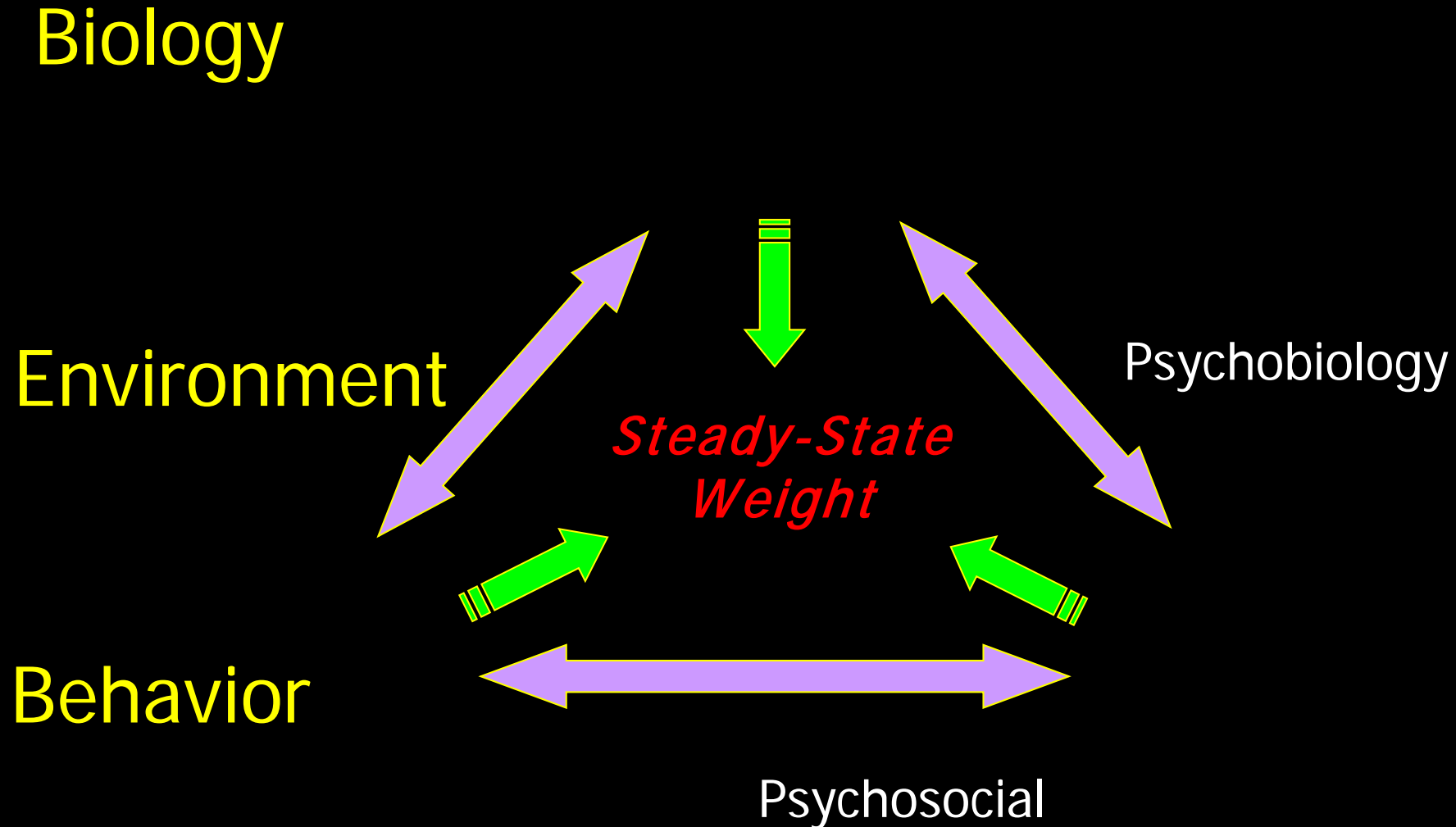
choice of friends and activities



# Framing the Discussion

## *Pressures Affecting Body Weight*

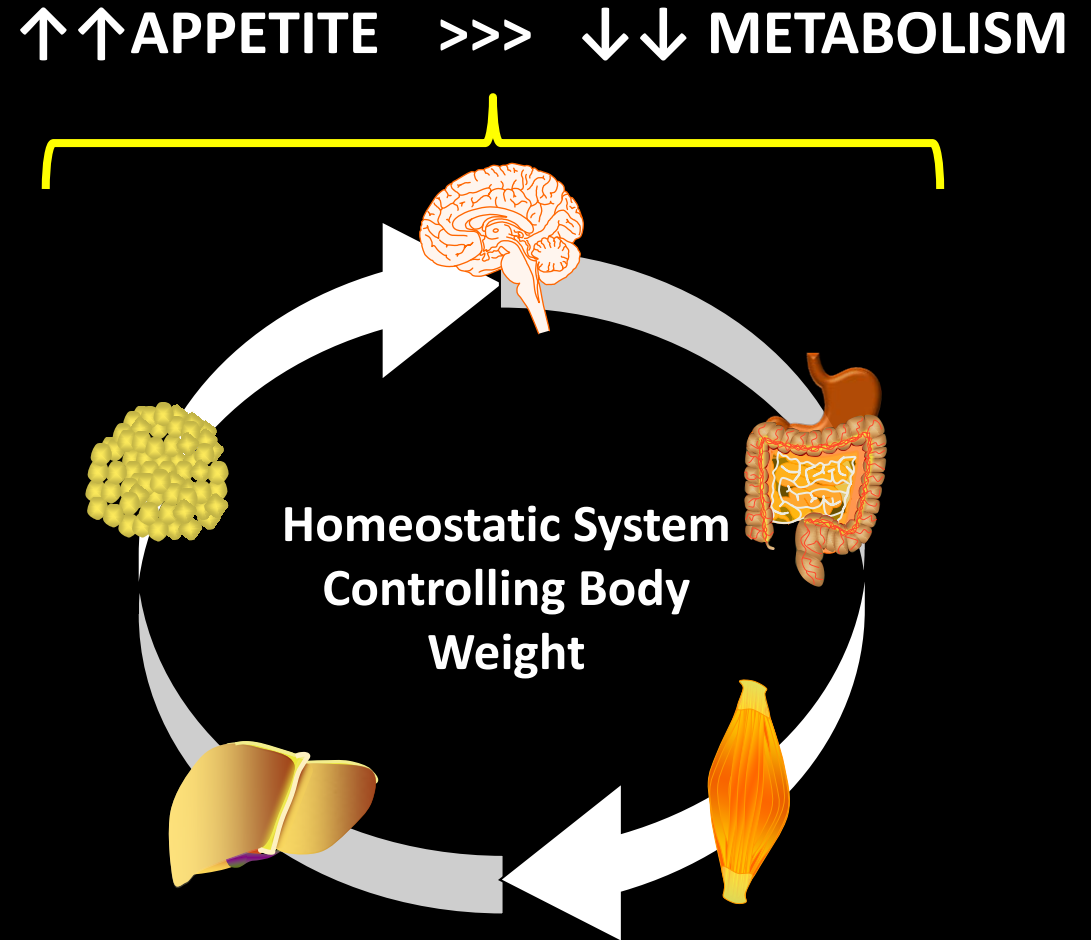
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# BARRIER 1

## Biological Drive to Regain Weight

- **Complex, strong, redundant**
  - Coordination of several tissues and regulatory nodes.
  - Extends to hedonic aspects of food intake.
  - May extend to the motivation to be physically active.
- **Persistent**
  - Does not resolve with time.
  - May even strengthen with time.



