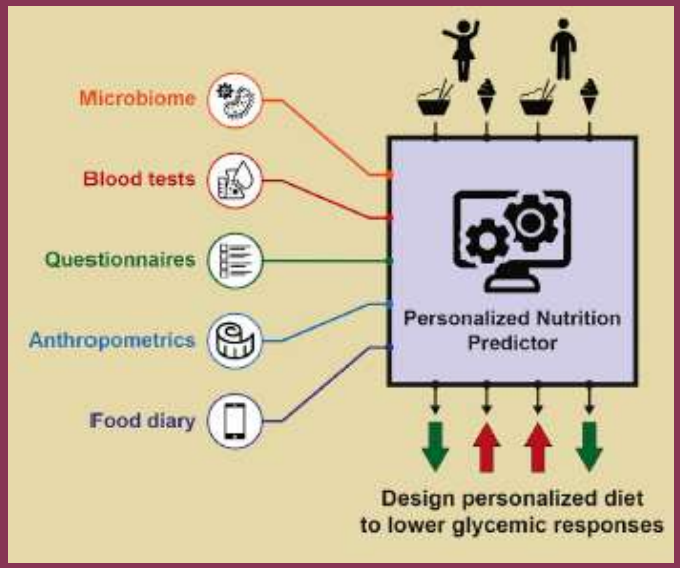
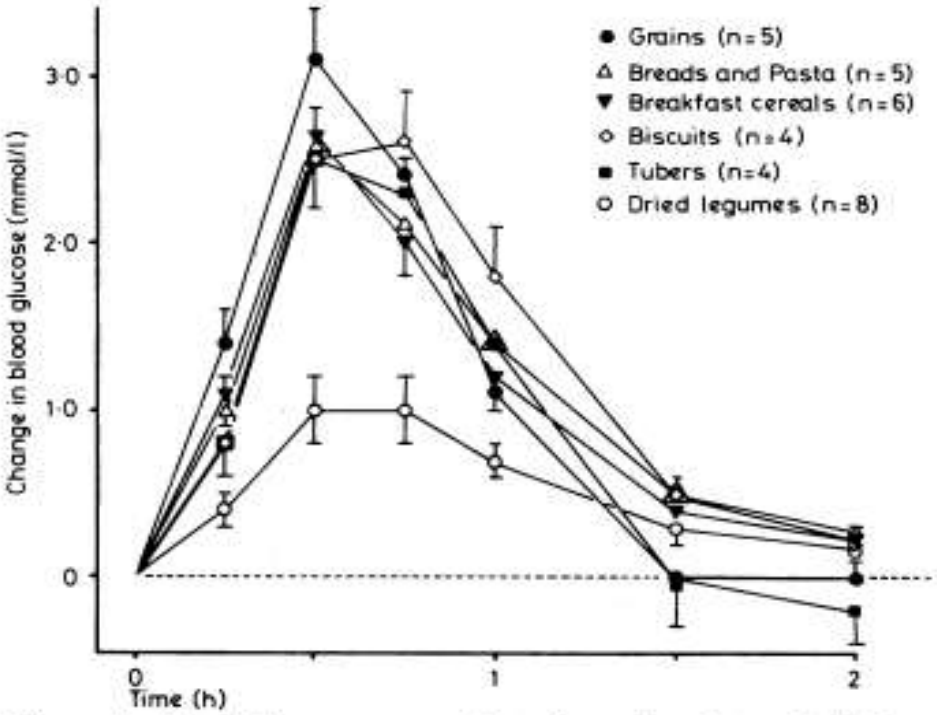
Siri, what should I eat?



Zeevi et al. Personalized Nutrition by Prediction of Glycemic Responses. Cell 2015;163(5):1079-94.

Vanessa Ha

What is Postprandial Glycemic Response?



Change in blood glucose concentration after eating 50-g carbohydrate portions of individual grains, breads and pasta, breakfast cereals, biscuits, tubers, and dried legumes.

Conversion: SI to traditional units— Glucose: 1 mmol/l ≈ 18 mg/100 ml.

Jenkins et al. BMJ 1980; 281(6240): 578–580.

