Quadram Institute Science Health Food Innovation

NCDs and personalised nutrition: The role of the microbiome

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…Treasure your exceptions…

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"If your results don't make physiological sense, think and think again! You may have made a mistake (in which case own up to it) or you may have made a discovery. Above all, **treasure your exceptions**. You will learn more from them than all the rest of your data."

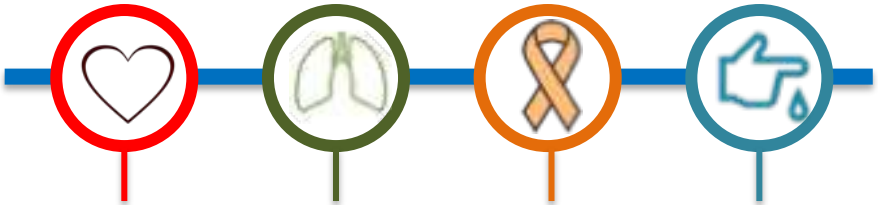
—Elsie Widdowson, 1906-2000

This is very true when we try to understand why people respond differently to diets

Forms the basis for personalized nutrition in the prevention of NCDs

NONCOMMUNICABLE DISEASES (NCDs)

World Health Organization



NCDs are responsible for

71%

of all deaths worldwide
(41 million people)

Every **2 seconds**
someone aged 30 to 70 years
dies prematurely from NCDs

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Spotlight on diabetes crisis

DIABETES UK
KNOW DIABETES. FIGHT DIABETES.

4.7 million
people in the UK have diabetes[1].

4 million
people in England have diabetes.

5m

By 2035
more than 5 million
people will be diagnosed with diabetes in England.[11]

Compared to people without diabetes, people with **Type 2 diabetes** are

nearly 2.5 times
more likely to have a heart attack

more than 2.5 times
more likely to experience heart failure

2 times
more likely to have a stroke.

Over 10 million
people are at increased risk of Type 2 diabetes in England.[23]

Diet & Lifestyle changes through human evolution

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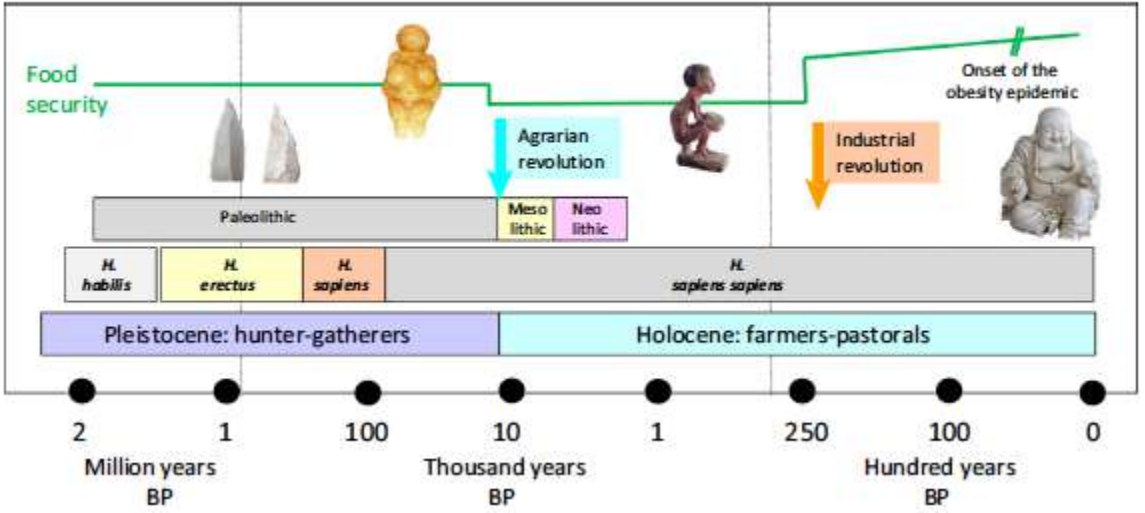
- Over nutrition with foods high in fat, processed meat, sugars, salt and refined grains
- Low in fruit and vegetables
- Limited physical activity
- Starting in the early 1980s, rapid increases in the prevalence of overweight and obesity began in high income countries.



Hochberg *et al.* (2018) Trends in Endocrinology & Metabolism

Ensuring the message is out

change 4 life

Eat well Move more Live longer

- Campaigns have successfully made people aware of healthy eating (reached 99% of mothers with children <10y)
- But the message is generalised (eg healthy vs unhealthy foods)

Successful in educating, but does it translate to effect?

Is there a clear message for consumers?