## BARRIER 2

# Persistence of the Obesogenic Environment (food and physical activity)

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- Food Availability and Security
- Socio-Economic Status
- Cultural Demands/Expectations
- Built Environment
- Home, Neighborhood, Work



# BARRIER 3

## Decline in Adherence to Behavioral Programs

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- Between 6 – 9 months of a weight loss program
  - Coincides with weight plateau
  - Both dietary and exercise prescriptions
- Gradual, intermittent
  - Very difficult to study
  - Complex, multi-factorial

### ***WHY?***

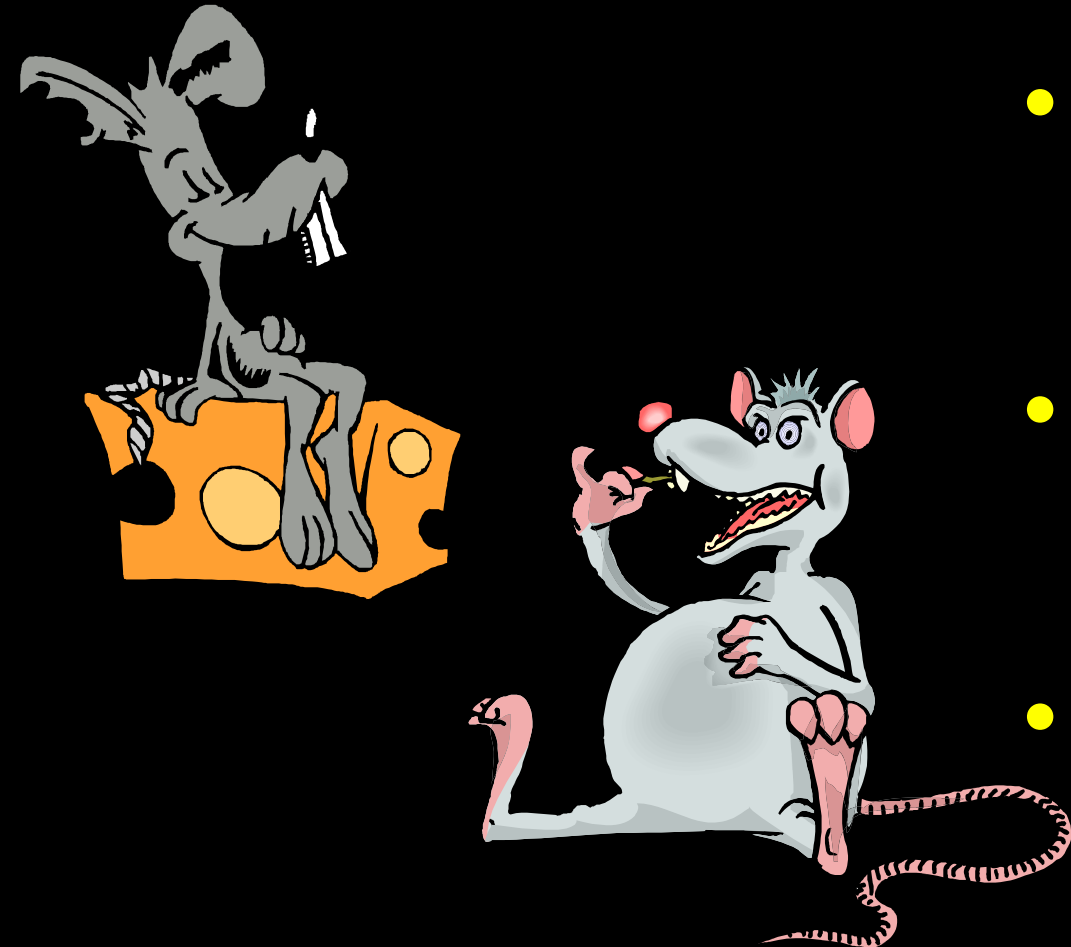
#### ***Psychosocial + Psychobiological***