PPGR and Survival

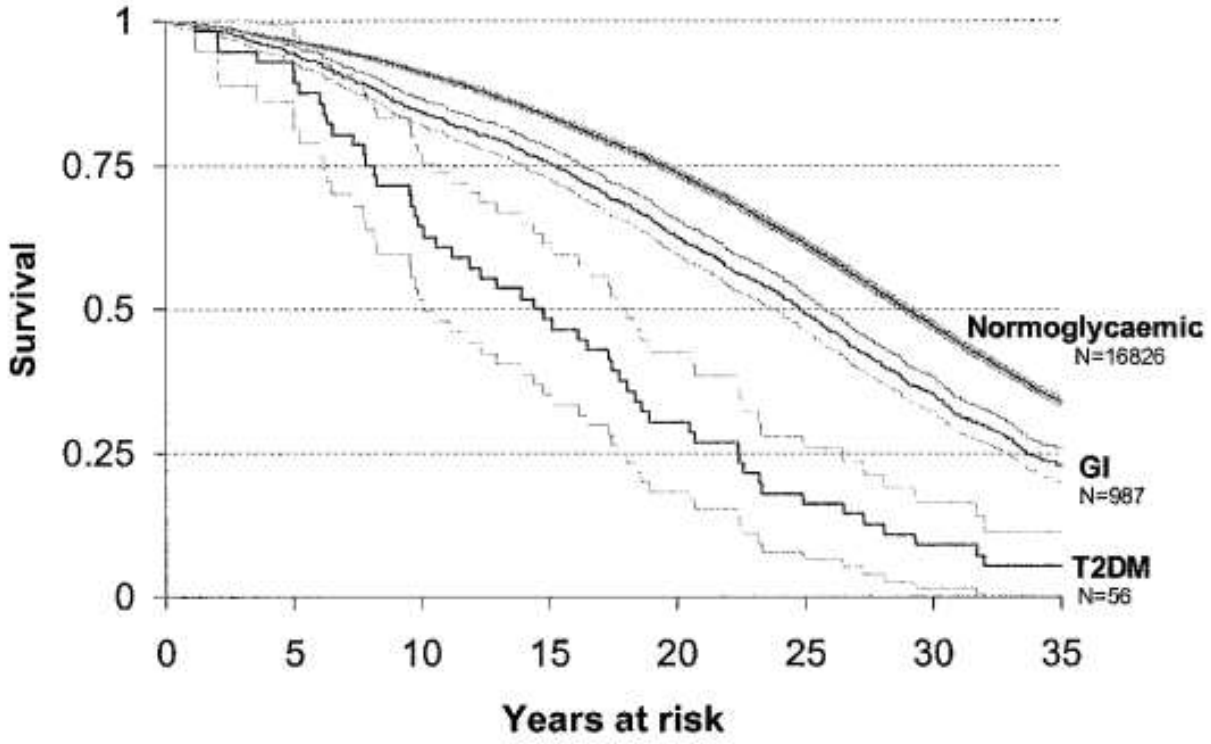


Figure 1—*Survival by baseline glucose tolerance status. Age-adjusted survival and 95% CI. Glucose intolerance (GI), 5.3 ≤ 2-h glucose < 11.1 mmol/l. Newly diagnosed diabetes (T2DM), 2-h glucose ≥ 11.1 mmol/l.*

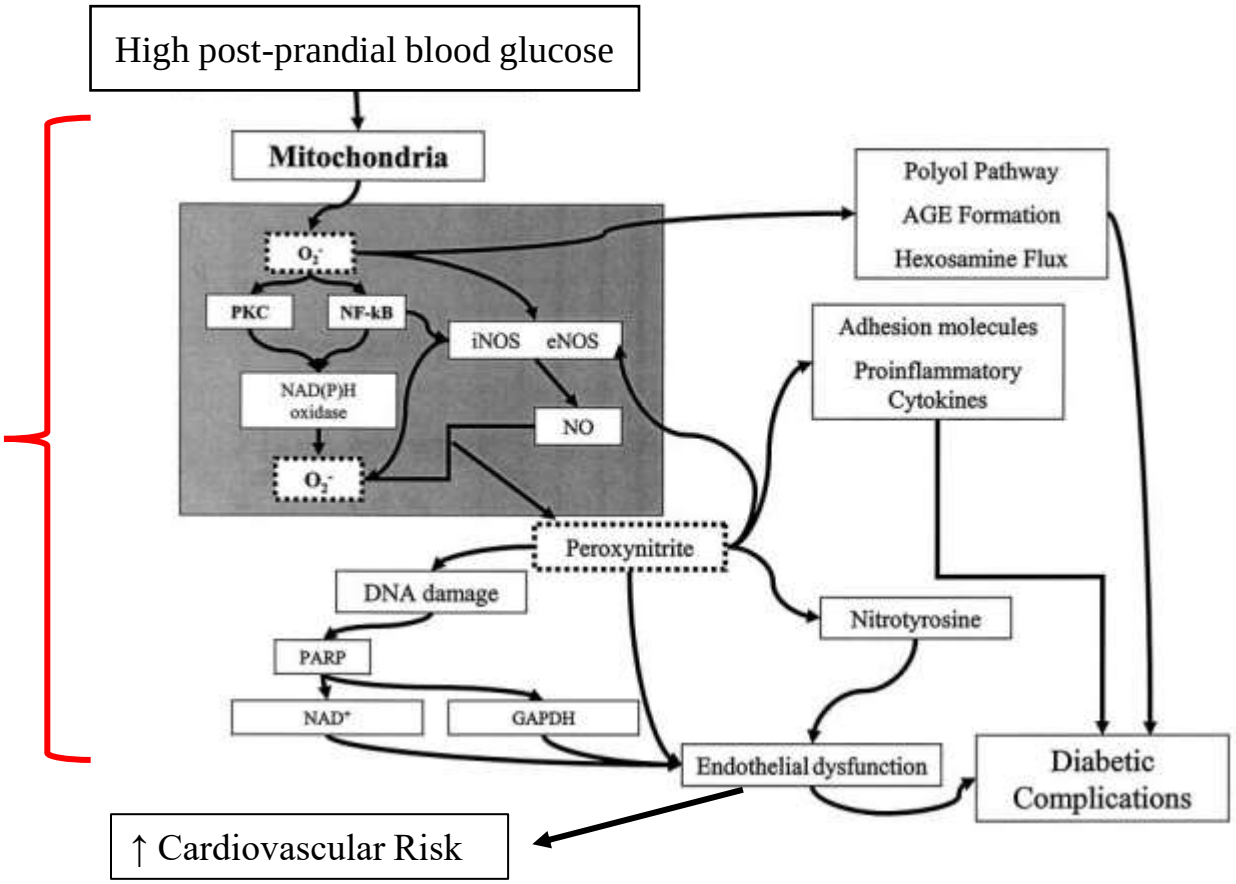
Brunner et al. Diabetes Care 2006. 29: 26 –31.

PPGR and Oxidative Stress

High PPGR

Oxidative Stress

↑ Disease Risk



Ceriello. Diabetes 2005. 54:1–7.

