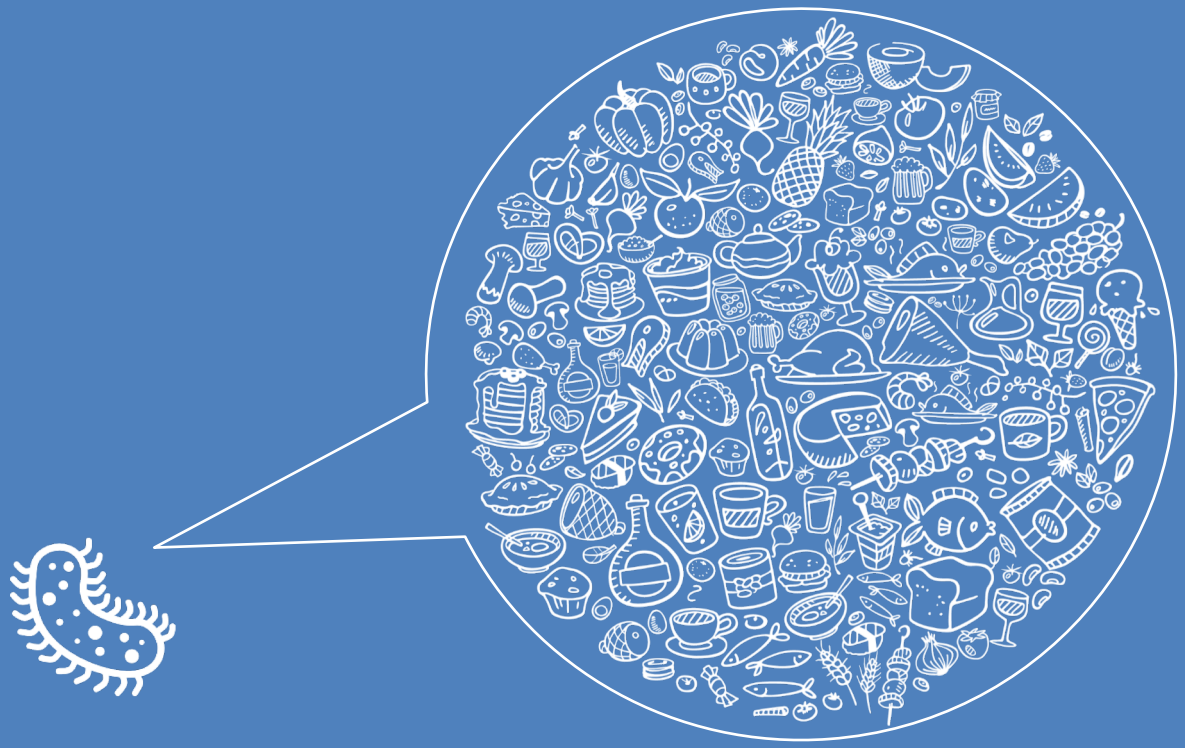
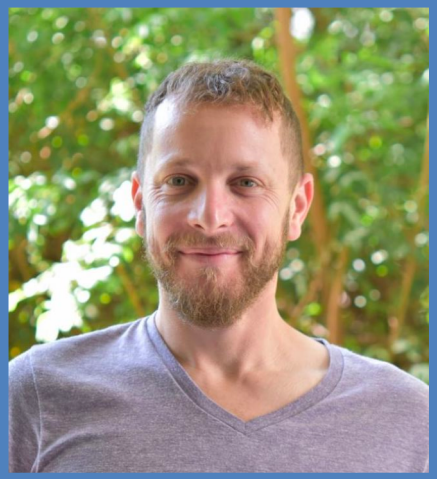


A data-driven approach for personalized dietary interventions

Tal Korem (@tkorem)
Departments of Systems Biology & OB/GYN
Columbia University

korem_lab()



Prof. Eran Segal

Dr. David Zeevi

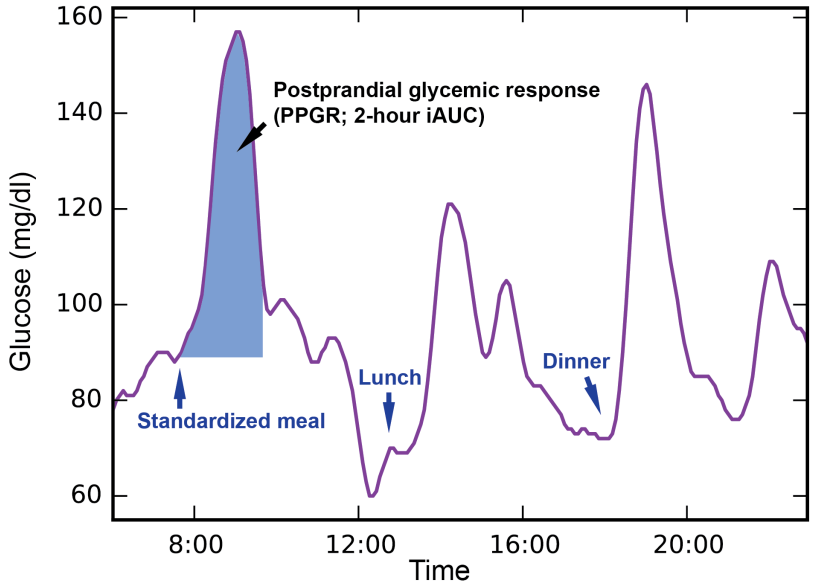
מכון ויצמן למדע

WEIZMANN INSTITUTE OF SCIENCE

Studying healthy nutrition through postprandial glycemic responses

Postprandial (post-meal) glucose response as a measure of healthy nutrition

Directly affects fat storage, weight gain and hunger



Associated with disease

- Diabetes
- Obesity
- Cardiovascular disease
- Chronic metabolic disorders

Bonora et al., Diabetologia 2001; Cavalot et al., Diabetes Care 2011; Wang et al., Diabetes Care 2004; Temelkova-Kurktschiev et al., Diabetes Care 2000; O'Keefe et al., Am J Cardiol 2007

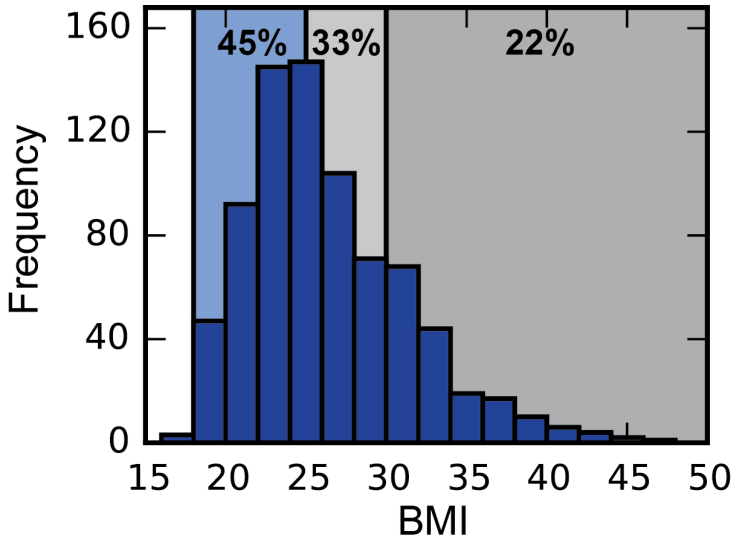
Glucose responses provide an immediate high-resolution feedback to every meal

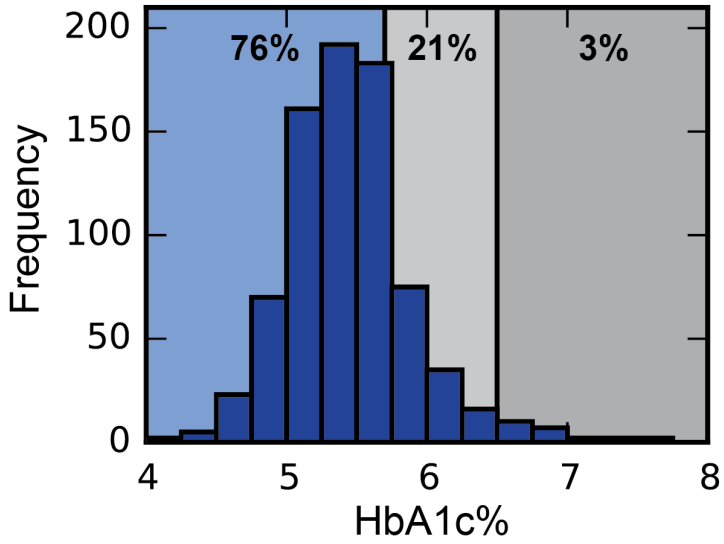
Weight	Post-meal blood glucose levels
Risk factor for many diseases	Risk factor for many diseases
Indirect measure of intervention	Direct measurement of meal effect
Periodic	Immediate
Low-resolution	High-resolution
Few data points per participant	Multiple data point per participant on short time-scales

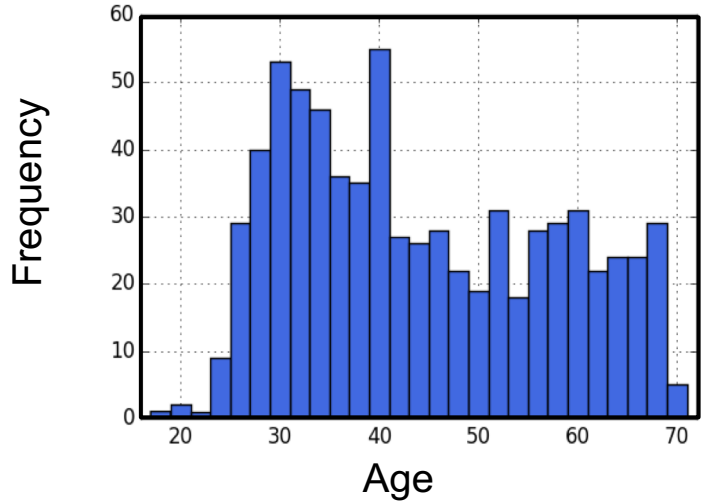
Maintaining normal blood glucose levels is key to fighting metabolic disease…

What's the best way to do this?