- Weight loss strategies are viewed as transient endeavors
- Perceived cost / benefit ratio changes
- Boredom/aversion to dietary/exercise regimen
- Return of entrenched eating/inactivity habits
- A strengthening biological drive to overeat

# Challenges to Developing Better Strategies

## *Individual Variability*

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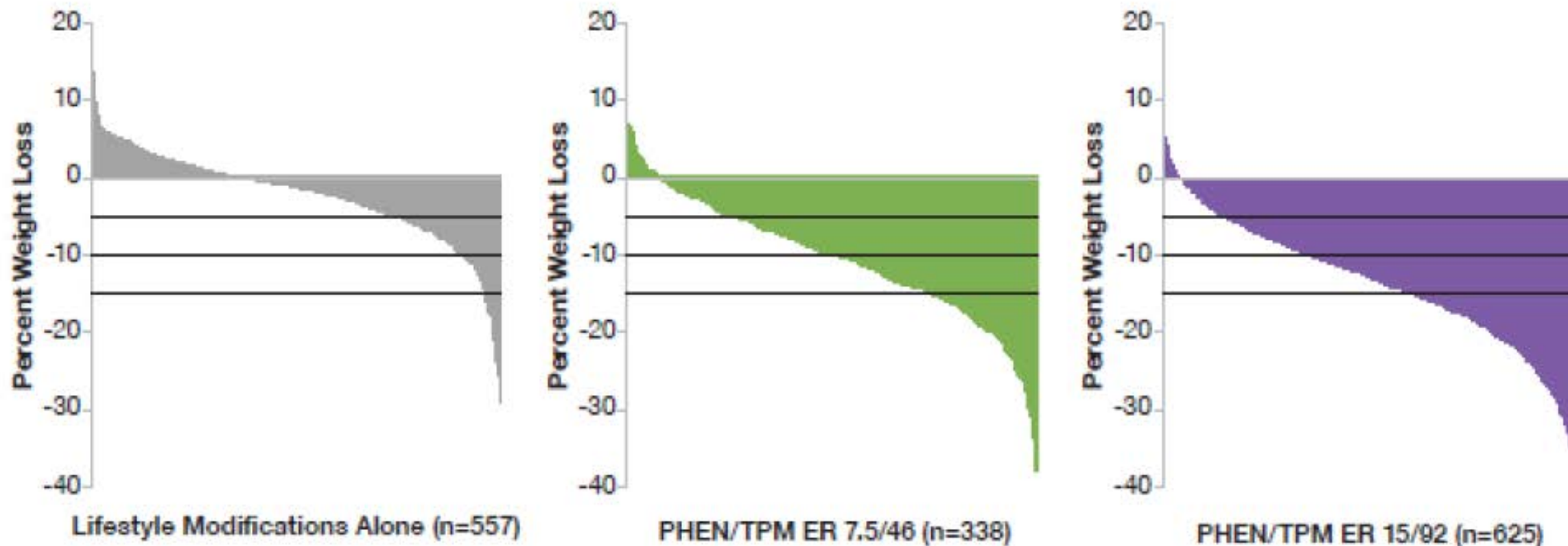
- **BIOLOGY**
  - Genetic and epigenetic variability
- **BEHAVIOR**
  - Psychological aspects of behavior change
- **ENVIRONMENT**
  - Diverse, and changing across the lifespan