Diet and PPGR

- Carbohydrate Quantity -> Carbohydrate Loading
- Carbohydrate Quality -> Glycemic Index/Glycemic Load

Study Purpose

To develop an algorithm that can predict individual postprandial glycemic responses

In the Media

SEARCH

The New York Times

FOOD

A Personalized Diet, Better Suited to You

By KATE MURPHY JANUARY 11, 2016 3:59 PM 74 Comments

The Atlantic

The Algorithm That Creates Diets That Work for You

It crunches hundreds of factors to make personalized plans for controlling blood sugar. Some people even get cake and cookies.

YouTube CA

Personalized Nutrition/ Cell November 19, 2015 (Vol. 163, Issue 5)

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日本語要約

Nutrition: A personal forecast

NHS choices Your health, your choices

Health A-Z | Live Well | Care and support

One diet 'doesn't fit all' – people 'metabolise food differently'

Study Objectives

Study 1

1. To conduct an observational study of 800 individuals to characterize the variability of postprandial glycemic response (PPGR)

Study 2

2. To develop an algorithm that integrates blood parameters, dietary habits, anthropometrics, physical activity, and gut microbiota that can be used to predict PPGR

Study 3

3. To conduct a randomized controlled trial that compared a dietary intervention based on the algorithm to lower PPGR to a dietary intervention that predicted high PPGR on PPGR and alterations to gut microbiome

Study 1

Characterization of postprandial glycemic response

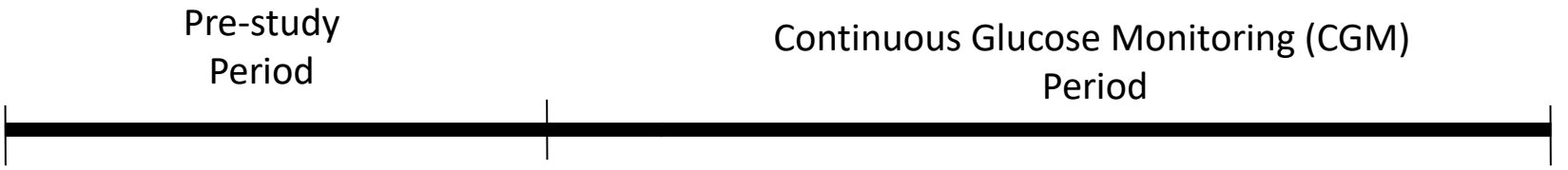
Methods

Eligibility Criteria

- individuals aged 18–70
- not diagnosed with T2DM

Study Design

- Participants were blinded to the results of CGM



- FFQ
- lifestyle and medical questionnaires
- anthropometric measures
- blood tests
- single stool sample

- Given standardized breakfast every day
- Recorded using smartphone website:
  - food intake
  - exercise
  - sleep

Results- Characteristics of Participants

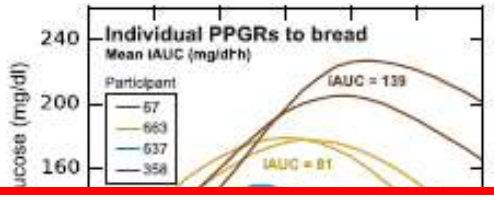
Number of participants (n)	800
Sex (% female)	60%
Age (y) Mean ± SD	43.3 ± 13.1
BMI (kg/m^2) Mean ± SD	26.4 ± 5.1
BMI ≥ 25	428 (54%)
BMI ≥ 30	173 (22%)
HbA1c% Mean ± SD	5.43 ± 0.45
HbA1c% ≥ 5.7	189 (24%)
HbA1c% ≥ 6.5	23 (3%)
Total cholesterol (non-fasting, mg/dl) Mean ± SD	186.8 ± 37.5
HDL cholesterol (non-fasting, mg/dl) Mean ± SD	59.0 ± 17.8
Waist-to-hip circumference ratio Mean ± SD	0.83 ± 0.12

Representative of the adult non-diabetic Israeli population as well as Western adult non-diabetic population

Results- Postprandial Glycemic Response

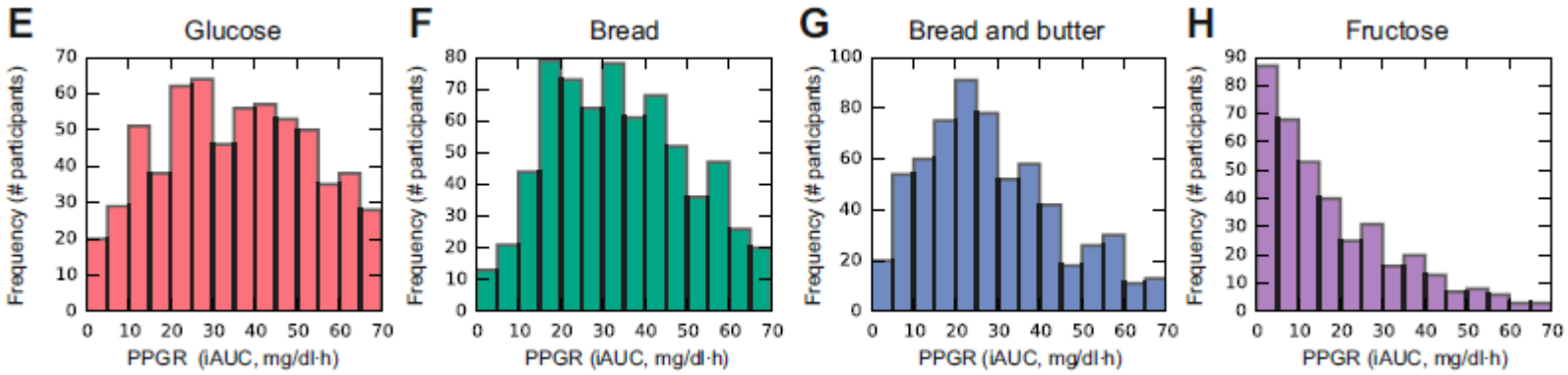
Intra-variability

R = 0.77 for glucose
R = 0.77 for bread with butter
R = 0.71 for bread, $p < 10^{-10}$



