NUTRITION 2019
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JUNE 8 - 11, 2019 | BALTIMORE, MARYLAND

Predicting personal metabolic responses to food using multi-omics machine learning in over 1000 twins and singletons from the UK and US: The PREDICT 1 Study

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Faculty Disclosure

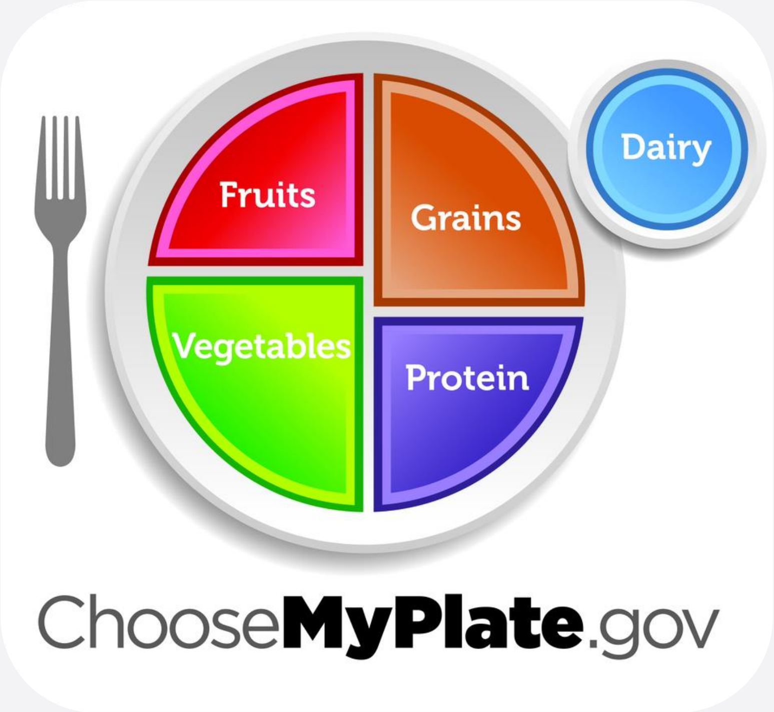
Financial Relationship (prior 12 months)	**Commercial Interest**
Grant/Research Support	Wellcome Trust, MRC, NHS NIHR, NIH, CDRF, Zoe Global, Danone.
Scientific Advisory Board/ Consultant/Board of Directors	SAB Zoe Global
Speakers Bureau	N/A
Stock Shareholder	Zoe Global
Employee	Kings College London
Other	

Food guidelines: Does one size fit all?

Why do some people respond to low fat and others low carb?

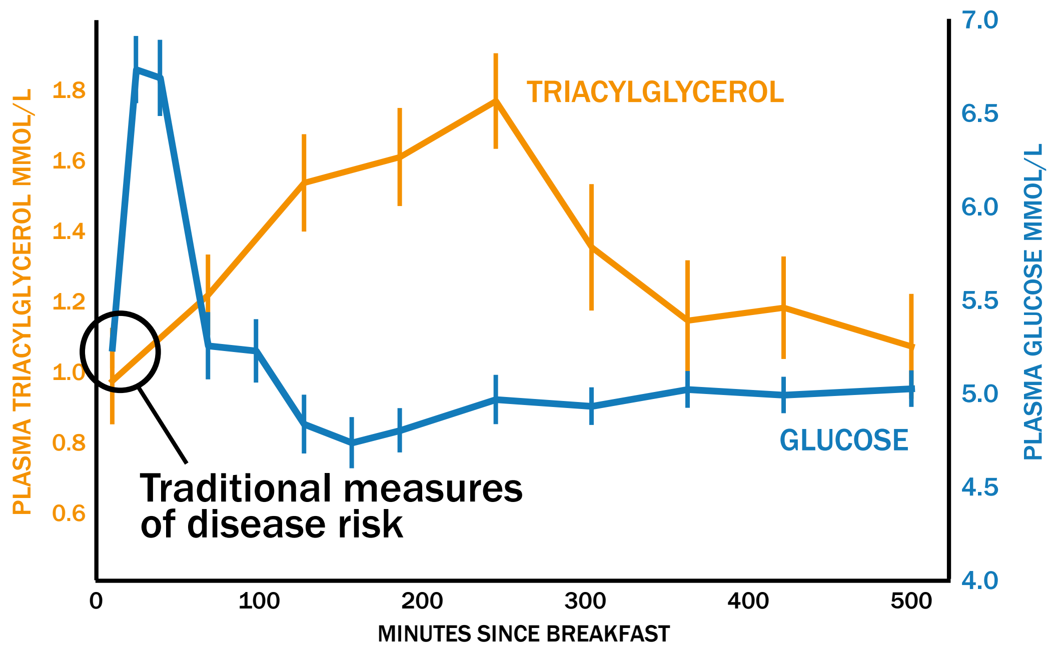
Maybe our individual responses to food are more variable than we believed?