The Personalized Nutrition Project: Cohort statistics







- 25-70 years of age
- 55% overweight
- 22% obese
- 21% pre-diabetic

Zeevi et al., Cell 2015

Collection of glycemic, nutritional, clinical and microbiome data on a large healthy cohort

Initiation

Gut microbiome
16S rRNA
Metagenomics

Blood tests

Questionnaires
Food frequency
Lifestyle
Medical

Anthropometrics

Continuous glucose monitoring
Using a subcutaneous sensor (iPro2)

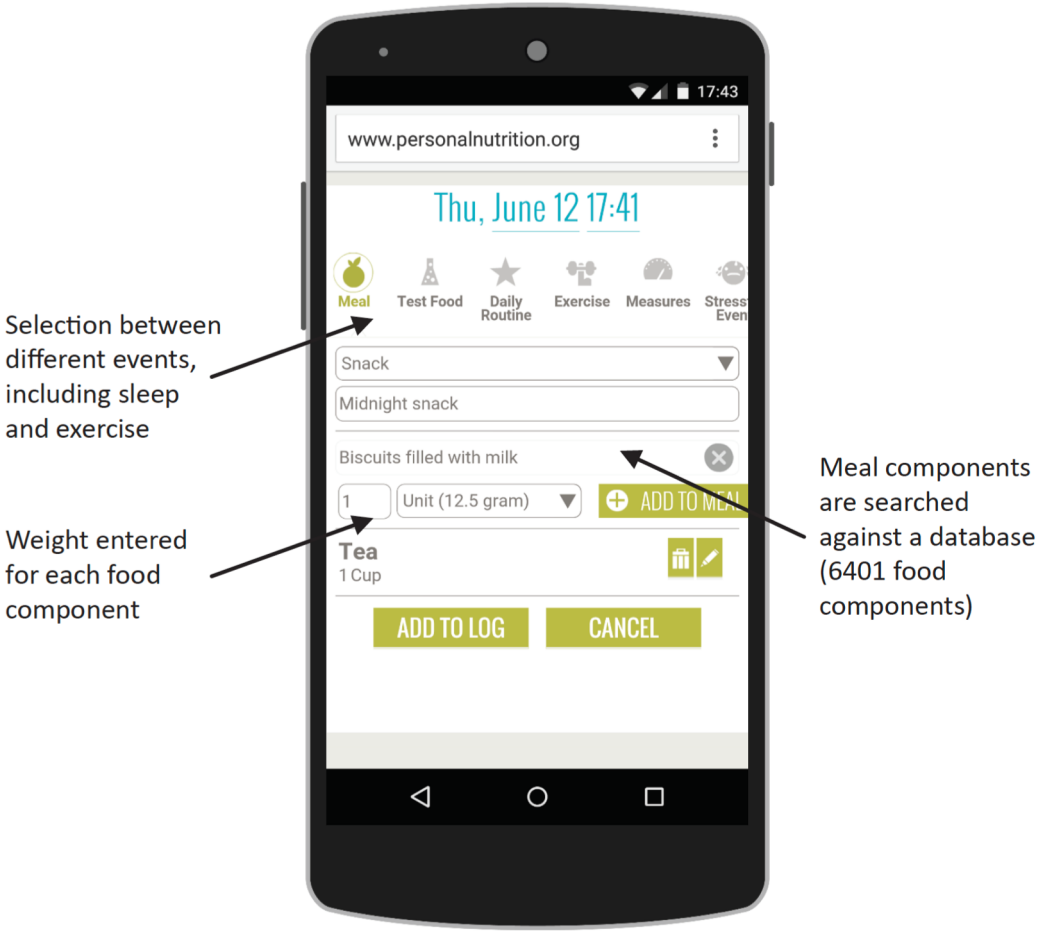
130K hours, 1.56M glucose measurements

Diary (food, sleep, physical activity)
Using smartphone-adjusted website

5,435 days, 46,898 meals, 9.8M Calories, 2,532 exercises

Zeevi et al., Cell 2015

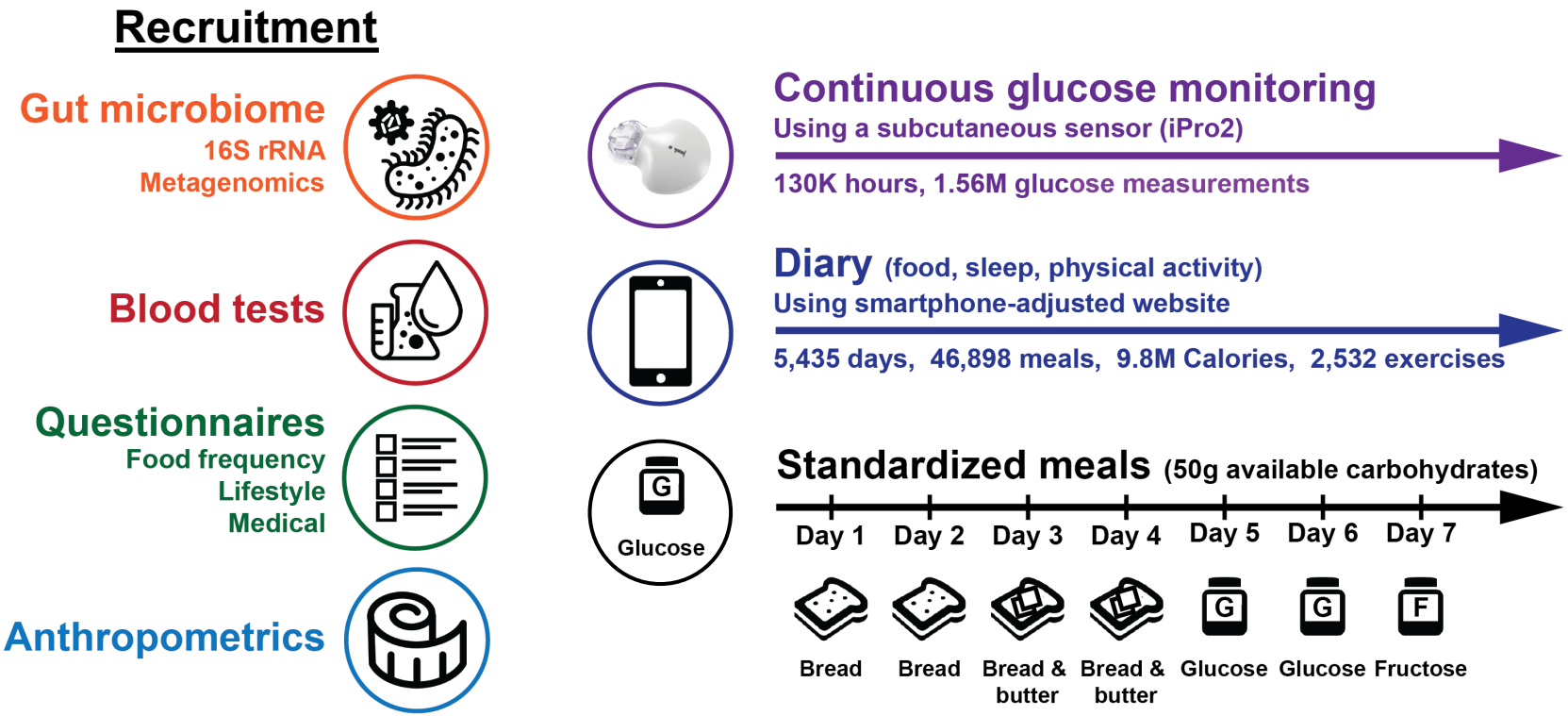
Real-time food logging



Benefits of real-time logging

- Consumption matched in real-time to actual products, brands, etc.
- Serving sizes considered in real-time
- ”Live” database
- Real-time compliance monitoring
- Generally improved compliance

Collection of glycemic, nutritional, clinical and microbiome data on a large healthy cohort

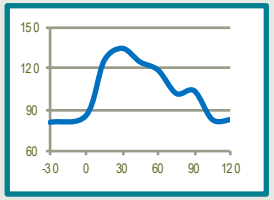


Zeevi et al., Cell 2015

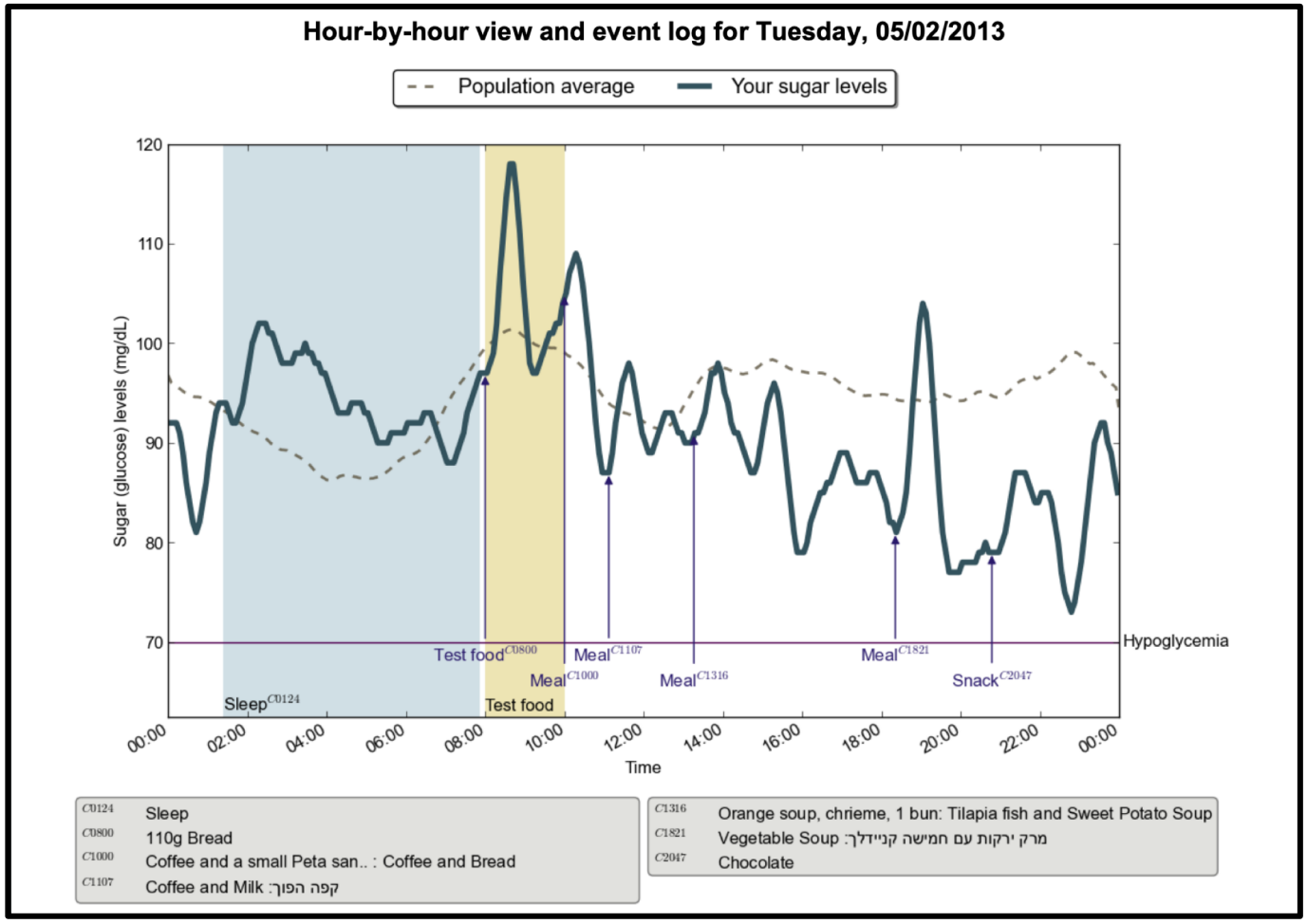
Why would anyone go through this?