-variability to the identical food is small in the same person
-variability to the identical food is big in different people

Inter-v

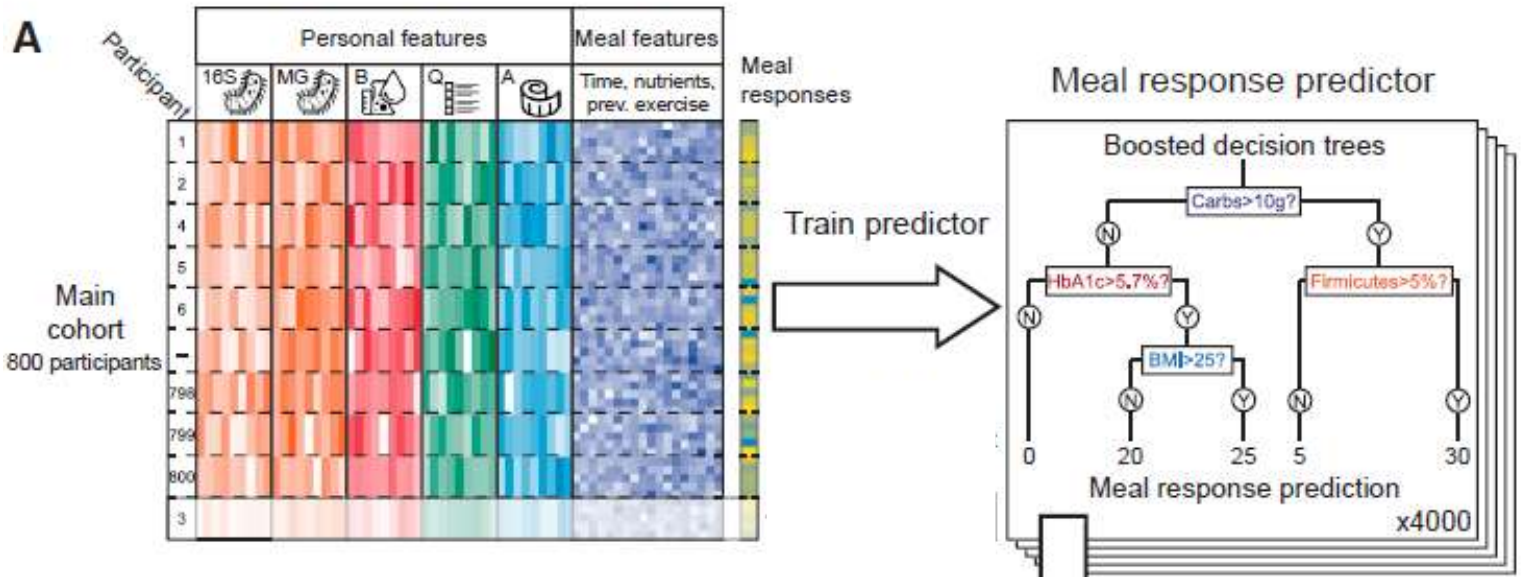


Study 2

Development of the Algorithm

Methods

Algorithm Development- Decision Tree



Methods

Algorithm Development- Predictors

1. **Meal features**- alcohol (g), caffeine (mg), carbohydrate (g), dietary fibers (g), energy (Cal.), fat (g), protein (g), sodium (mg), sugars (g), water (g), carbohydrates-to-fat ratio
2. **Lifestyle features**- time to next and last exercise and sleep; amount of water consumed one hour before and in the two hours following the meal; total amount of carbohydrates consumed in the 3, 6 and 12 hours prior to the meal; total amount of calories consumed in the 2, 3, 6, and 12 hours prior to the meal; total amount of fibers consumed 12 and 24 hours prior to the meal; and the hour of the day in which the meal was consumed
3. **CGM-derived features**- iAUC and glucose trend of 1, 2, and 4 hours prior to the meal
4. **Clinical features-** blood test results
5. **Personal features** - age, sex, smoking habits, and self reported hunger, physical activity, stress levels and defecation routine
6. **Microbiome features** - relative abundances of 16S rRNA based phyla existing in more than 20% of the cross-validation training cohort; relative abundance of the 30 KEGG modules, 20 metagenome-based species relative abundances selected similarly to the KEGG modules; 10 PTRs; Percentage of reads mapped to host genome, gene-set database, and database of full genomes

Methods

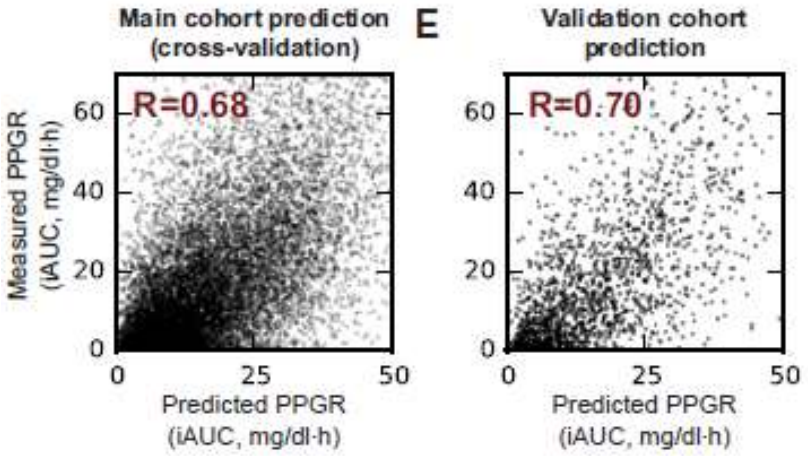
Algorithm Validation

- Internal Validation
  - standard leave-one-out cross validation scheme
    - Whereby PPGRs of each participant were predicted using a model trained on the data of all other participants