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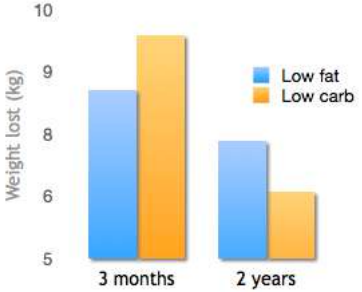
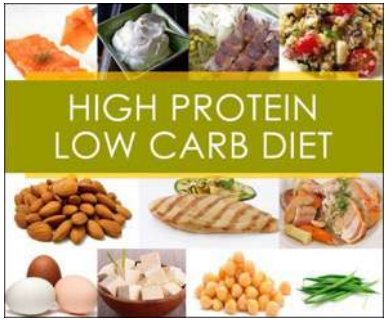


Foster *et al.* (2010) Ann Intern Med. 153(3):147-57

Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion: The DIETFITS Randomized Clinical Trial.
Gardner *et al.* (2018) JAMA. 2018;319(7):667-679.



A carbohydrate-reduced high-protein diet acutely decreases postprandial and diurnal glucose excursions in type 2 diabetes patients
Samkani *et al.* (2018) British Journal of Nutrition,119: 910–917

No grains or legumes (**low fibre**)

Increased satiety in healthy (Bligh *et al.,* 2015)/**improved glucose tolerance** in obese (Frassetto *et al*., 2009)

Iodine deficiency (Manousou et al. 2018, Eur J Clin Nutr.72:124-129)

Does a clear message even exist?

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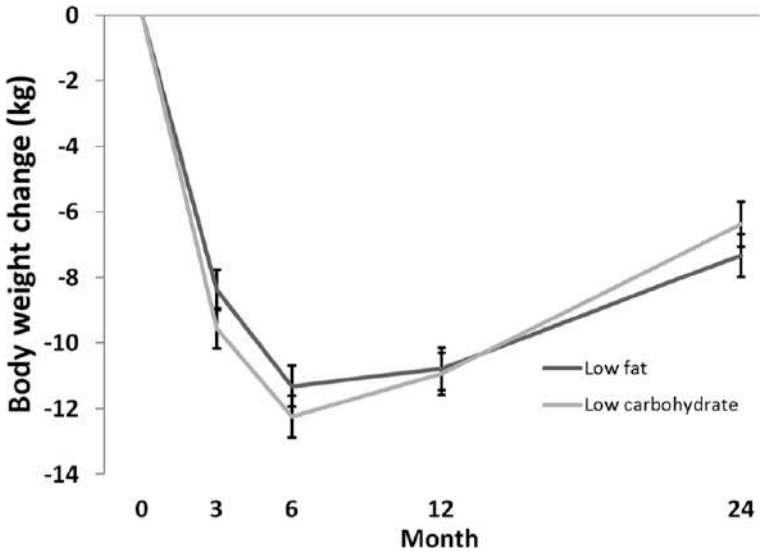

N=307 obesity patients

- 2y later **no difference in weight loss**

…BUT

Baseline fasting plasma glucose and insulin were strong predictors of weight loss

- **High FI** : lost more on low-fat diet
- **Low FI**: lost more on low-carb

Hjorth *et al.* (2019) Int. J. Obesity. 2:e188102

A personalized approach… is it necessary?

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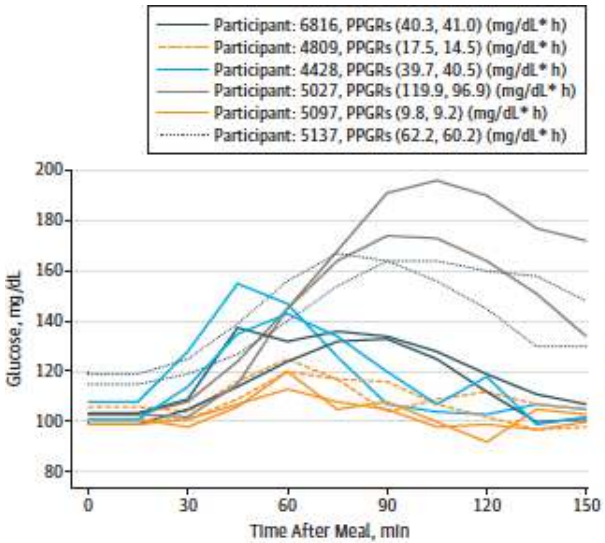
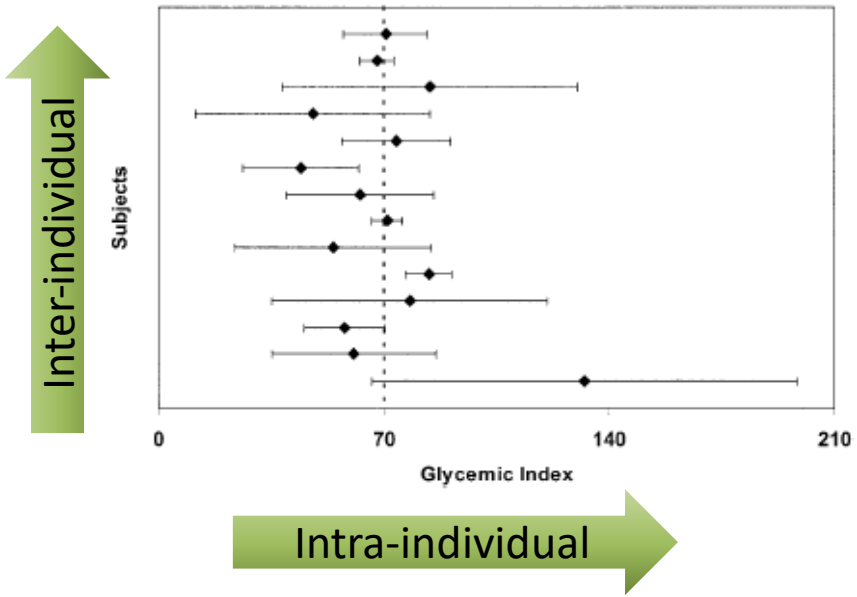
Inter-individual variability in glycemic response to the same meal