Understanding these factors is key to predicting individual food responses



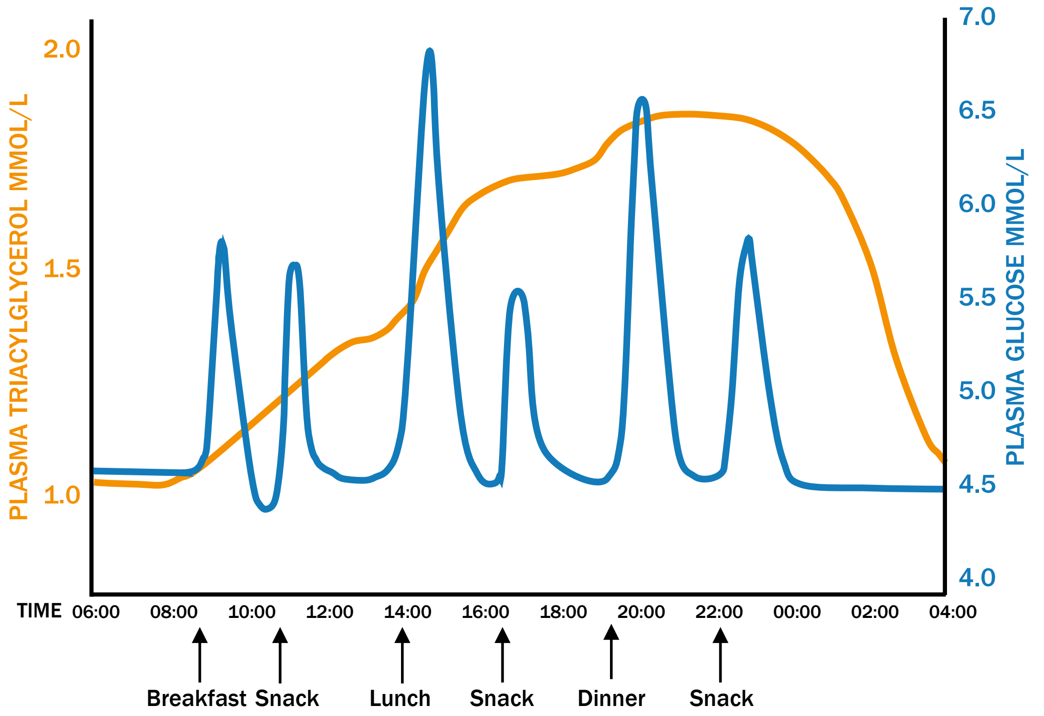
Why do we need to look at postprandial responses?

Single Meal

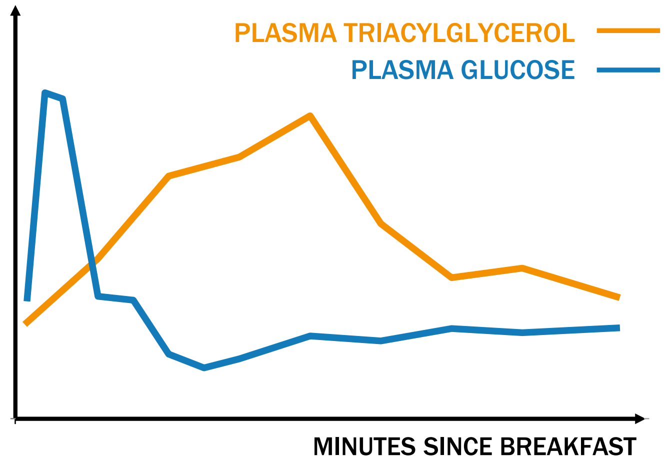


50g fat, 85g carb. AJCN. 2011. 94, 1433-41. n=50

Typical Day



Why do prolonged post-prandial peaks matter?



Raised Insulin Secretion

Lipoprotein Re-modelling

Oxidative Stress Inflammation

Endothelial Dysfunction

Weight Gain

Increased risk for

- **Cardiovascular Disease**
- **Metabolic Disease (Type 2 Diabetes, Fatty Liver, Insulin Resistance)**

Astley, C. M. *et al. Clin Chem* **64**, 192-200, doi:10.1373/clinchem.2017.280727 (2018). Bansal, S. *et al. JAMA* **298**, 309-316, doi:10.1001/jama.298.3.309 (2007). Lindman, A. S., . *et al.* . *Eur J Epidemiol* **25**, 789-798, doi:10.1007/s10654-010-9501-1 (2010). Nordestgaard, B. G., . *et al.* . *JAMA* **298**, 299-308, doi:10.1001/jama.298.3.299 (2007). Levitan, . *et al.* . *Arch Intern Med* **164**, 2147-2155, doi:10.1001/archinte.164.19.2147 (2004).

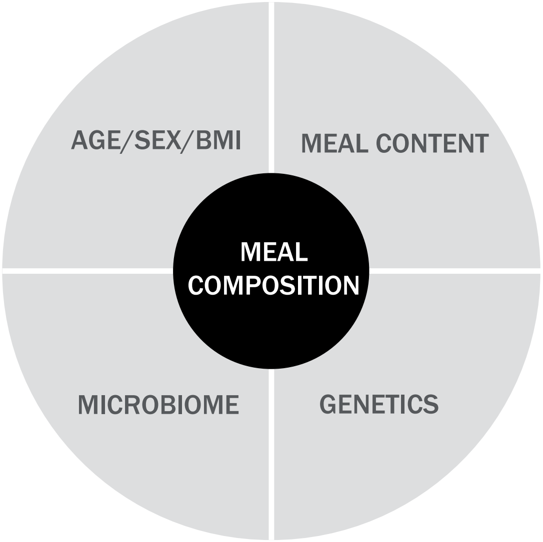
PREDICT STUDY

Aim:

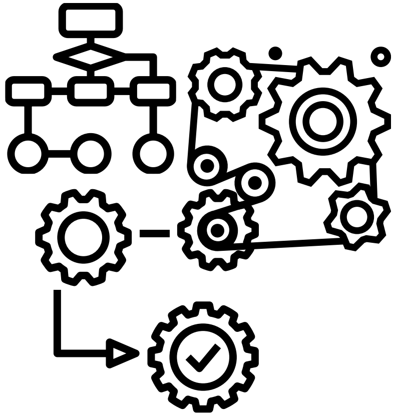
Use genetic, metabolomic, metagenomic and meal-context information to predict individuals' metabolic response to food

1\. How much variability between people?