- External Validation
  - Recruited independent cohort of 100 participants and their PPGRs were predicted using the model trained only on the main cohort

Results

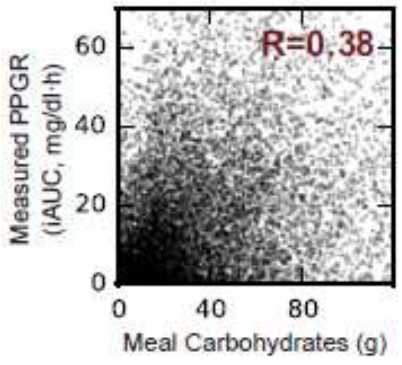
Study's Algorithm



R= 0.68
p-value< 10^{-10}

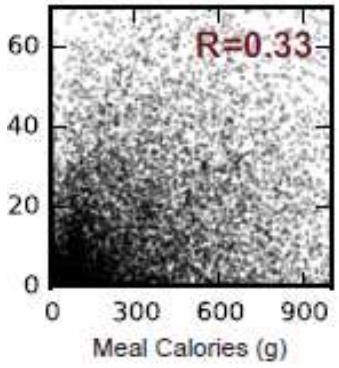
R= 0.70
p-value< 10^{-10}

Carbohydrate Counting



R= 0.38
p-value< 10^{-10}

Calories



R= 0.33
P-value< 10^{-10}

Study 3
Dietary Intervention

Objective

Objective

- ❑ whether personally tailored dietary interventions based on the algorithm could improve PPGR and cause changes to the gut microbiome over 1-week period

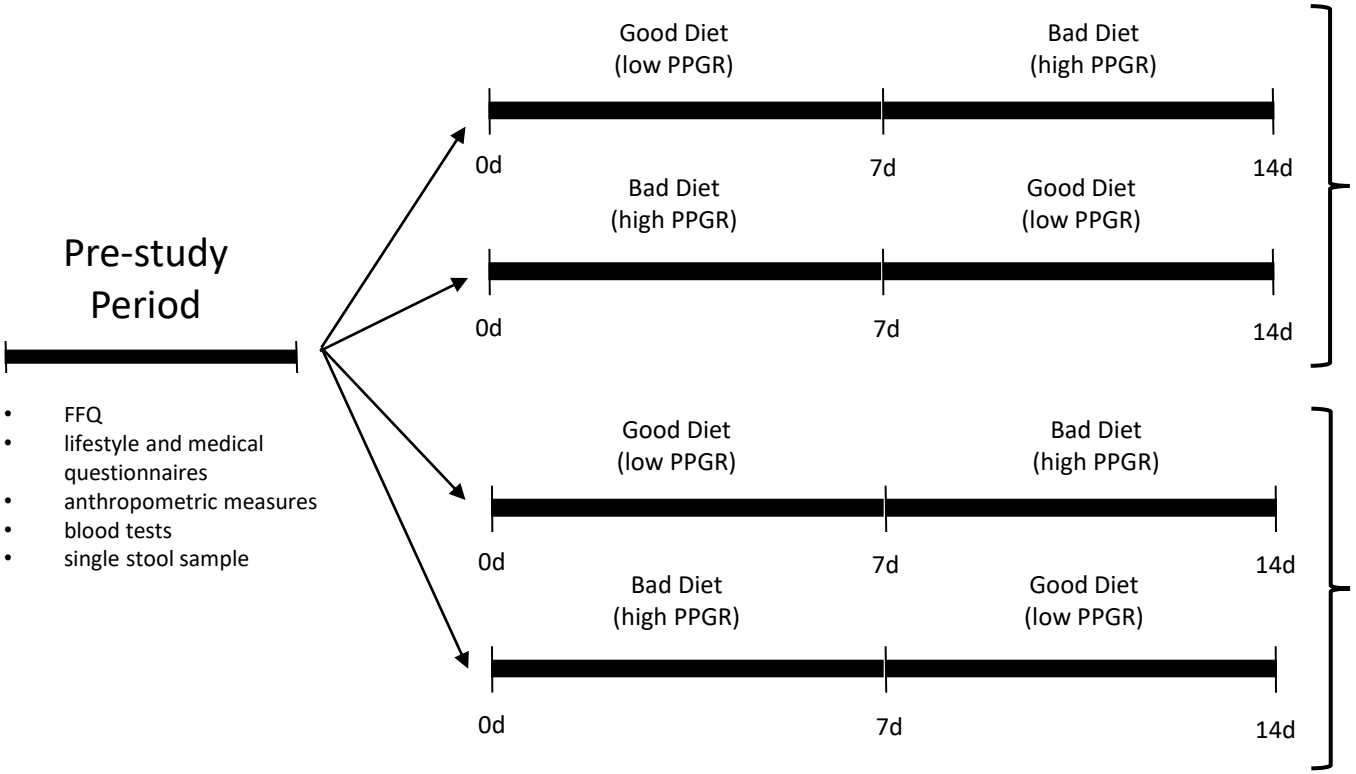
Participants

- ❑ n= 26
  - 12 individuals in the predictor arm and 14 in the expert arm
  - Eligibility Criteria: 1) individuals aged 18–70; 2) not diagnosed with T2DM