What will I learn?

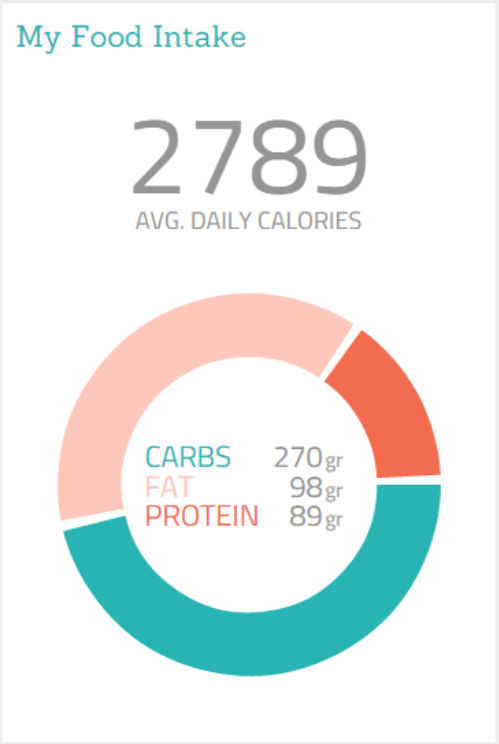
- My response to food
- Know my microbiome
- In the future: Plan a better diet

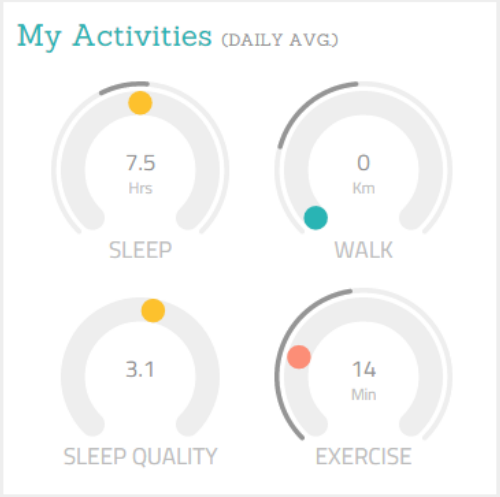


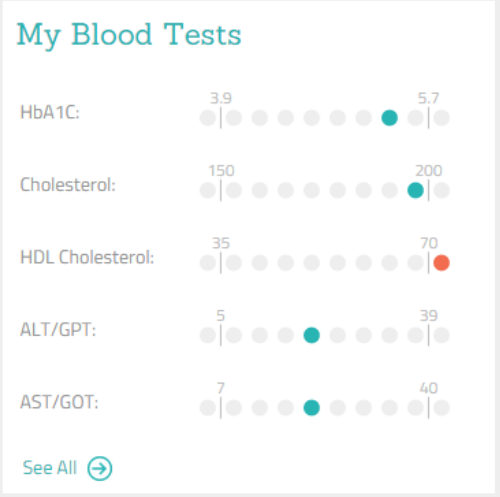
Full accessibility to collected data



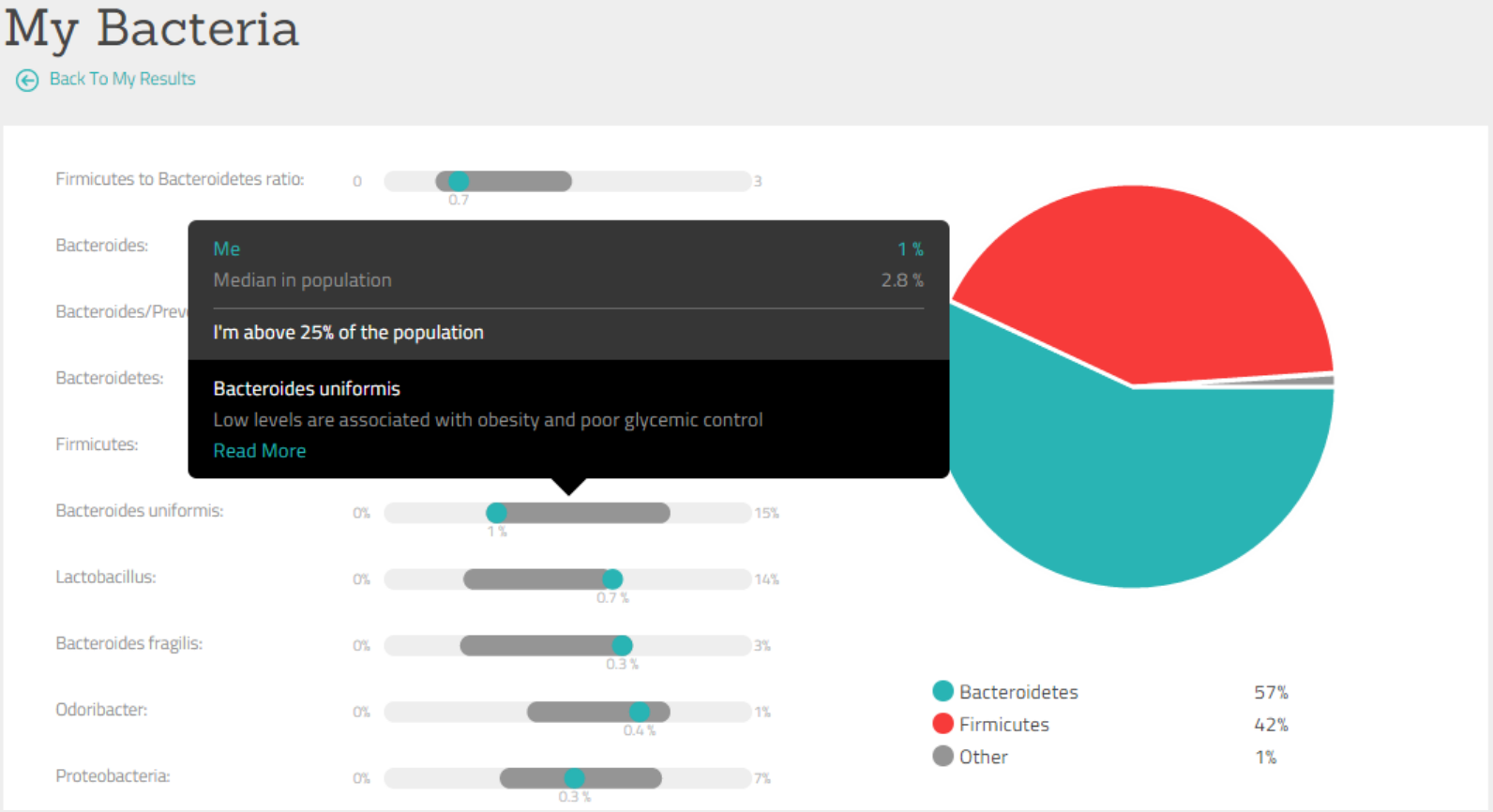
Participant analysis: nutrition, activity & blood tests