# Manifestations of Individual Variability

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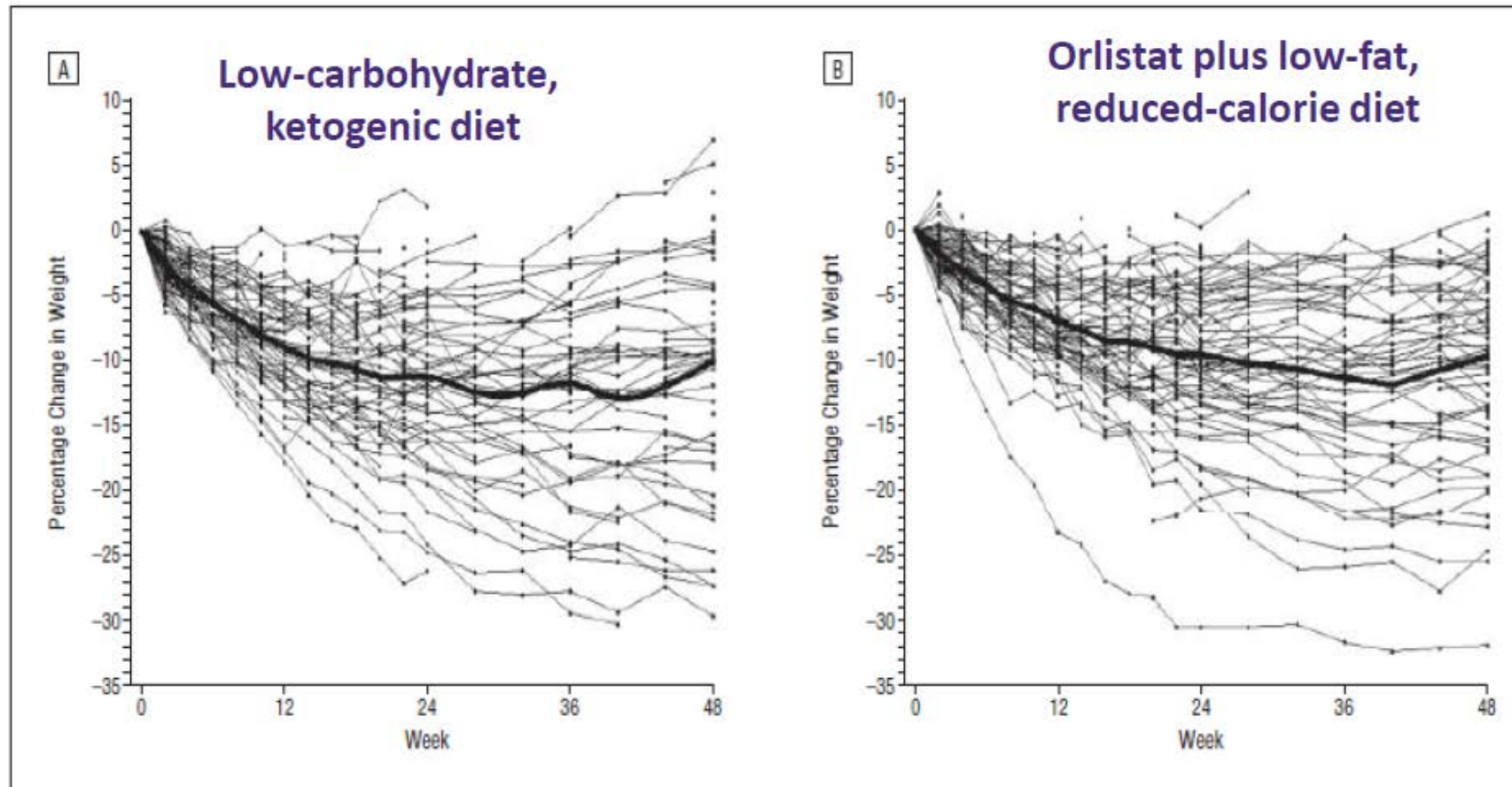
- Predisposition for obesity
  - Biological adaptations to weight loss
  - Motivations behind behavior change/failure
  - Food/Activity environmental pressures
- 
- ★ • Response to diet, exercise, drug, surgery, and other behavioral interventions

# When individual weight loss is displayed, it looks like this:



Each vertical bar represents a single subject experience in subjects completing 56 weeks on study drug

# Mean and Individual Weight Loss Response with Low-carbohydrate Ketogenic Diet or Orlistat with Low-fat, Reduced-calorie Diet



**Variability in response, regardless of the treatment.**

*Yancy W, et al  
Arch Intern Med 2010.*



# Advancing the Science

One next step in this effort



- Pursue the individual variability in the effectiveness of obesity treatments.
  - Acknowledge the “responder/non-responder” phenomenon.
  - Targeting specific treatment(s) to “responders” to give individual the best chance for success.

- Long Range Goal:

Targeted or personalized treatments in obesity medicine.