Methods

Study Design

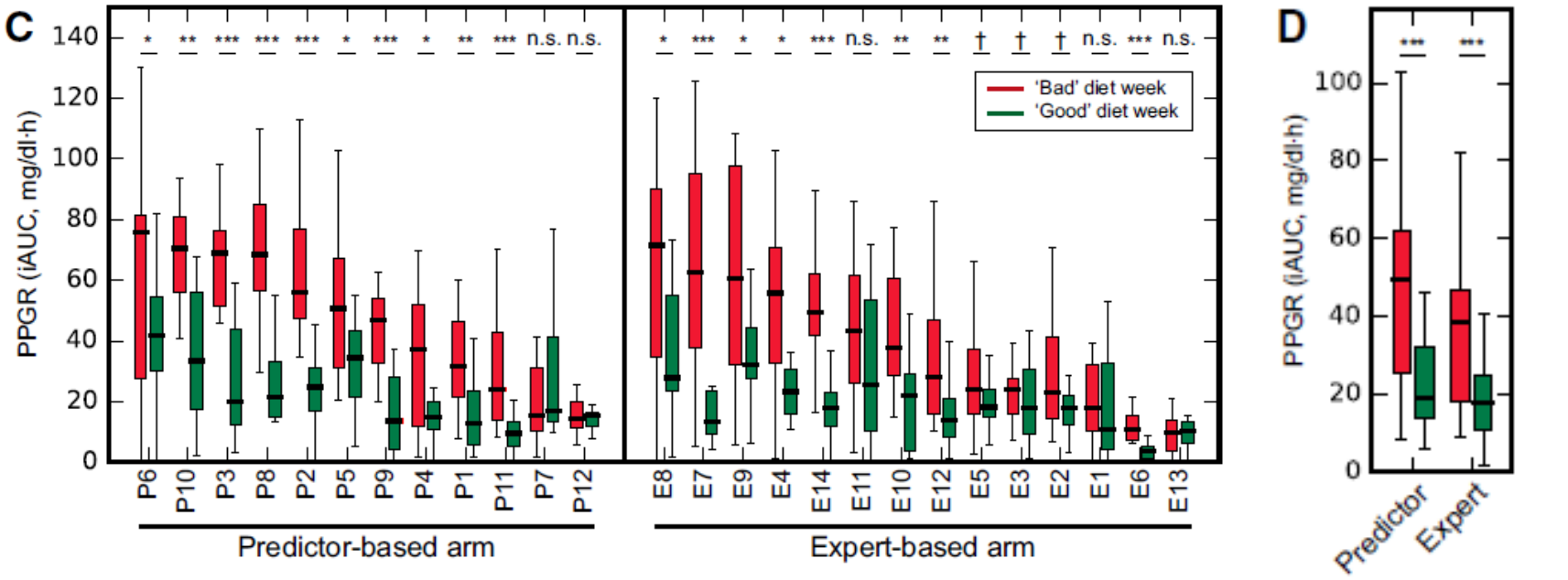
- blinded randomized controlled trial



Results- PPGR

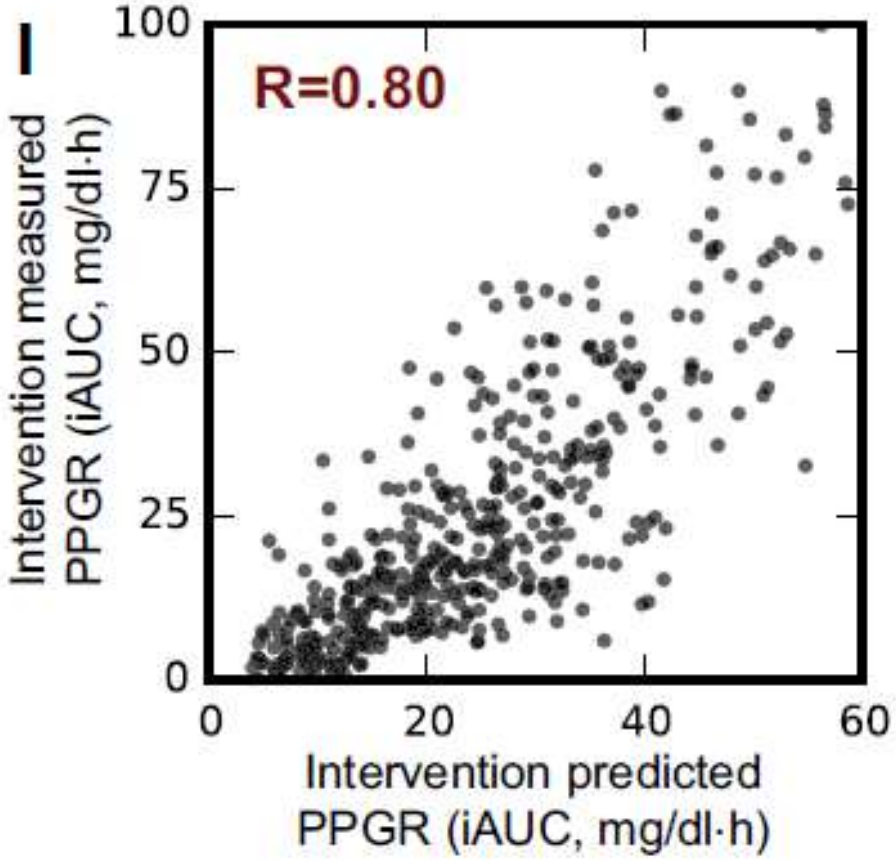
Individual Data

Average Data

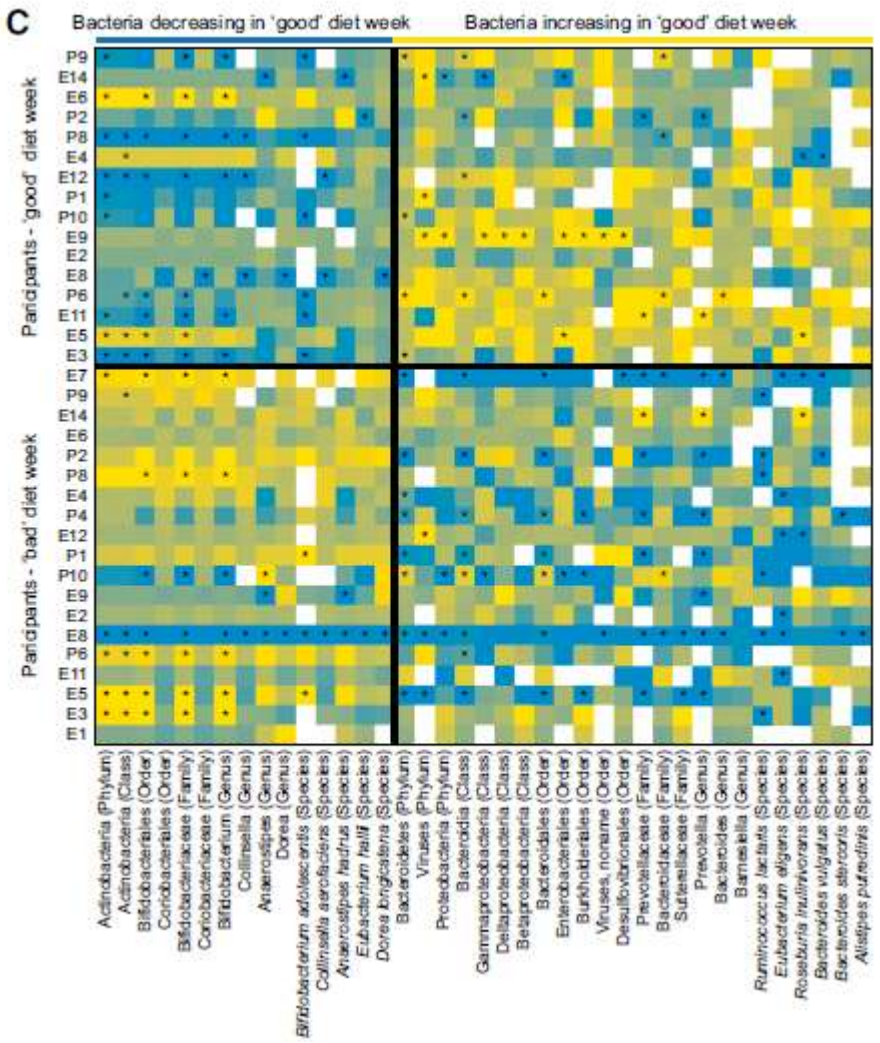


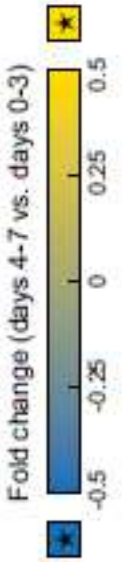
Overall one either the predictor or expert arm, the bad diet significantly had higher PPGR than the good diet ($p < 0.05$)

Results- PPGR



Results- Microbiome





Statistically significant increase($p < 0.05$)

Statistically significant decrease($p < 0.05$)

The abundance of several types of bacteria changed when comparing the bad diet to the good diet

Discussion

Conclusions

- First study to develop a personalized algorithm to predict PPAR
- Using personal and microbiome features enables accurate PPGR prediction
  - Prediction is accurate and superior to the current gold standard, carbohydrate counting
- Short-term personalized dietary interventions successfully lower PPGR