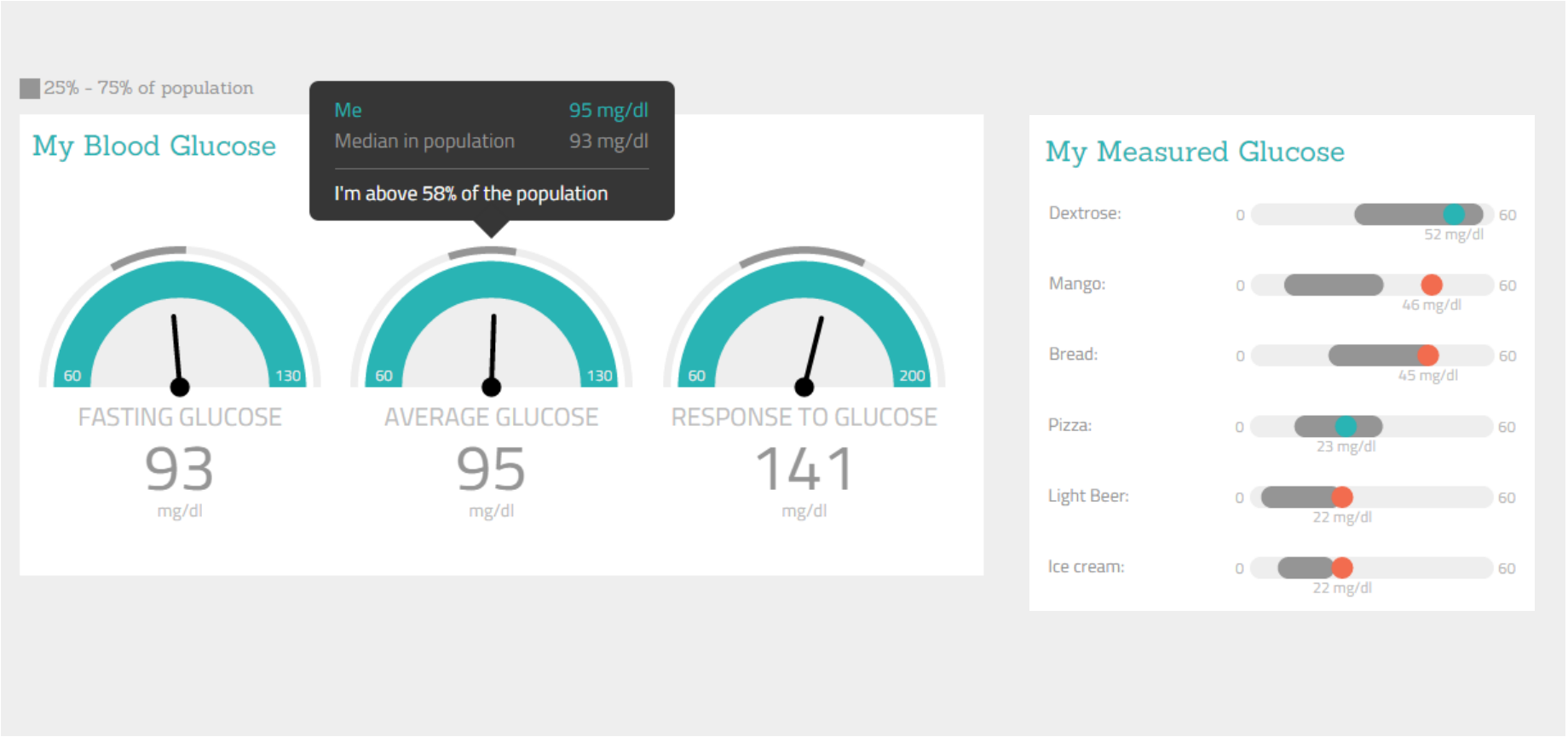




Participant analysis: Overview of microbiota composition



Participant analysis: Glucose spiking foods



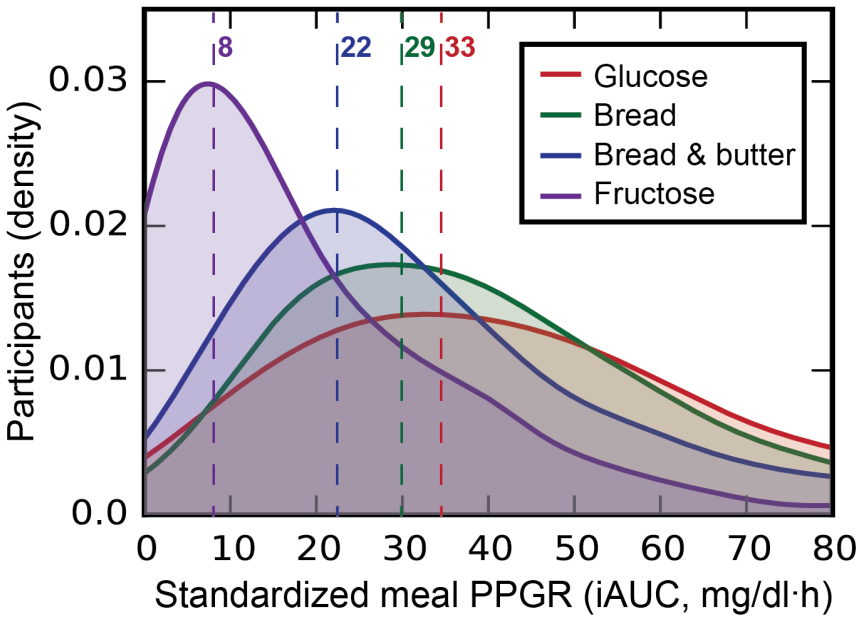
Participants engagement and retention

- Better data
- Easier trial management
- Minimal recruitment effort
  - Finished recruitment of 900 individuals with a wait-list of 3,000

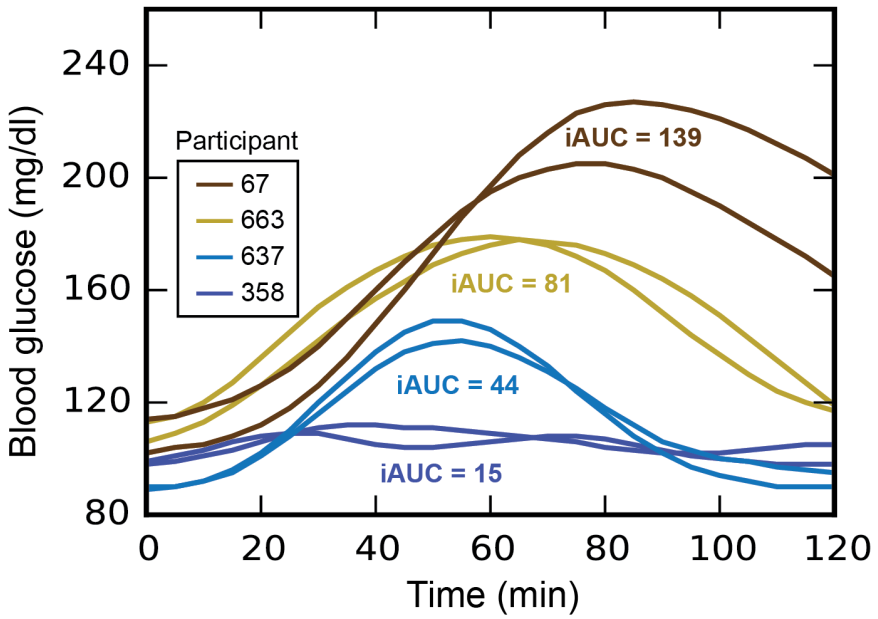
What is the variability across people in the response to the same food?

Different people have widely different post-meal responses to the same standardized meal

Population Responses to Standardized Meals



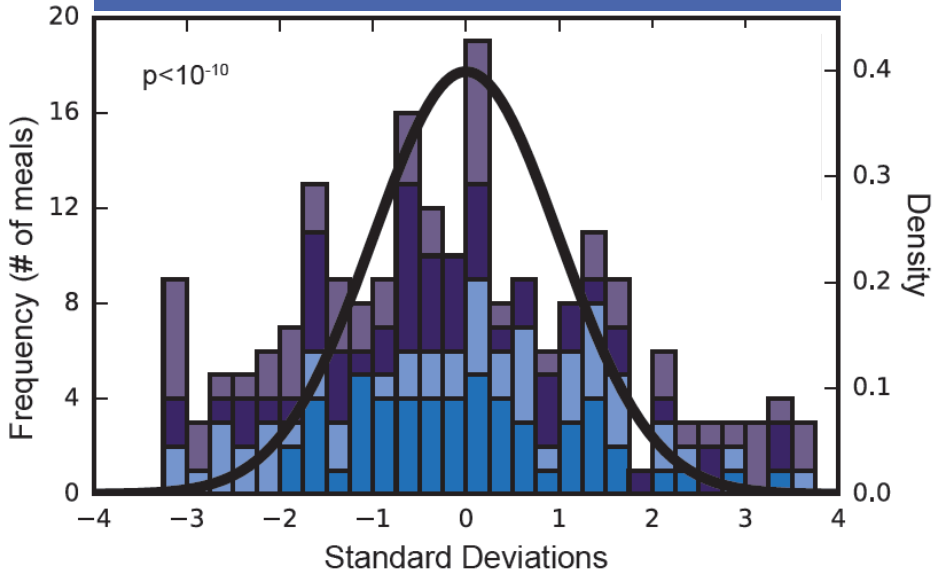
Four Individual Responses to Bread



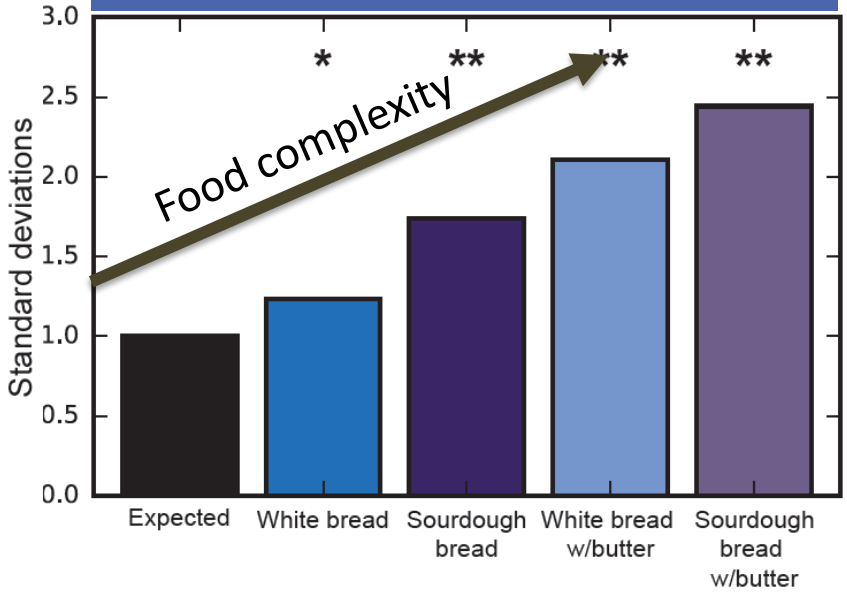
Zeevi et al., Cell 2015

Significant personalized response which increases with food complexity

Null hypothesis rejected: significant interpersonal variability



Variability increases with food complexity



Standard normal

Measured GI

* $p < 0.05$

** $p < 10^{-3}$

Korem et al., Cell Metab. *2017*

Results replicated and validated by subsequent studies

JAMA Network | Open™

Original Investigation | Diabetes and Endocrinology

Assessment of a Personalized Approach to Predicting Postprandial Glycemic Responses to Food Among Individuals Without Diabetes

Helena Mendes-Soares, PhD; Tali Raveh-Sadka, PhD; Shahar Azulay, BSc; Kim Edens, MSc; Yatir Ben-Shlomo, BSc; Yossi Cohen, MSc; Tal Ofek, PhD; Davidi Bachrach, BSc, MBA; Josh Stevens, BSc; Dorin Colibaseanu, MD; Lihi Segal, LLB, MBA; Purna Kashyap, MBBS; Heidi Nelson, MD

See corresponding editorial on page 955.