2\. What explains these differences?



3\. Can we PREDICT individual responses using machine learning?



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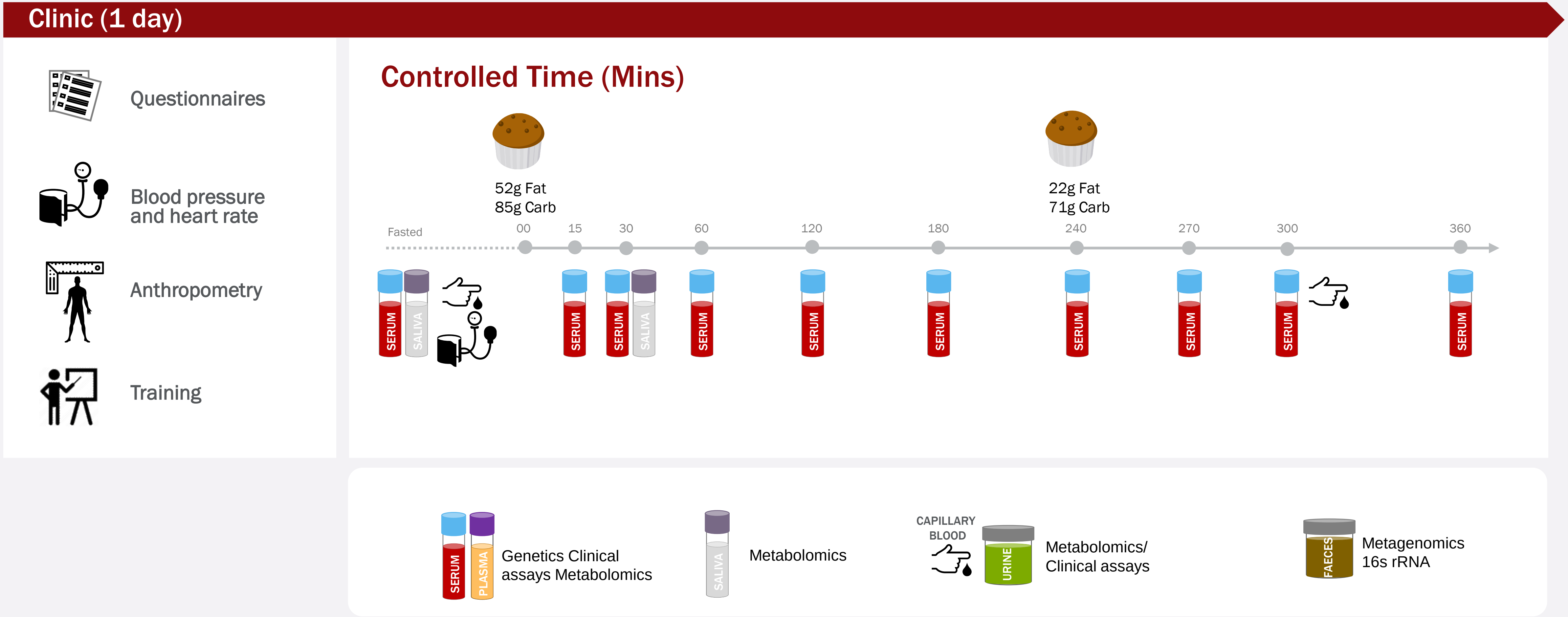
PREDICT STUDY DESIGN

Multiple Test Meal Challenge study: Clinic day + 2 weeks at home

Inclusion criteria
- Aged 18-65 years
- Healthy volunteers



PREDICT STUDY DESIGN

Multiple Test Meal Challenge study: Clinic day + 2 weeks at home

Home (2 Weeks) Standardized set meals + Free-living meals

Test Meal Challenges

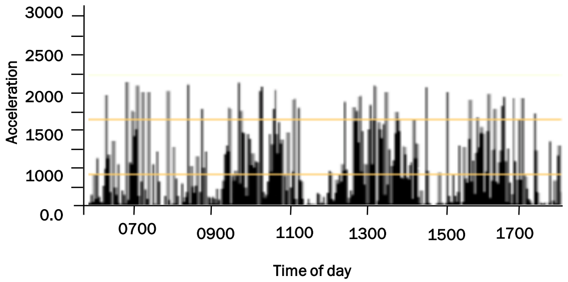
12 days of standardized meals in duplicate

75g OGTT

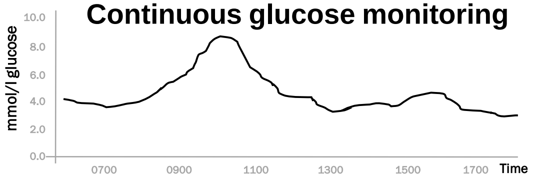
Isocaloric muffins with varying macronutrient composition