Mendes-Soares *et al.* (2019) JAMA Network Open. 2:e188102

Inter- & intra- individual variability in glycemic response to the same food



Vega-Lopez *et al.* (2007) Diabetes Care 30:1412–1417

Sources of variability

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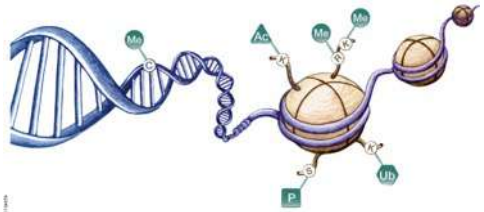
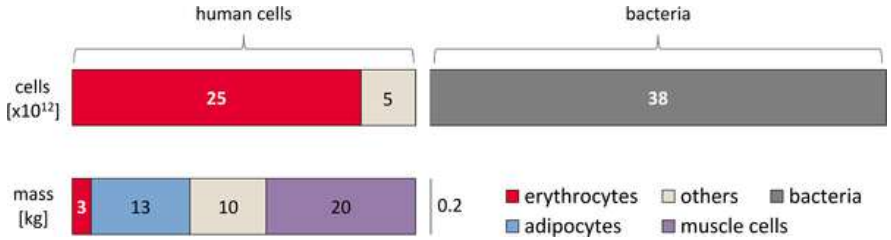
- **GENETICS** (SNPs, Mutations, CNVs)
  - **EPIGENETICS**
    - **ENVIRONMENT & LIFESTYLE** (Exercise, Sleep, Stress)
      - **GUT MICROBIOTA**

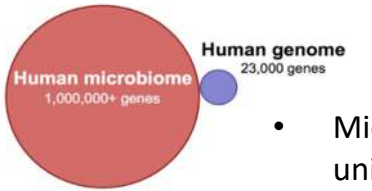


The human microbiota: we are home to highly diverse and dynamic microbial communities

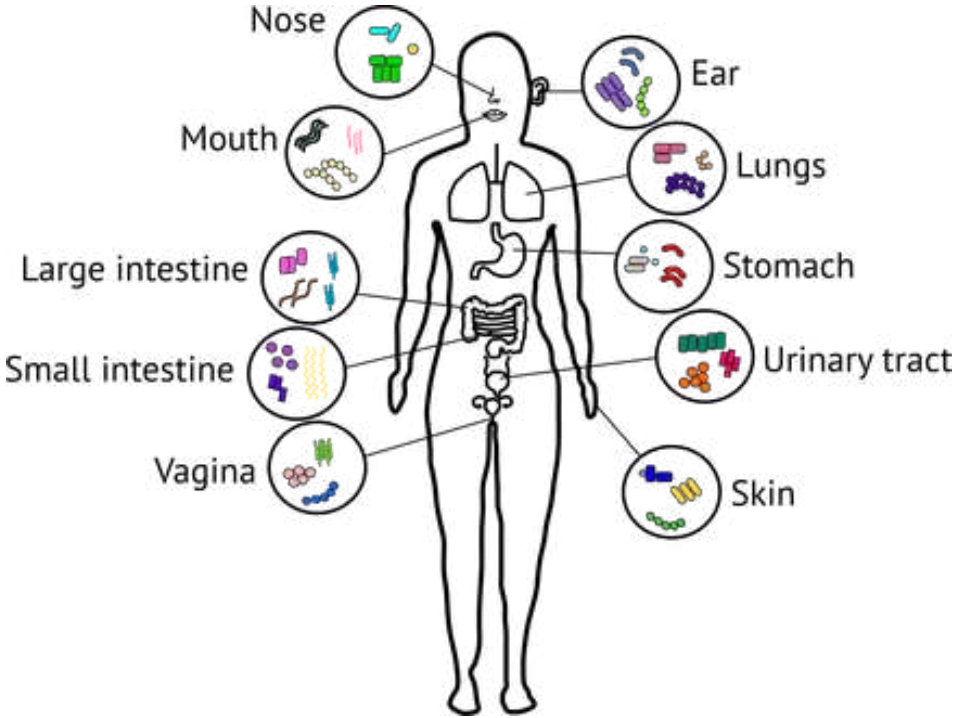
- **Are we more human or microbial?**
  - **1:1 ratio**
  - **10:1 ratio (nucleated cells)**