Estimating the reliability of glycemic index values and potential sources of methodological and biological variability[1–3]

Nirupa R Matthan,[4] Lynne M Ausman,[4] Huicui Meng,[4] Hocine Tighiouart,[5] and Alice H Lichtenstein[4]*

[4]Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA; and [5]Tufts Clinical and Translational Science Institute, Tufts Medical Center, Boston, MA

General recommendations in nutrition are suboptimal

1943

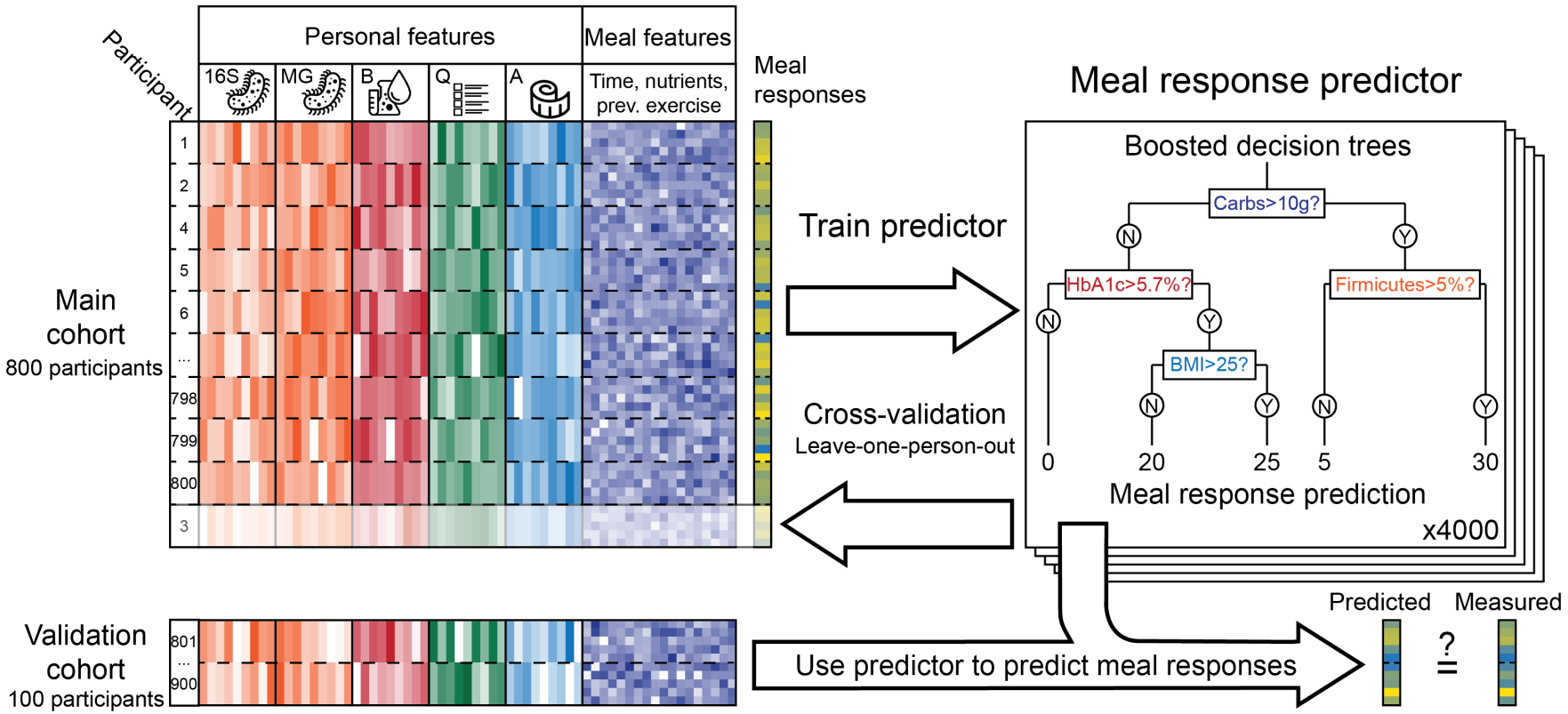
1992

2015

Source: USDA

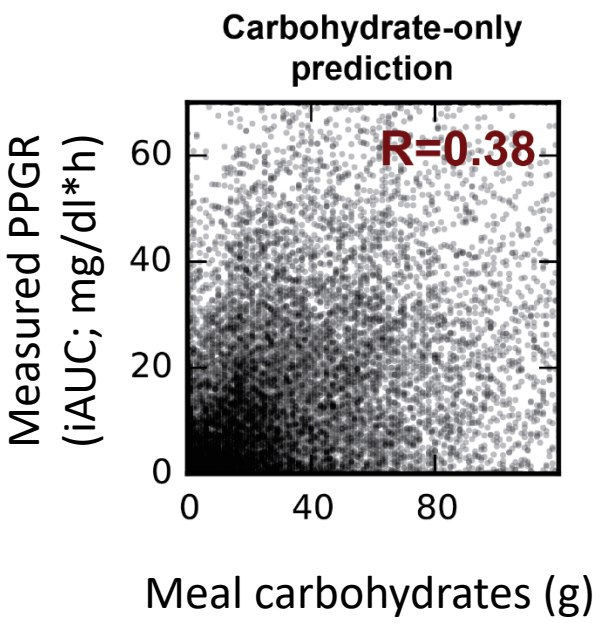
Can we predict the personal post-prandial glucose response to any complex meal?