Self-selected Free-living meals

Sleep and Exercise



Metabolites



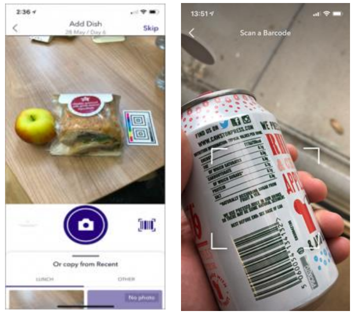
Capillary Blood

Metabolomics/
Clinical assays

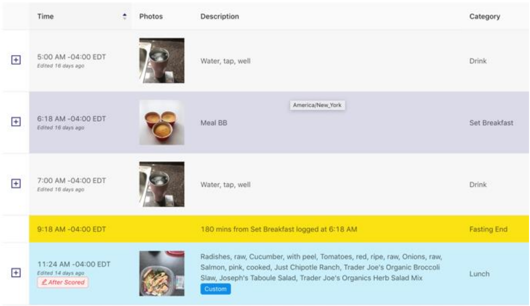
Microbiome

Metagenomics
16s rRNA

Dietary Assessment: Real-time App by Zoe



Dietary Assessment: Real-time Dashboard by Zoe



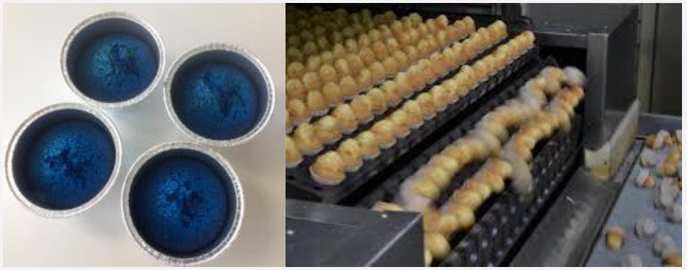
PREDICT STUDY RESULTS

Sample n=1,100	
MZ Twins	479
DZ Twins	172
Non-Twins	351
Drop-out	2.5%

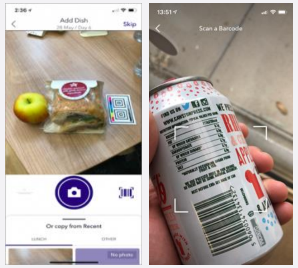
	Mean (SD)*
Age (yr)	45.7 (12.0)
BMI (kg/m^2)	25.6 (5.0)
Sex (%)	72 F/ 28 M
Triacylglycerol (mmol/L)	1.1 (0.5)
Insulin (IU/mL)	6.1 (4.3)
Glucose (mmol/L)	5.0 (0.5)
Total cholesterol (mmol/L)	5.0 (1.0)

*n = 1, 001

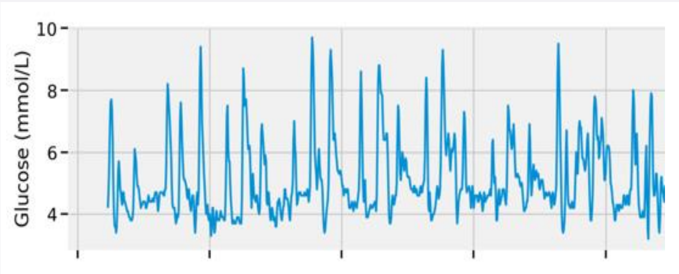
32,000
muffins consumed



132,000
meals logged



2,022,000
CGM glucose readings



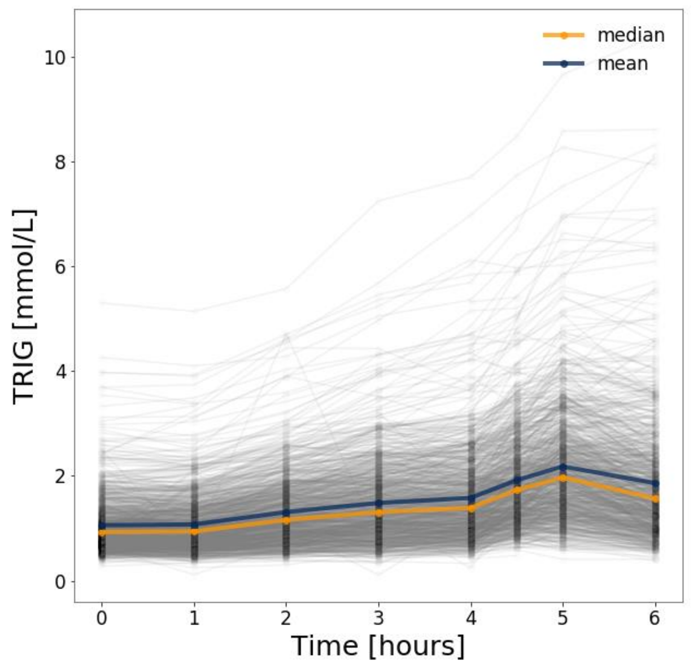
28,000
TAG readings

INTERIM UNPUBLISHED DATA

PREDICT STUDY RESULTS

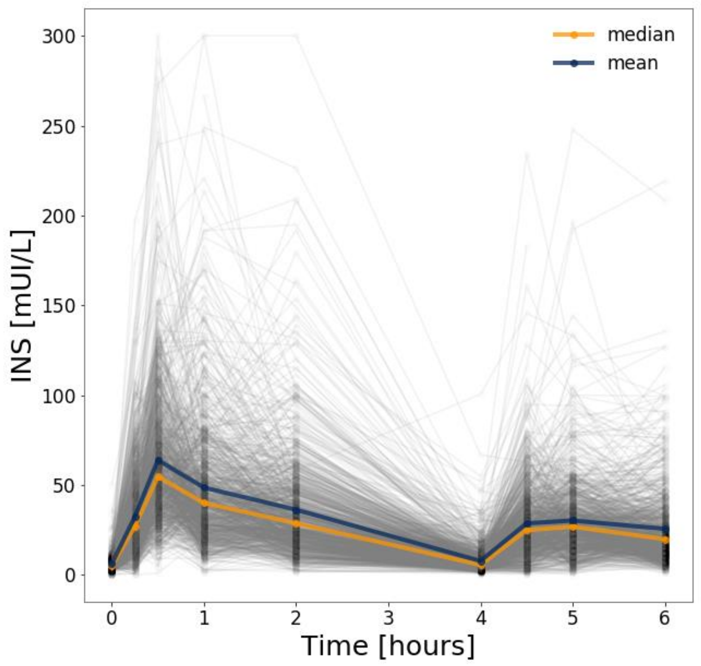
Significant variability between healthy individuals