# Demand for This Effort



- Patients are asking for it.
  - Too many programs, too much misinformation
- Clinicians are asking for it.
  - Trial and error is frustrating and expensive
- Many clinicians are already doing it.
  - Based upon personal experience
- The scientific community is already pursuing it.
  - Studies that are too limited in scope or size
  - Not gauging all domains in the effort to find predictors, moderators, and mediators of treatment response

# NIH Working Group

*May 26-27, 2016*



- Organized by NIH in December of 2015
- Leadership Team
  - Co-Chairs:
    - Alex Rothman and Paul MacLean
  - NIH Program Staff:
    - Catherine Loria, Holly Nicastro, Tanya Agurs-Collins, Susan Czajkowski, Elise Rice, Katrina Serrano

## **ADOPT Core Measures Project**

( Accumulating Data to Optimally Predict obesity Treatment )

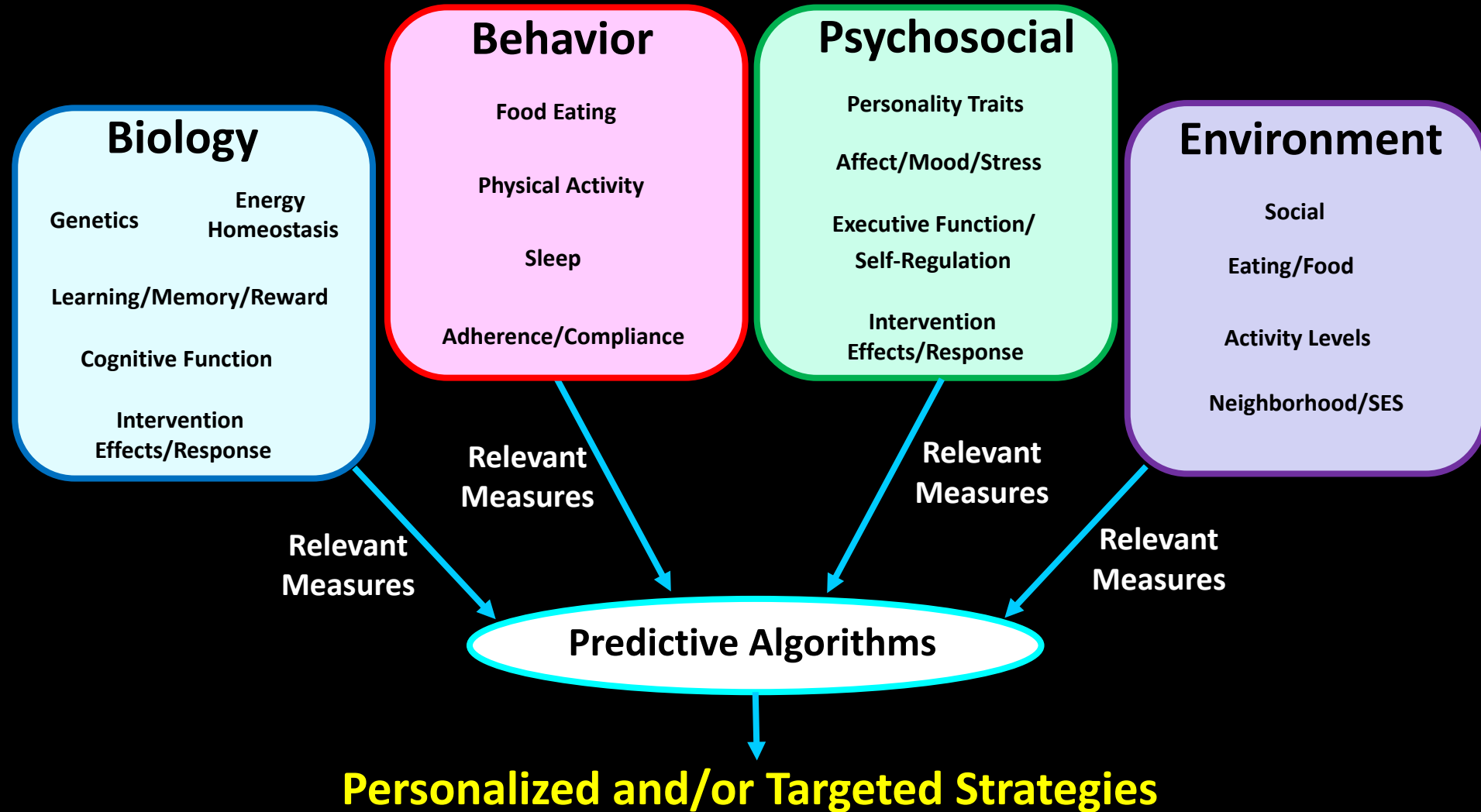
**Focus on Adult Obesity**

# Long Term Vision

**A D O P T**  
**CORE MEASURES**

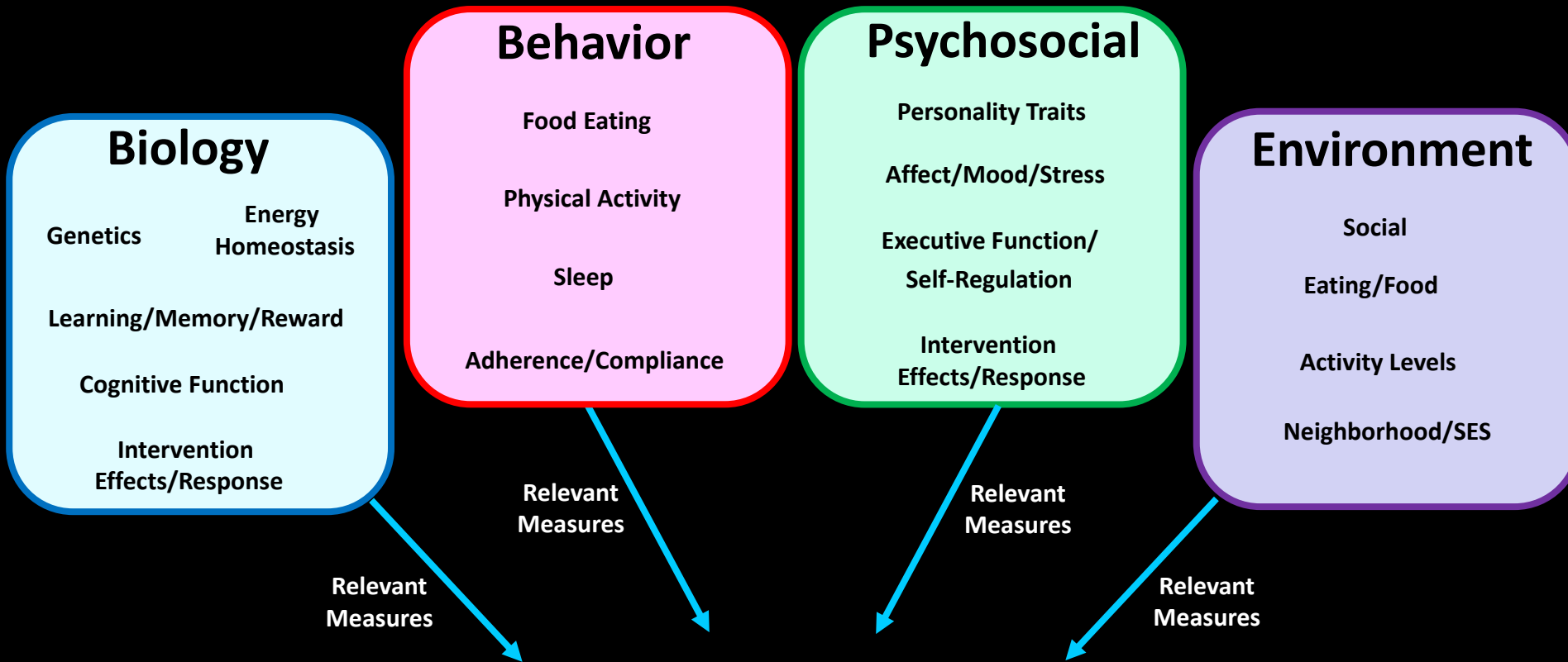


National Institutes  
of Health



# Short Term Objectives

**A D O P T**  
**CORE MEASURES**



Core set of high-priority measures that when consistently used in studies will identify constructs and parameters that predict or moderate treatment response.

# Recruiting the Panel

## Affiliations of 43 Panel Members



## 19 Universities

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Banner Alzheimer's Institute

Brown University

Columbia University College of Physicians  
& Surgeons

Florida State University College of  
Medicine

Johns Hopkins University

Pennington Biomedical Research Center

Sheffield Hallam University

University of California, San Diego

University of California, San Francisco

University of Illinois at Chicago

University of Colorado School of Medicine

University of Connecticut

University of North Carolina, Chapel Hill

University of Pittsburgh Medical Center

University of Minnesota

University of Texas at Austin

University of Washington

Tufts University

Yale Medical School