Prediction scheme

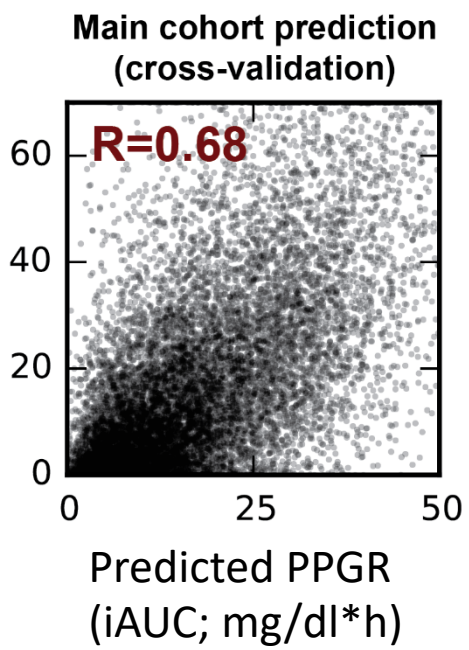


Accurate predictions of personalized glucose responses

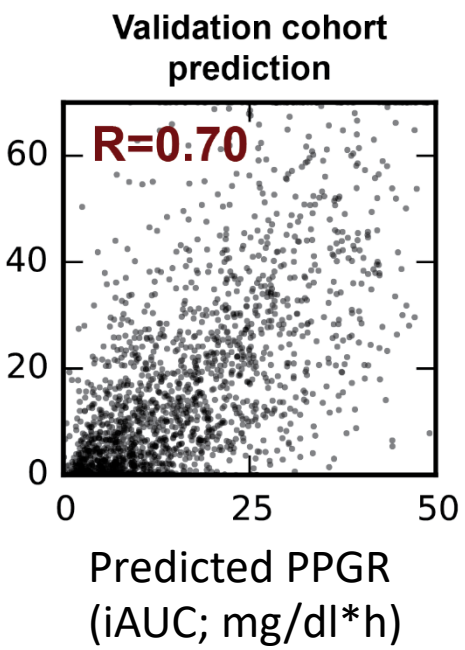
State of the art



Our prediction
800 participants

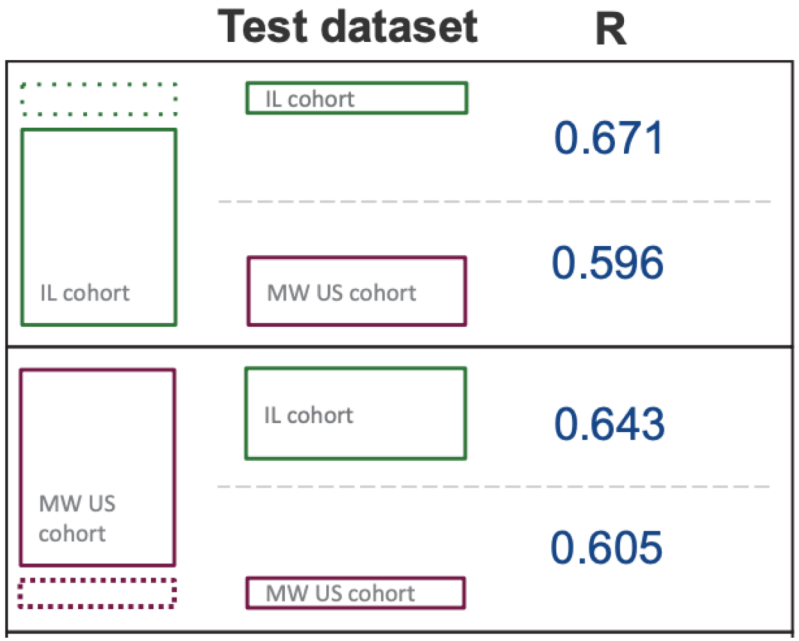


Prediction validation
100 participants



Zeevi et al., Cell 2015

Replication and validation by subsequent studies

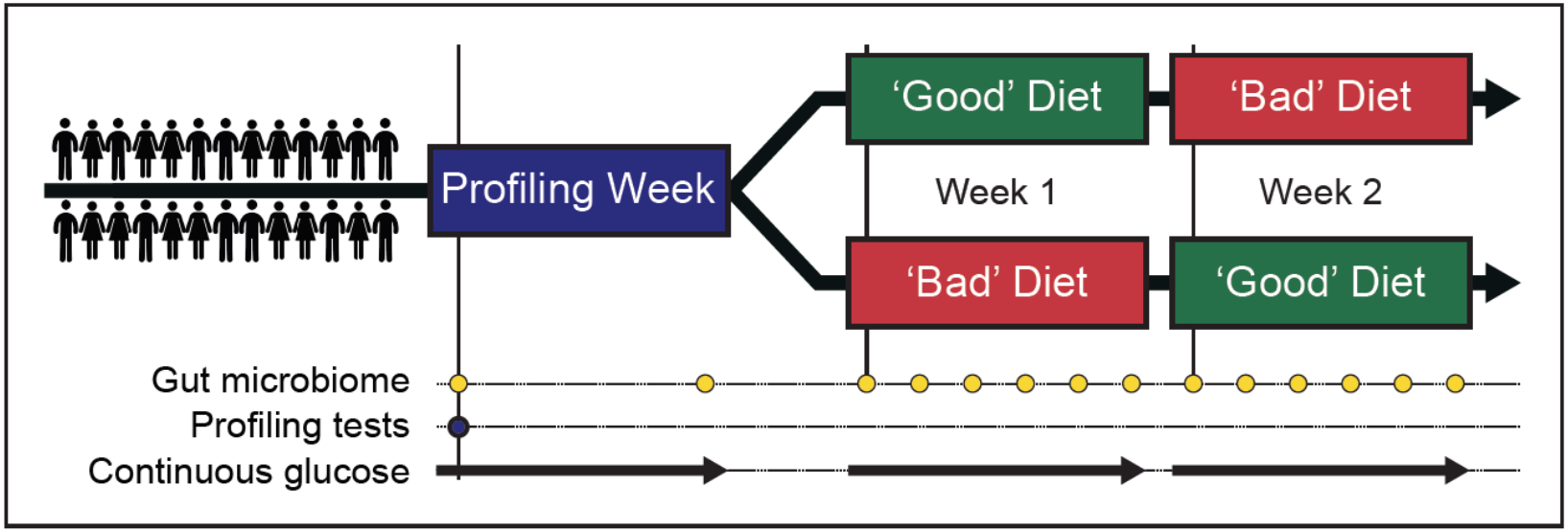


Mendes-Soares et al., JAMA Netw. Open. 2019, AJCN 2019

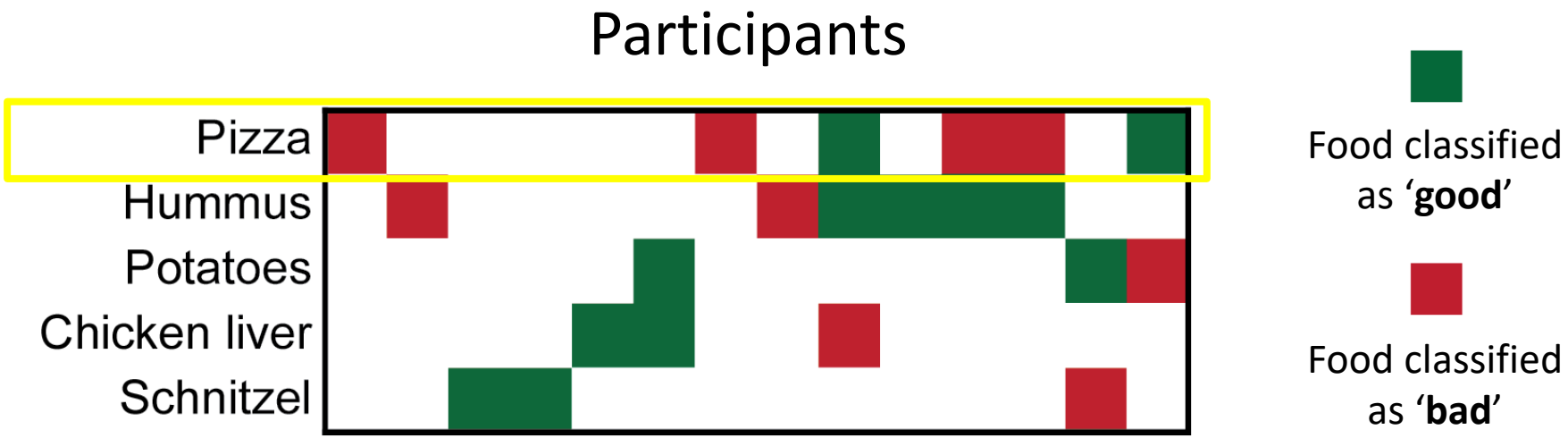
Can glucose response predictions improve post-prandial glucose responses?

Constructing personally tailored diets that achieve normal post-prandial glucose responses

- 12 subjects, mostly prediabetics
- Profiled for one week
- Self-selected isocaloric meals, categorized as good / bad
- Good and bad diets assigned double-blindedly, one week each

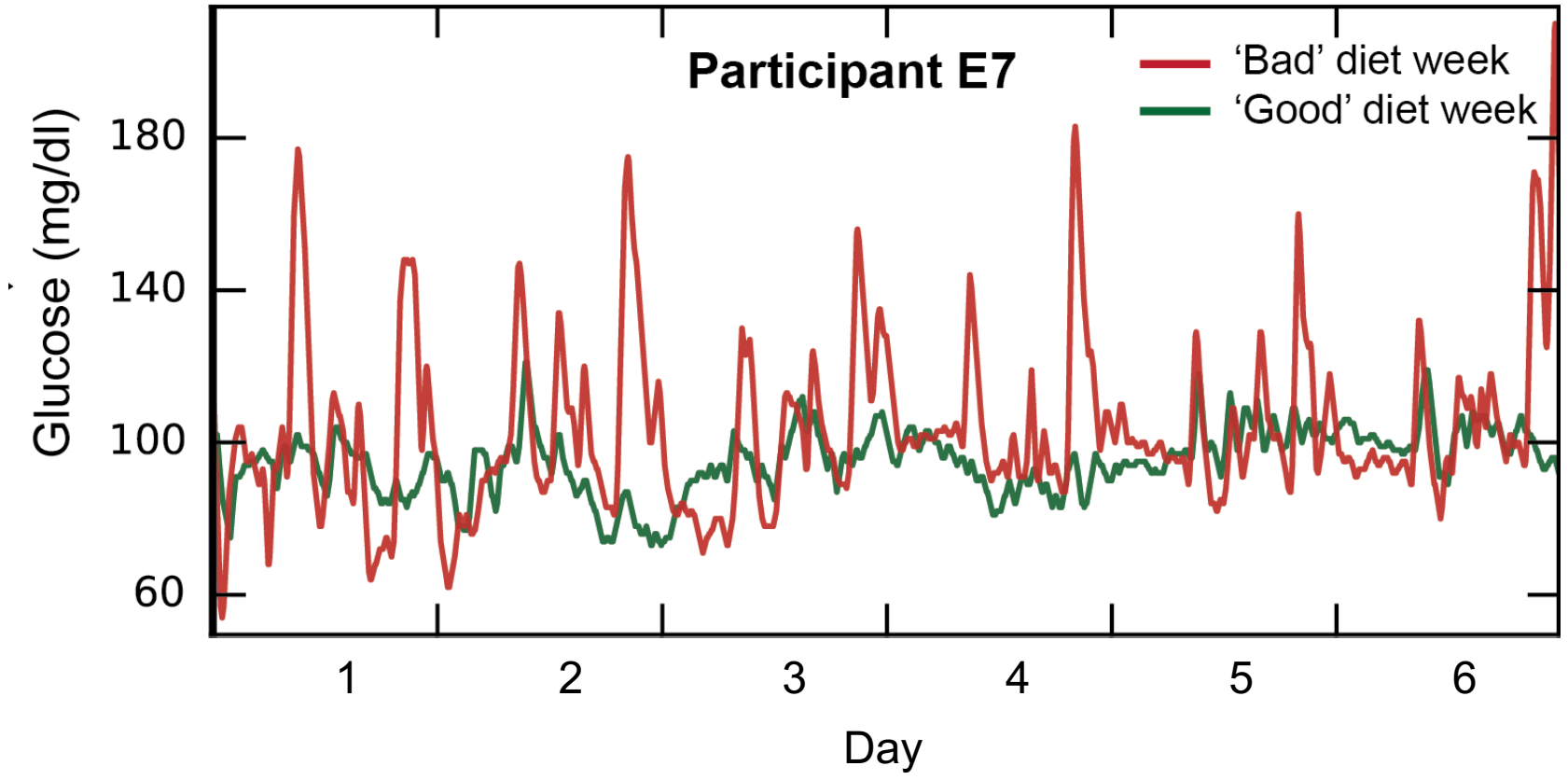


A ‘good’ meal for one person can be a ‘bad’ meal for another



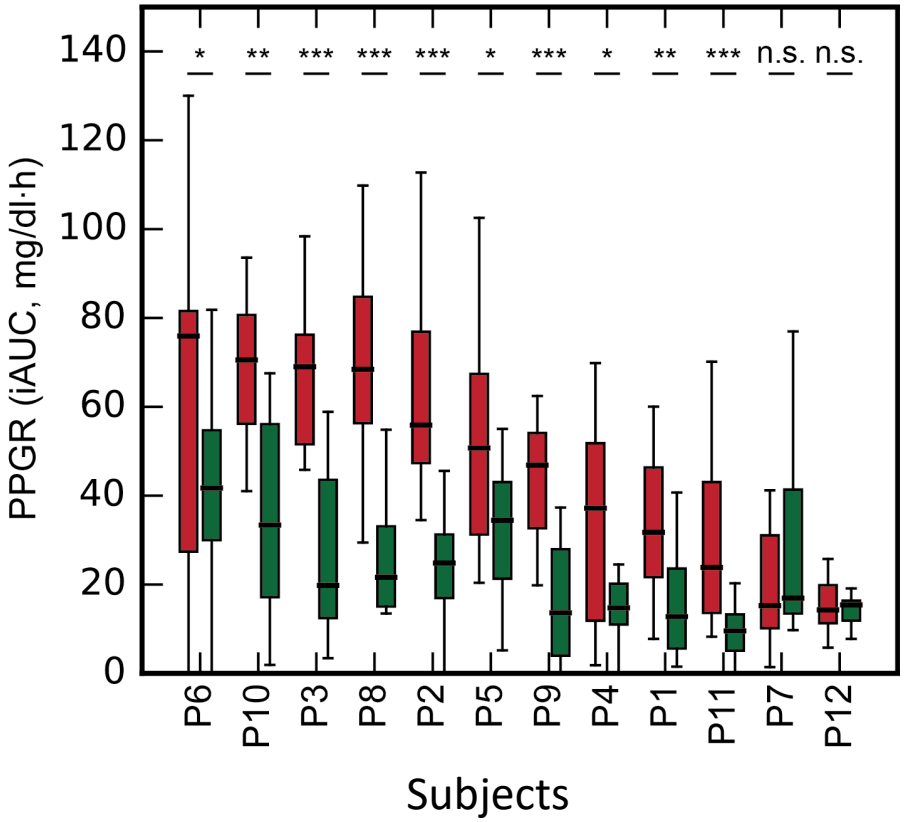
Zeevi et al., Cell 2015

Personally tailored diets reduce the post-prandial glucose response



Zeevi et al., Cell 2015

Personally tailored diets improve post-meal responses



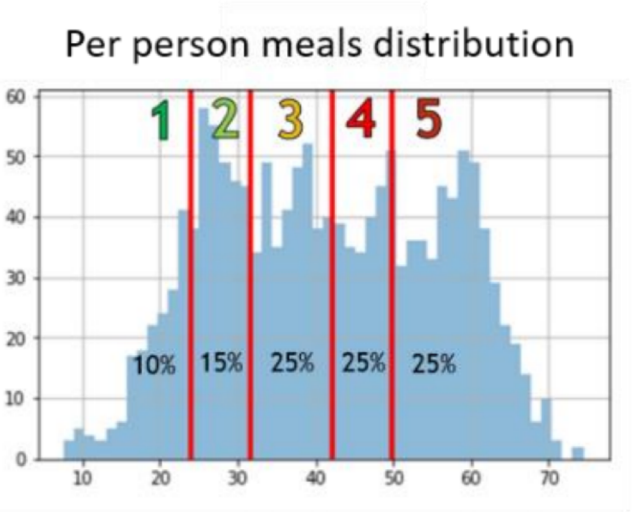
Zeevi et al., Cell 2015

Is this useful for long-term interventions?