Triacylglycerol



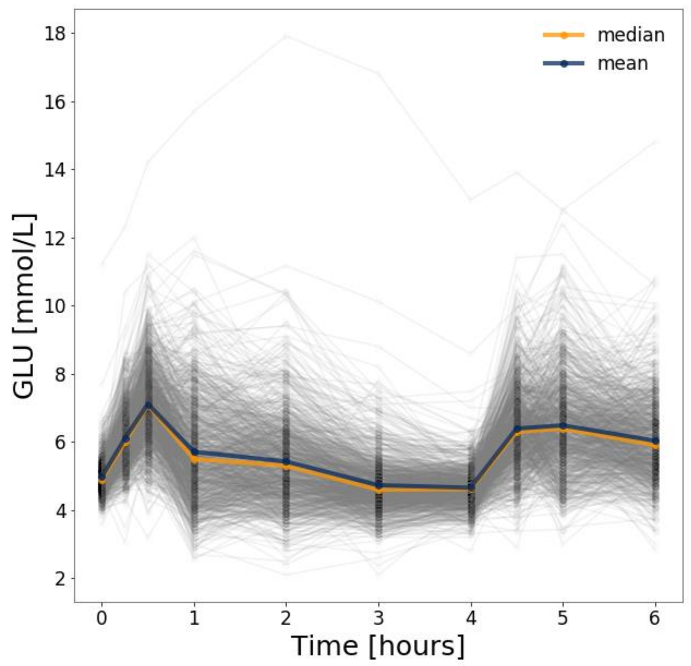
	Baseline	6h rise
CV	50%	103%

Glucose



	Baseline	2h iAUC
CV	10%	68%

Insulin



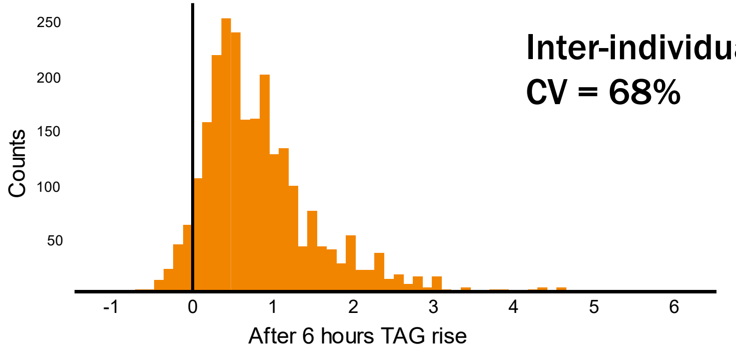
	Baseline	2h iAUC
CV	69%	59%

n = 1,001

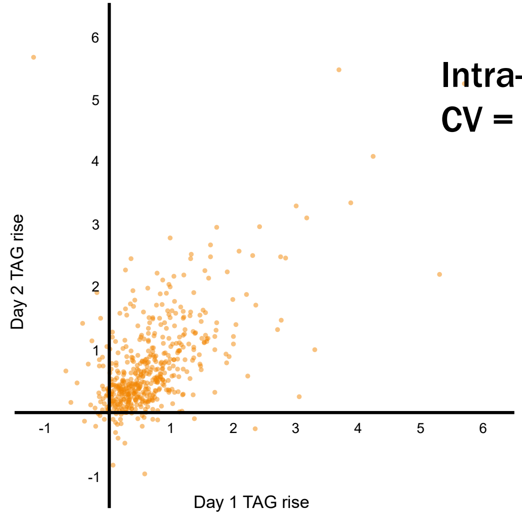
INTERIM UNPUBLISHED DATA

Intra-individual variability is lower than inter-individual variability

Triacylglycerol (6h rise, n=1018 meals at home and in clinic)

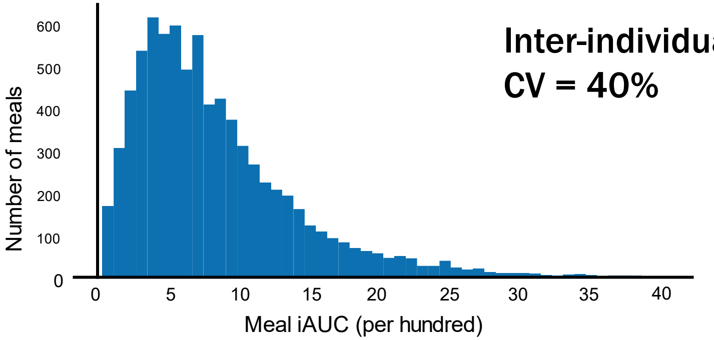


Inter-individual CV = 68%

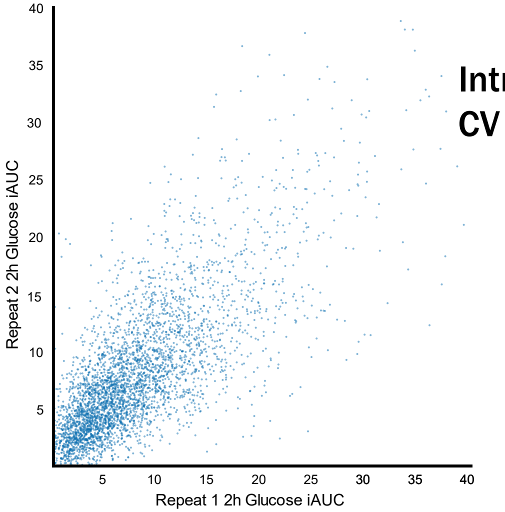


Intra-individual CV = 36%

Glucose (iAUC 0-2h, n=7898 meals at home)