## 5 NIH

## Centers/Institutes

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National Heart, Lung, & Blood Institute  
(NHLBI)

National Cancer Institute (NCI)

National Institute on Aging (NIA)

National Institute of Diabetes,  
Digestive & Kidney Diseases (NIDDK)

Office of Behavioral and Social  
Sciences Research (OBSSR)

# Biological Domain

## Subdomain Experts

Molly Bray

Michael Rosenbaum

Dana Small

Cary Savage

Mark Hopkins

Susan Roberts

Genetics

Energy Homeostasis

Learning/Memory/Reward

Cognitive Function

Exercise Response/Variability

Diet Response/Variability

## NIH Co-Leads

Tanya Agurs-Collins

Aynur Unalp-Arida

Luke Stoeckel

Maren Laughlin

Padma Maruvada

# Behavioral Domain

## Subdomain Experts

Leslie Lytle

John Jakicic

Naresh Punjabi

Food/Eating  
Behavior

Physical Activity/  
Sedentary Behaviors

Sleep Behaviors

## NIH Co-Leads

Holly Nicastro

Mary Evans

Aaron Laposky



# Psychosocial Domain

## Subdomain Experts

Angelina Sutin

David Williams

Elissa Epel

Kerri Boutelle

Personality/Dispositional  
Traits

Social Cognitive

Affect/Mood/Stress

Executive Function/  
Self Regulation

## NIH Co-Leads

Lis Nielson

Christine Hunter

Paige Green

Deborah Young-  
Hyman

# Environmental Domain

## Subdomain Experts

Shannon Zenk

Brian Saelens

Amy Gorin

Tiffany Powell-  
Wiley

Food Environment

Activity Environment

Social Environment

Neighborhood/SES

## NIH Co-Leads

Jill Reedy

David Berrigan

Sonia Arteaga

Charlotte Pratt

# Perspectives, Input on All Domains



## Added Perspectives

Daniel Bessesen

**Pharmacotherapy  
Variability in Response**

Anita Courcoulas

**Surgery/Devices  
Variability in Response**

Donna Ryan

**Behavioral Interventions  
Variability in Response**

Kevin Hall

**Complex Data Modeling**

# Charge to Panel Members



- Prioritize the “BEST” constructs that could be predictors or moderators of treatment responses.
- Prioritize the “BEST” measure for those constructs that could be used in weight loss trials.