- Future Directions: Can algorithm be used on other ethnic populations? Are there other predictors that can be added to the algorithm to further increase accuracy? What are the long-term metabolic consequences of changing microbiome by changing PPAR?
  - Larger and longer high-quality research is needed!

Time for Discussion

Thank you!

Extra

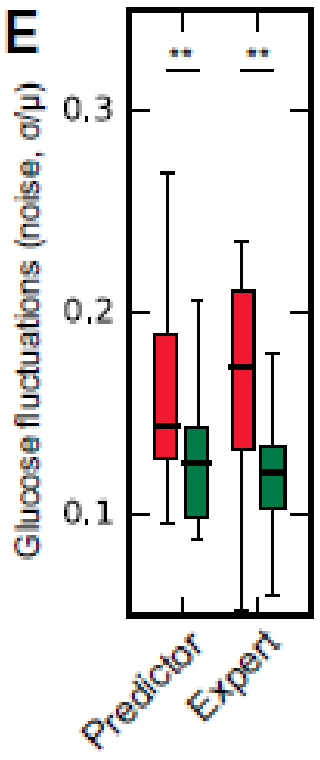
Participant Characteristics

	Main Cohort	Validation Cohort	KS p Value
Number of participants (n)	800	100	
Sex (% female)	60%	60%	1
Age (y) Mean ± SD	43.3 ± 13.1	42.4 ± 12.6	0.972
BMI (kg/m^2) Mean ± SD	26.4 ± 5.1	26.5 ± 4.8	0.867
BMI ≥ 25	428 (54%)	50 (50%)	
BMI ≥ 30	173 (22%)	18 (18%)	
HbA1c% Mean ± SD	5.43 ± 0.45	5.50 ± 0.55	0.492
HbA1c% ≥ 5.7	189 (24%)	31 (31%)	
HbA1c% ≥ 6.5	23 (3%)	3 (3%)	
Total cholesterol (non-fasting, mg/dl) Mean ± SD	186.8 ± 37.5	182.7 ± 35.7	0.231
HDL cholesterol (non-fasting, mg/dl) Mean ± SD	59.0 ± 17.8	55.0 ± 16.1	0.371
Waist-to-hip circumference ratio Mean ± SD	0.83 ± 0.12	0.84 ± 0.07	0.818