Inter-individual CV = 40%



Intra-individual CV = 24%

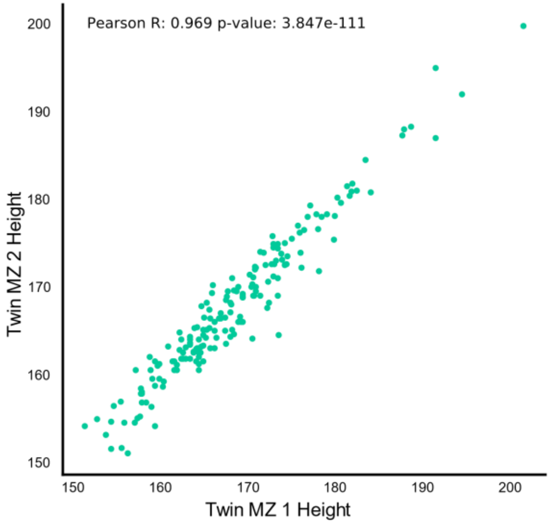
Differences between individuals are repeatable

Interindividual CV is calculated for identical meals, between random pairs of individuals. Intraindividual CV is calculated between pairs of nutritionally identical meals for the same individual

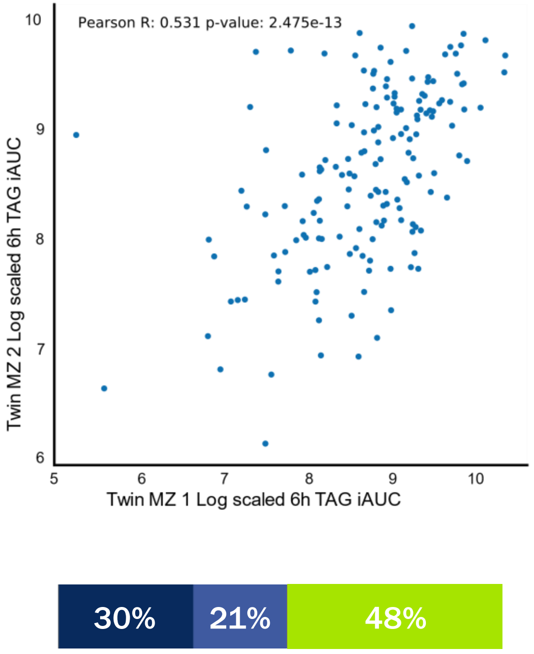
INTERIM UNPUBLISHED DATA

Identical twins have very different responses

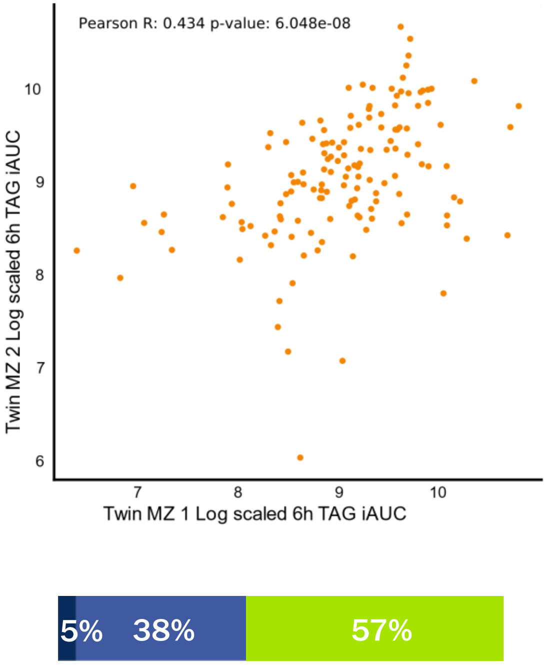
Height



Glucose (iAUC 0-2h)



Triacylglycerol (6h iAUC)



Genetics do not explain most nutritional differences

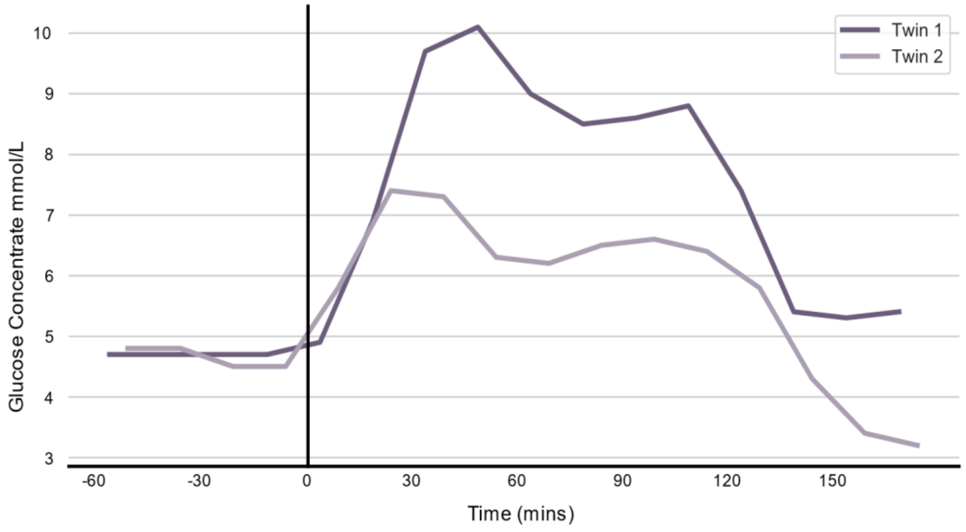
Key:

GENETICS | UPBRINGING | ENVIRONMENT

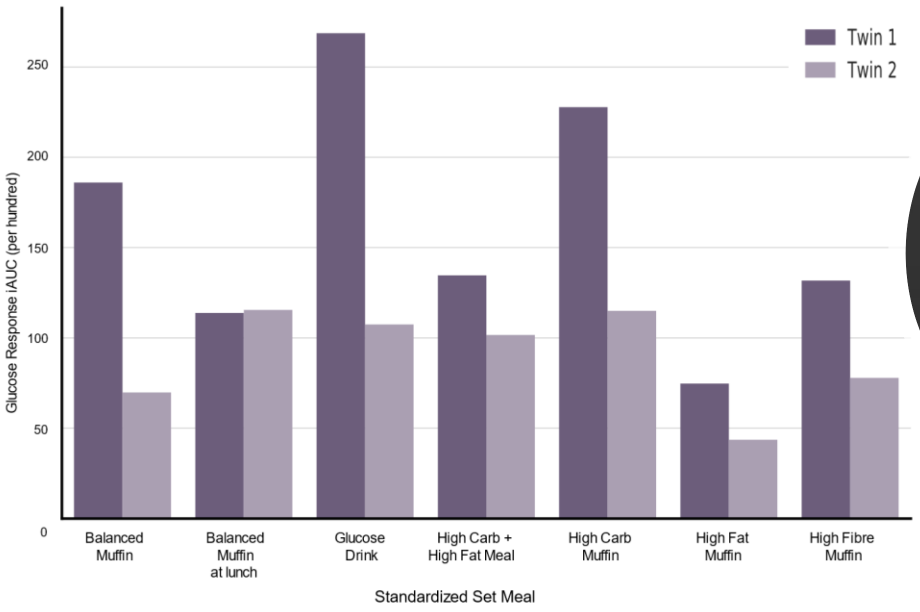
INTERIM UNPUBLISHED DATA

Case Study
Example of a twin pair with different responses

Twin's responses to High Carb muffin



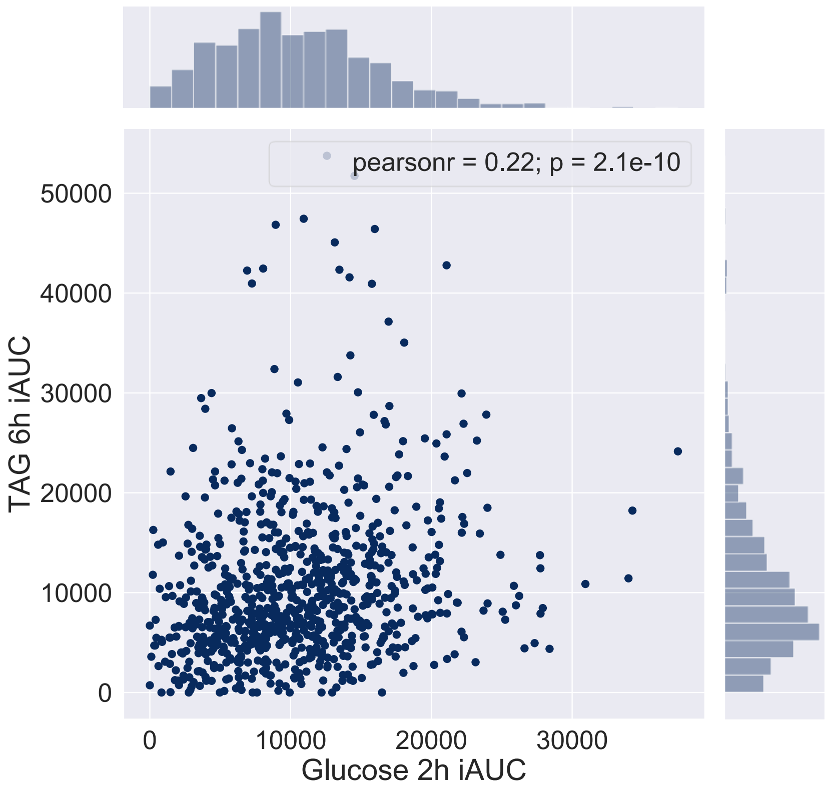
Twin's responses to set meals



INTERIM UNPUBLISHED DATA

Glucose and TAG responses are not well correlated

TAG iAUC 0-6h *vs.* Glucose iAUC 0-2h

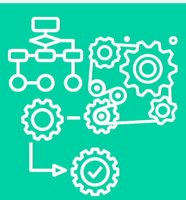


Knowing glucose responses won't tell you a person's fat responses

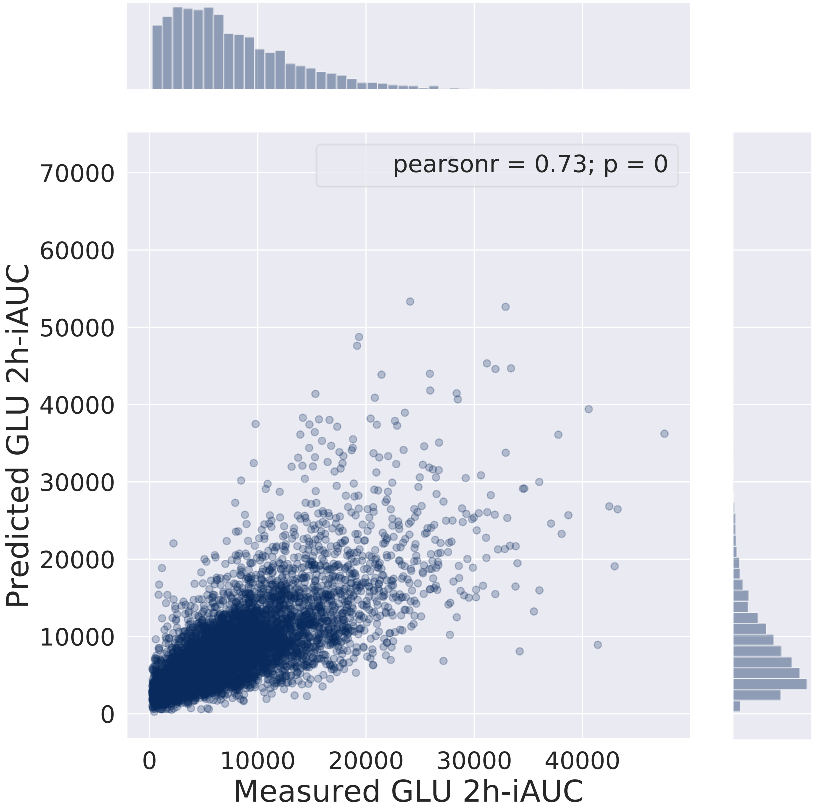
PREDICT STUDY

Machine Learning can predict individual responses

Individual takes test



Machine Learning model uses test results to predict responses to new meals



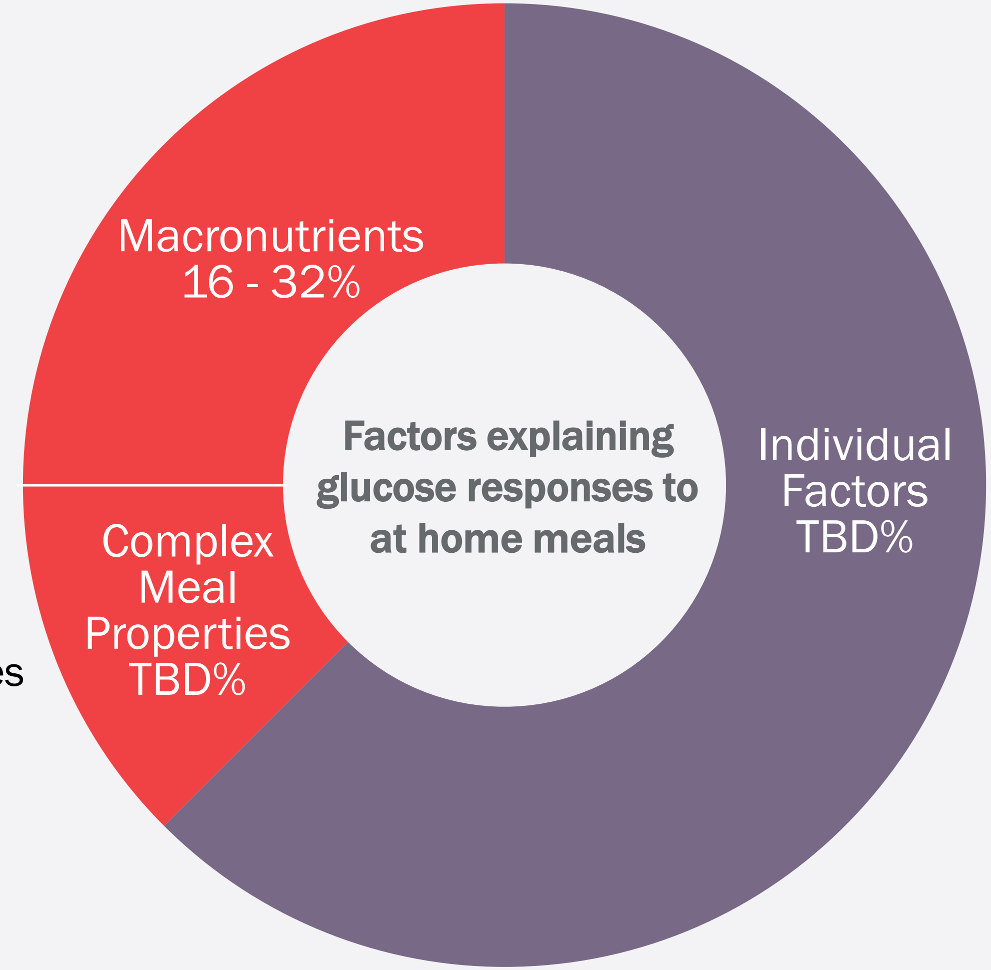
Initial machine learning model correlates

73%

to measured glucose responses

INTERIM UNPUBLISHED DATA

Macronutrients explain 16-32% of responses to at home meals



- Microbiome, genetics, health, medication, etc
- Timing: meal timing, meal order, circadian rhythm
- Sleep
- Exercise

- Carb/fiber types
- Food matrix
- Cooking, etc

n=9376 free living meals. Impact of macronutrients varies depending on meal dataset used

INTERIM UNPUBLISHED DATA

Conclusion

- Everyone is unique in food response – even identical twins
- Genetics explains less than half of metabolic response: most is potentially modifiable
- The macronutrient composition of foods only explains 16-32% of our responses
- Initial machine learning model already correlates 73% to measured glucose responses

What next?

- Build more sophisticated machine learning models, using all the data collected
- Launch PREDICT 2 home study today with MGH and Stanford: https://predict.study

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Stanford University

ZOE

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