# Criteria for “BEST” Constructs and Measures



- Strength and Source of the evidence
  - Relevance to obesity, weight loss
- Quality of measure (validity, reliability)
- Feasibility of measure
  - Researcher cost/expertise
  - Study size
- Subject burden

# Expected Products



- Core set of high priority list of constructs/measures
  - Based on the current state of the science
  - Modifiable with advancements in the science
  - With input from the scientific community
- Online accessible database of measure protocols
  - To facilitate consistency in obesity research
- Identification of Gaps in Knowledge or Process
  - Better constructs, measures, or measurement schedules
  - More helpful study designs
- Roadmap for future efforts and applications



# GEM Grid-Enabled Measures Database

National Cancer Institute

U.S. National Institutes of Health | [www.cancer.gov](http://www.cancer.gov)

Hello Alex Rothman [Logout](#)

GEM Grid-Enabled Measures Database

- Home
- Constructs
- Measures
- Datasets
- Workspaces
- About
- My GEM
- Glossary

## Content Areas

- Anthropometrics
- Cancer
- Cardiovascular
- Diabetes
- Education, Training, and Career Development
- Environment
- HIV/AIDS
- Mental Health
- Methods
- Nutrition
- Obesity
- Occupational Health
- Pain
- Physical Activity
- Pregnancy
- Risk and Decision Making
- Sexual Behaviors
- Sleep
- Smoking/Tobacco

### Welcome to GEM, a web-based collaborative tool containing behavioral, social science, and other relevant scientific measures.

The goal of GEM is to support and encourage a community of users to drive consensus on best measures and share the resulting data from use of those measures.

GEM enables users to:

- Add constructs or measures to the database
- Contribute to and update existing information (metadata) about constructs and measures
- Rate and comment on measures to drive consensus on best measures
- Access and share harmonized data
- Search for and download measures

[Learn more about GEM](#)

- ▼ Community News
- ▲ Recent Additions

#### Check out the Team Science Toolkit blog about GEM

See a recent blog by Richard Moser and Kisha Coa about how GEM can be used to facilitate team science on the Team Science Toolkit website (<https://www.teamsscience toolkit.cancer.gov>). Make sure to explore this helpful site that has information and... [More](#)

[Click here to read the blog](#)

#### Inaugural GEM-inar! GEM Care Planning: Advancing Survivorship Care Planning

In case you missed it, click the link below to watch the first GEM-inar that highlights real-world application and use of GEM. NCI's Carly Perry, PhD, MA, MSW and University of Pittsburgh's Ellen Beckjord, PhD, MPH presented on the GEM-Care... [More](#)

[Click here to watch the Gem-inar](#)

### Recent Workspaces

Customizable virtual areas to collaborate on a specific project

Consortia... [More](#)

- ADOPT Core Measures: Psychosocial Workspace  
To identify a core set of high-priority psychosocial... [More](#)
- ADOPT Core Measures: Behavioral Workspace  
To identify a core set of high-priority behavioral measures... [More](#)
- ADOPT Core Measures: Biological Workspace  
To identify a core set of high-priority biological measures... [More](#)
- ADOPT Core Measures:

### My Subscriptions

You have no subscription activity to report.

Publically Available

4 Workspaces/Measures

Biology – 29

Behavior – 46

Psychosocial – 129

Environment - 34

# ADOPT Working Group: Biological Domain

## Initial *Draft* of High Priority Measures



Construct	Measure
<i>Hormones: Long-Term Regulators</i>	<i>Insulin, Leptin, Glucagon, Amylin (ELISA)</i>
<i>Hormones: Long-Term Regulators</i>	<i>Thyroid Hormone Panel (T3, fT3, T3/T4)</i>
<i>Biological Affectors of Energy Balance</i>	<i>Metabolite Panel (Glucose; NEFA, TG; Colorimetric)</i>
<i>Genetic Markers</i>	<i>SNPs (DRB3, FTO, GNPDA2, LYPLA, MTCH2, MTIF3, NEGR1, PLIN, RANK)</i>
<i>Body Composition: Fat Mass/Fat Free Mass</i>	<i>Dual Energy X-ray Absorptiometry (DXA)</i>
<i>Energy Intake</i>	<i>Model Calculated Energy Intake</i>
<i>Expended Energy: REE, TEF</i>	<i>Metabolic Cart (Indirect Calorimetry)</i>
<i>Fuel Utilization: Respiratory Exchange Ratio</i>	<i>Metabolic Cart (Indirect Calorimetry)</i>
<i>Metabolic Function: Diabetes Status</i>	<i>Fasting Glucose, HBA1c, HOMA</i>
<i>Metabolic Response to Fast/Feed Challenge</i>	<i>Hunger/Satiety Hormone Panel (Ghrelin, GLP1, GIP, PYY)</i>
<i>Biobanking Tissues (-omics)</i>	<i>Whole Blood and Saliva</i>