Challenges with translation to interventions

- Scores a meal rather than provide insights
  - Really not what people expect
  - Not straight forward to devise interventions
  - Accounting for preferences is challenging
  - Maintaining caloric target is external to prediction framework
- Strong assumptions on causality
  - Probably easier to make than for “long-term” outcomes
- Requires extensive variables
  - Real potential of using the gut microbiome

Long term, algorithm based intervention



~2000 meals

Compute Caloric Target (per person)

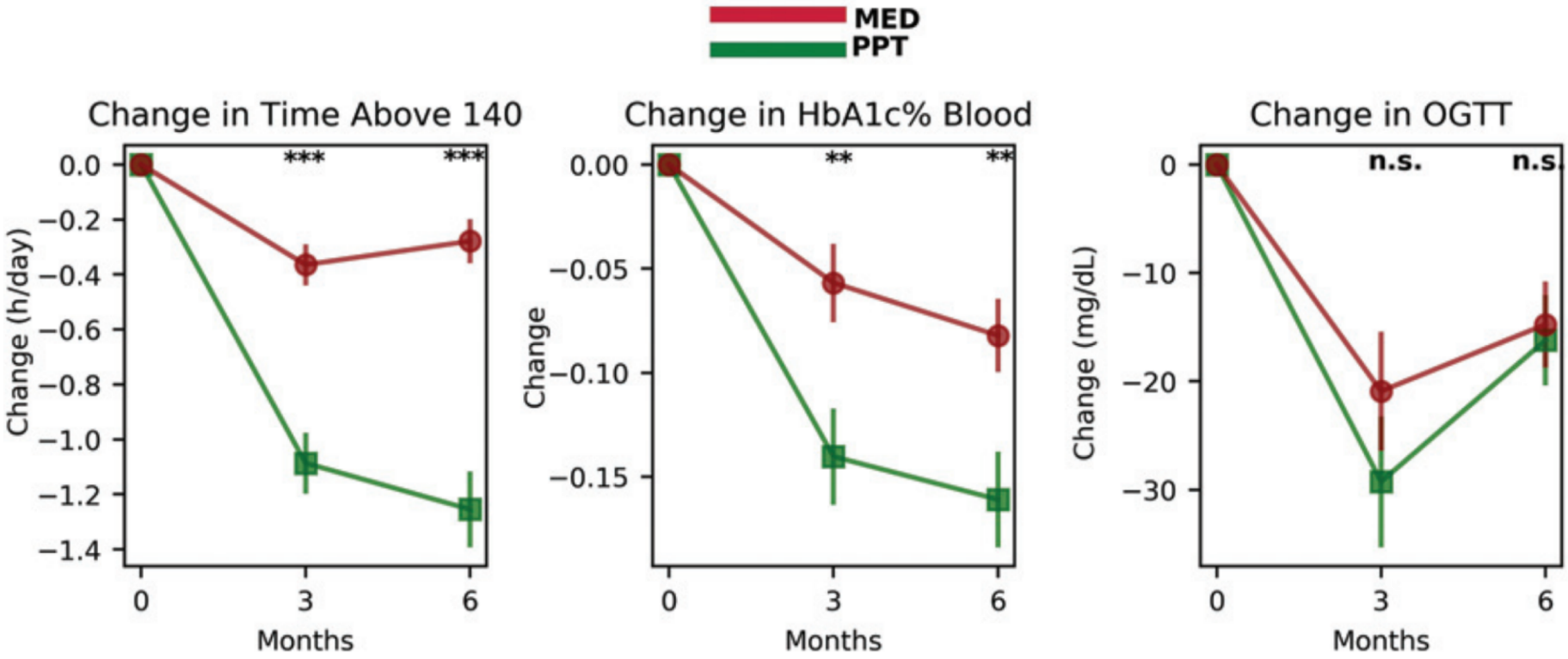
Score meals

Select meals to menu

+ Real-time app-based feedback

Ben-Yacov et al., Diabetes Care 2021

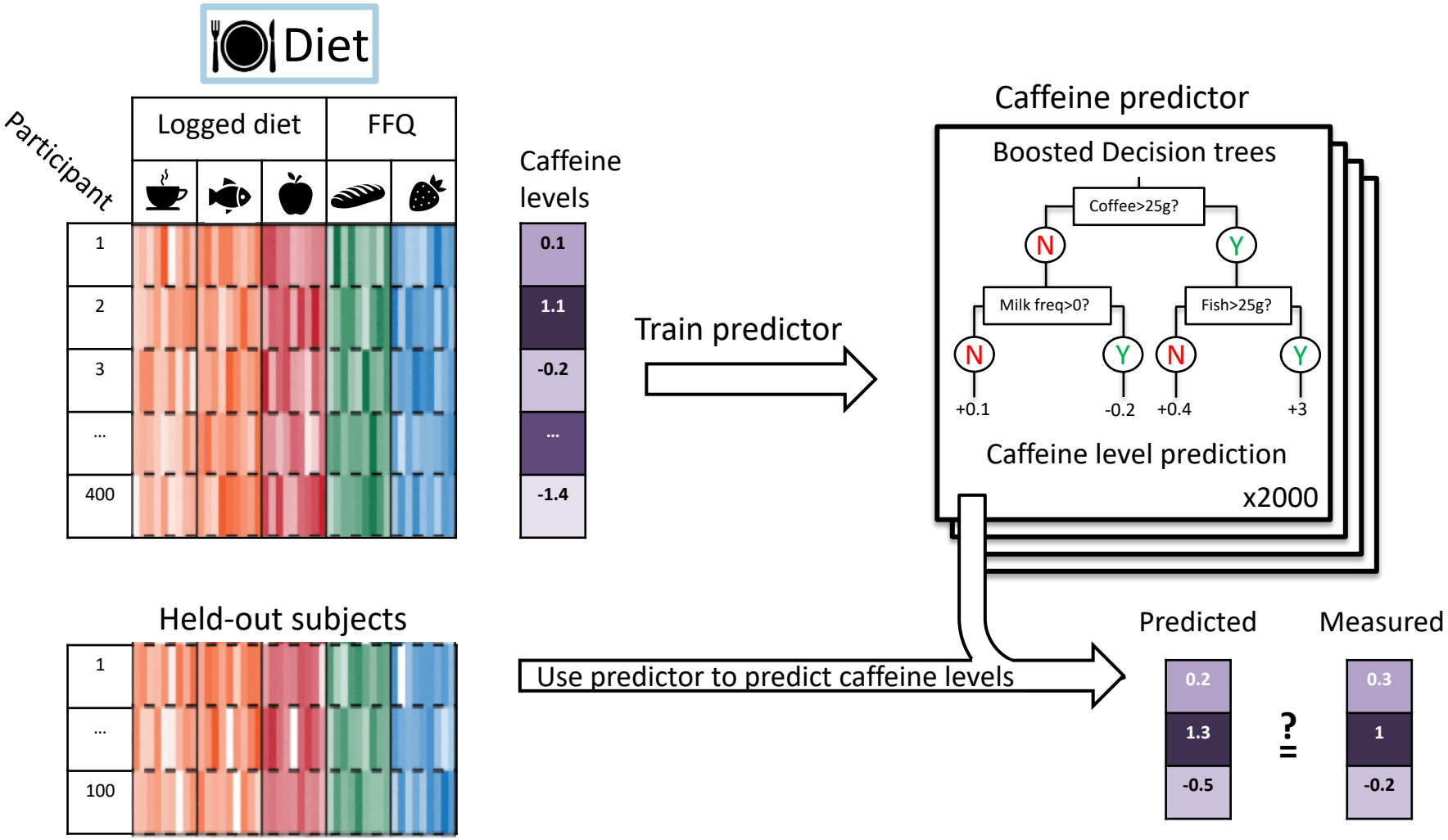
Long term ”algorithm-diet” achieves greater glycemic normalization



Ben-Yacov et al., Diabetes Care 2021

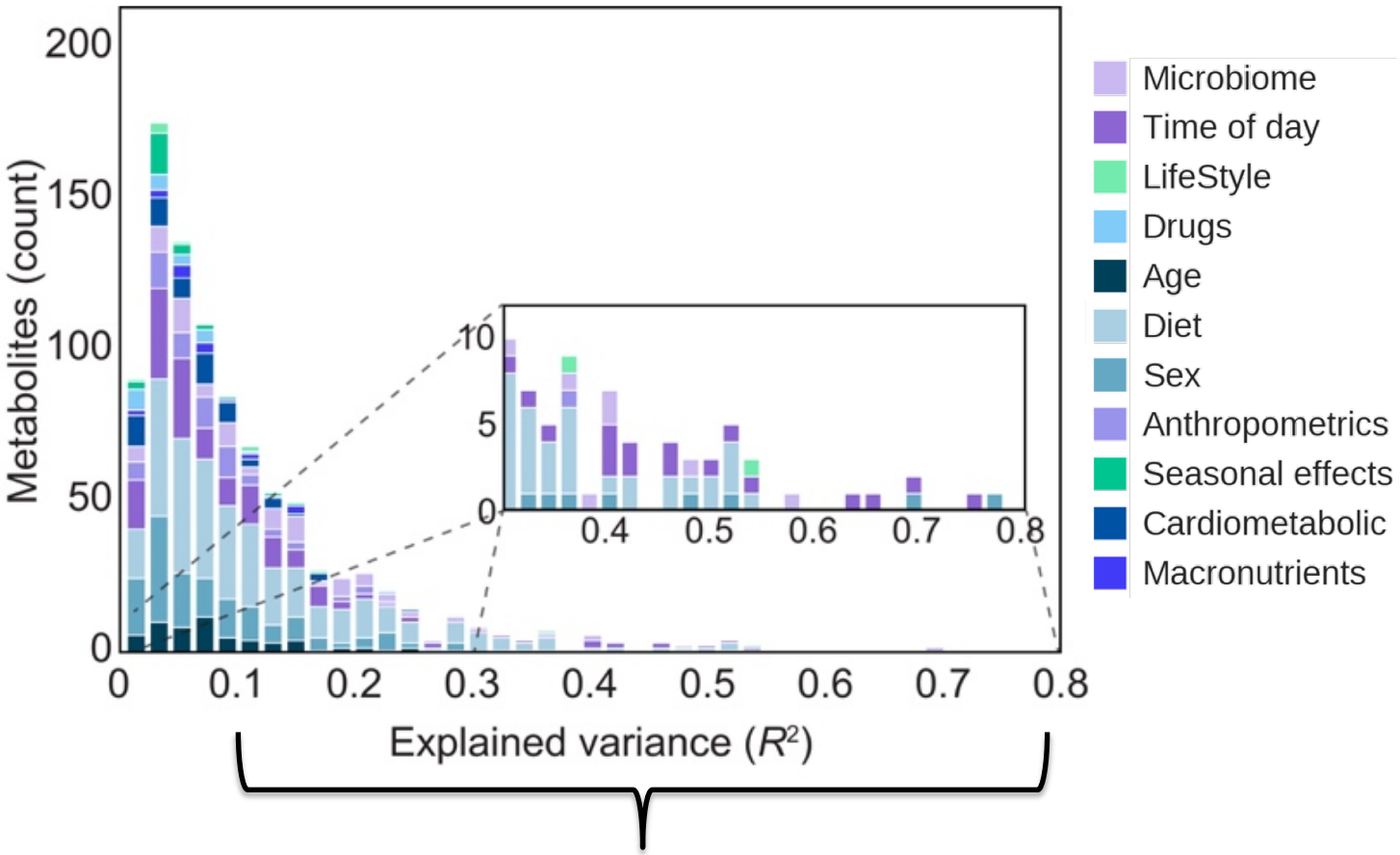
Rich data-sets facilitates multiple data-driven investigations