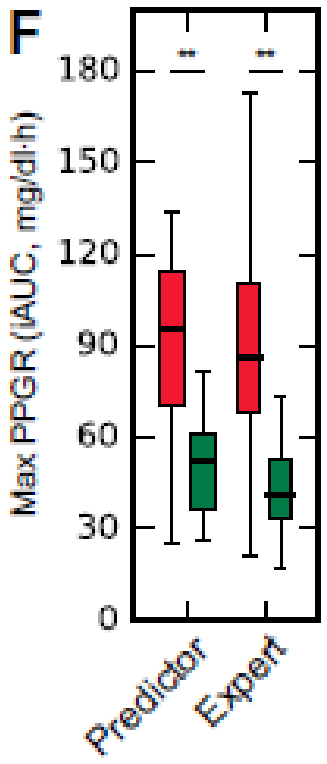
Statistically non-significant difference

Results

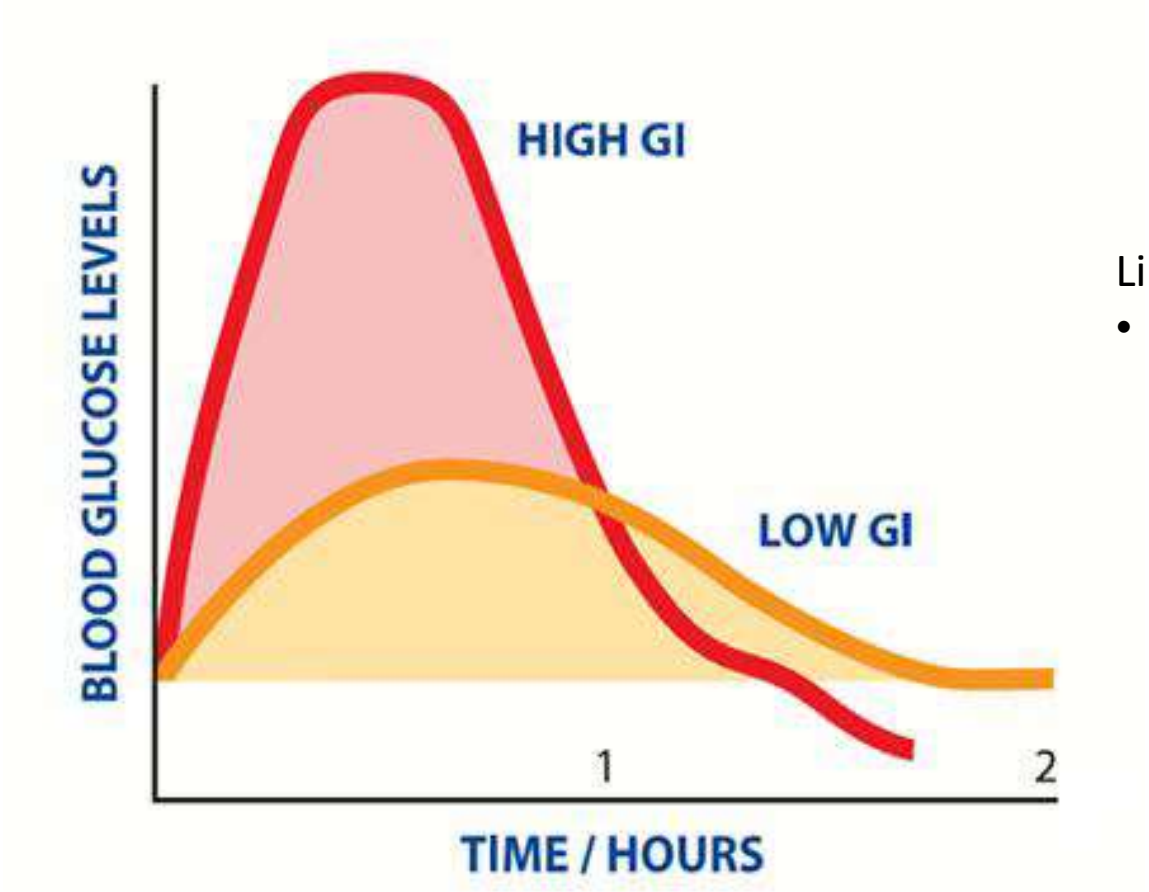
Glucose Fluctuations



Max PPGR



Glycemic Index



Limitations:

- Number of factors effect the GI

Limitations

Postprandial Glucose and Disease Risk

TABLE 1
Epidemiological studies showing an association between postprandial hyperglycemia with risk of CVD and mortality

Hoorn Study	2-h glucose better predictor of mortality than HbA_{1c}
Honolulu Heart Program	1-h glucose predicts coronary heart disease
Chicago Heart Study	2-h postchallenge glucose predicts all-cause mortality
DECODE	High 2-h postload blood glucose is associated with increased risk of death, independent of fasting glucose
Coutinho et al.	2-h glucose associated with CHD
Whitehall Study, Paris Prospective Study, and Helsinki Policemen Study	2-h postchallenge glucose predicts all-cause and CHD mortality
Diabetes Intervention Study	Postmeal but not fasting glucose is associated with CHD

CHD, coronary heart disease.

Ceriello. Diabetes 2005. 54:1–7.