**Good  
Constructs**

**Good  
Measures**

**Good  
Predictive Potential**

**Needed Work  
Psychobiology  
Metabolic Flexibility  
Feasibility/Cost**

*Working Draft*



# ADOPT Working Group: Behavioral Domain

## Initial Draft of High Priority Measures



Construct	Measure
Total Dietary Intake	Interview-administered 24hr recall
Eating Away from Home	EARLY Eating Away from Home Questionnaire
Sugar-sweetened beverage (SSB) consumption	EARLY SSB Consumption Questionnaire
Food hedonics and Preference	Leeds Food Preference
Appetite Sensations	Appetite (Visual analogue scale)
Overall Physical Activity	Global Physical Activity Questionnaire
Moderately Vigorous Physical Activity	Paffenbarger Questionnaire
<b>(1) Physical Activity/ (2) Sleep Duration</b>	<b>Actigraphy (wrist-worn)</b>
Sleep Disorders	Berlin Questionnaire for Sleep Apnea
Sleep Timing	Munich Chronotype Questionnaire
Self-Weighing Behavior	EARLY Self-weighing Questionnaire
Weight Management Practices	EARLY Weight Management Practices Quest.

**Good  
Constructs**

**OK  
Measures**

**Good  
Predictive Potential**

**Needed Work  
Food Intake  
Feasibility/Burden**

*Working Draft*

# ADOPT Working Group: Psychosocial Domain

## Initial *Draft* of High Priority Measures



Construct	Measure
Affect (Trait/State)	Positive and Negative Affect Scale/ EMA Daily Diary
Restraint/Inhibition/Hunger	Three Factor Eating Questionnaire
Eating Behaviors: Stress and Emotion	Palatable Eating Motives: Coping Subscale
Eating Behaviors: Food Craving	Food Craving Questionnaire (Trait, Reduced)
Personality: Big Five Factors	Mini-international Personality Item Pool (Short form)/ Big Five Inventory (Long form)
Behavioral Intention	Behavioral Intention Scale(s)
Self-Efficacy	Self-Efficacy Scale(s)
Executive Function	Behavior Rating Inventory of Executive Function –Adult Version (BRIEF-A)

**OK  
Constructs**

**OK  
Measures**

**OK  
Predictive Potential**

**Needed Work  
Construct Definition  
Measure Validation**

*Working Draft*

# ADOPT Working Group: Environmental Domain

## Initial *Draft* of High Priority Measures



Construct	Measure
Geographic Location	Home address(es)
<i>Neighborhood Food Accessibility</i>	<i>(1) Supermarkets, (2) Fast food restaurants, convenience stores</i>
Neighborhood Food Accessibility	NEWS walking proximity (1) Supermarkets, (2) Fast food restaurants, convenience stores
<i>Neighborhood Food Availability</i>	<i>MESA Neighborhood Healthy Food Availability</i>
<i>Neighborhood Socioeconomic Deprivation</i>	<i>Neighborhood Deprivation Index (Diez Roux; Lian)</i>
<i>Neighborhood Socioeconomic Deprivation</i>	<i>Neighborhood Socioeconomic Position Index</i>
<i>Neighborhood Socioeconomic Deprivation</i>	<i>Neighborhood Police-Reported Crime</i>
Neighborhood Socioeconomic Deprivation	Perceived Neighborhood Safety
<i>Neighborhood Physical Activity</i>	<i>Block Group Level Walkability</i>
Perceived Land Use Mix Access	NEWS Land Use Mix Access Subscale
Autonomy Support	Perceived Autonomy Support Scale

**Good  
Constructs**

**Good  
Measures**

**OK  
Predictive Potential**

**Needed Work  
Absence of Research  
Predictability**

*Working Draft*

# Follow-Up Workshop

*February 8-9, 2017*



- Final curation of the core measure lists
  - Hone and merge the lists
  - Develop the GEM website resource
  - Assess feasibility/cost of application in weight loss trials
  - Identify gaps and problems
- Dissemination plan
  - Publication
    - Overview + 4 domain papers in 2017
  - Integration with other NIH and professional initiatives
  - Plans and steps for the future

# Perspectives

**A D O P T**  
**CORE MEASURES**



National Institutes  
of Health

- This is challenging, complicated, and difficult.
- The need to fill this gap in knowledge is great.
- The pay off for obesity therapeutics could be substantial.
  - We won't know, unless we try.

# A D O P T CORE MEASURES



National Institutes  
of Health

ACCUMULATING DATA TO OPTIMALLY PREDICT OBESITY TTREATMENT



**GEM** Grid-Enabled  
Measures Database