Predicting caffeine levels from diet data



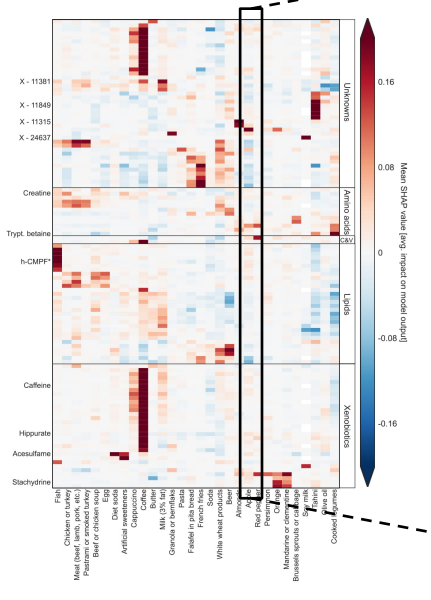
Bar *et al.*, Nature 2020

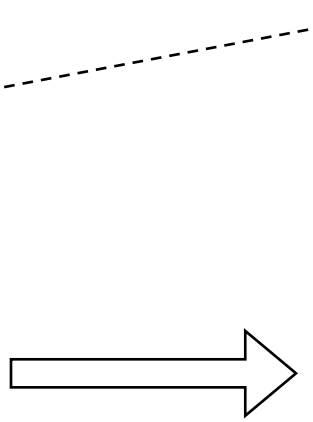
Our predictive models explain over 10% of the variance for 543 metabolites



Bar *et al*., Nature 2020

Metabolites associated with sourdough consumption increase after sourdough (but not white bread) intervention



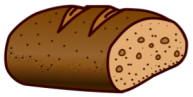


Top 5% negatively driven metabolites

betaine

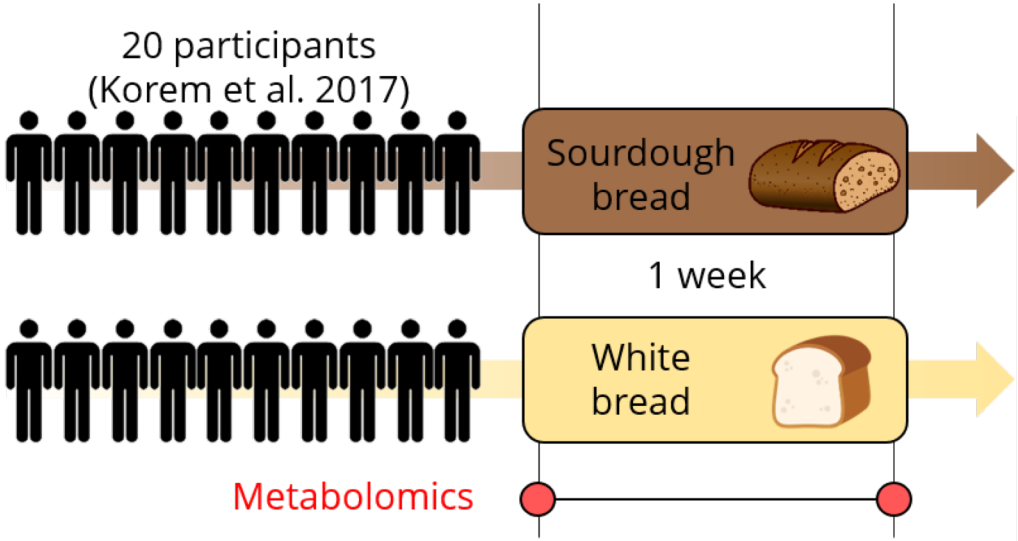
cytosine

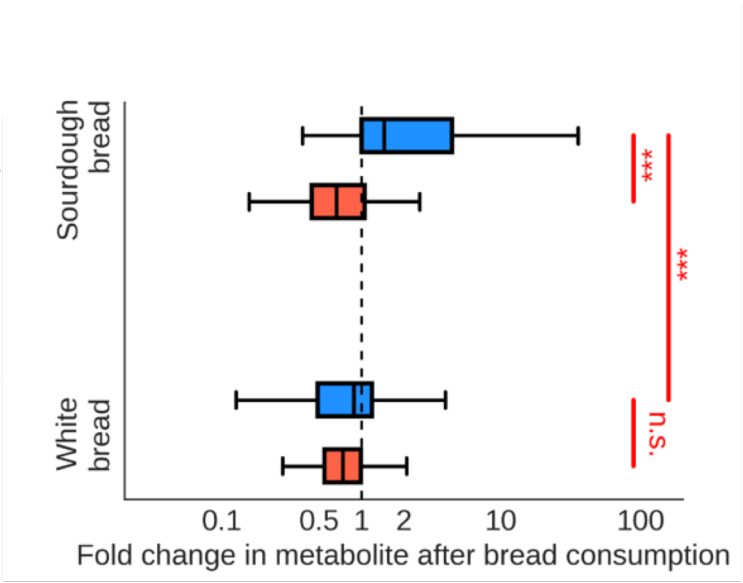
Top 5% positively driven metabolites



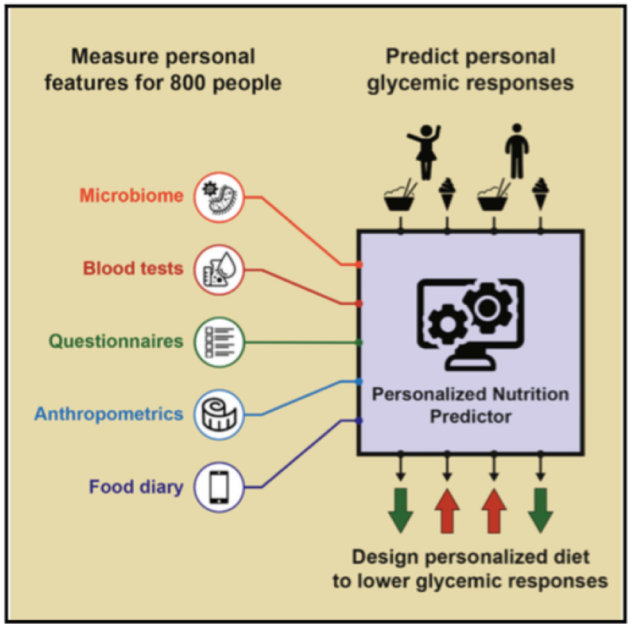
Whole-wheat bread

Metabolites associated with sourdough consumption increase after sourdough (but not white bread) intervention



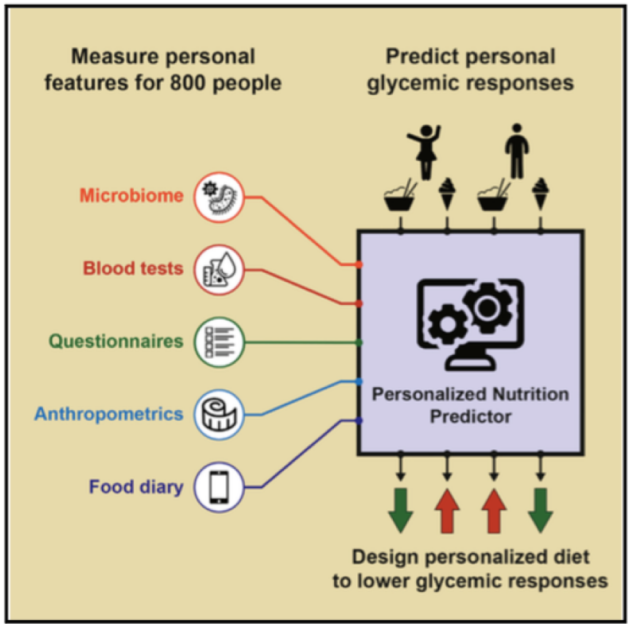


Summary



- **High interpersonal variability** in post-meal glucose response to identical meals
- Personal and microbiome features enables **accurate glucose response prediction**
- Personalized dietary interventions **successfully lower post-meal glucose**

Summary



- Importance of **real-time logging**
- Benefits of **participant engagement** and **data-sharing**
- The **challenges** of using this approach for **long-term dietary interventions**

Acknowledgements

Prof. Eran Segal

Noam Bar
Adina Weinberger
Omer Weissbrod
Noam Bar
Orly Ben-Yacov
Dar Lador
Tali Avnit-Sagi
Maya Lotan-Pompan
Elad Matot
Daphna Rothschild
Gal Malka
Noa Kosower
Michal Rein
Rony Bikovsky
Sigal Leviatan

Dr. David Zeevi

Prof. Eran Elinav

Niv Zmora
Jotham Suez
Jemal Ali Mahdi
Gili Zilberman
Lenka Dohnalova
Meirav Pevsner-Fischer

Prof. Avraham Levy
Ben Z. Goldberg

Dr. David Israeli
Kfar Shaul Medical Center

Prof. Zamir Halpern
Tel-Aviv Sourasky Medical Center

IMI DIRECT consortium
Dr. Tim D. Spector