Sender et al, 2016. PLOS Biology 14(8): e1002533.



- Microbiome contains **150X** more unique genes than human genome



Function of the gut microbiota – energy harvest

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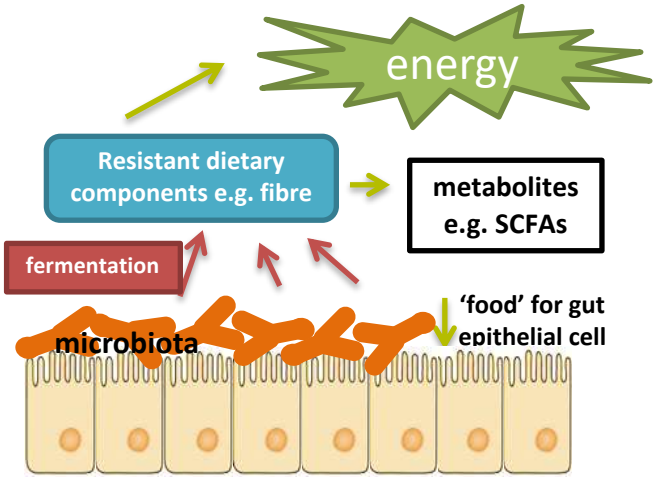
Nutrient metabolism

- Fermentation of CHO and glycans such as resistant starch, inulin, lignin, pectin, cellulose and fructo-oligosaccharides



Butyrate

- main **energy** source for human colonocytes
- activates intestinal **gluconeogenesis** | beneficial effects on glucose and energy homeostasis
- prevents gut microbiota **dysbiosis**

Propionate

- regulates **gluconeogenesis** and satiety signalling through interaction with the gut fatty acid receptors

Acetate

- essential metabolite for the **growth** of other bacteria
- reaches peripheral tissues where it is used in **cholesterol metabolism and lipogenesis**
- plays a role in central **appetite regulation**

Function of the gut microbiota – other

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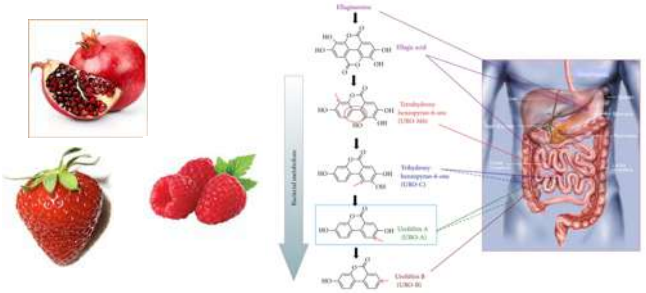
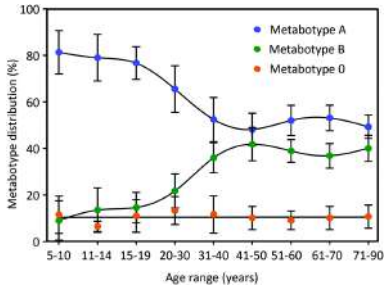
- **Nutrient metabolism**
  - Protein metabolism (eg conversion of L-histidine to histamine)
  - Synthesis of vitamin K and several components of vitamin B
- **Non-nutrient metabolism**

Polyphenols



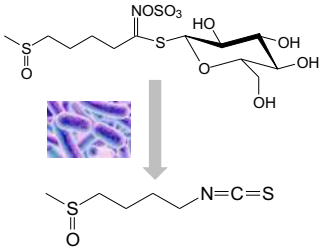
Espin *et al.* (2019) Evidence-Based Complementary and Alternative Medicine. Article ID 270418



Cortes-Martin *et al.* (2018) Food & Function

Glucosinolates

4-methylsylphinylbutyl glucosinolate –
Glucoraphanin



4-methylsylphinylbutyl isothiocyanate –
Sulforaphane

Traka *et al.* (2014) Drug Discovery Today

Diet modifies gut microbiota

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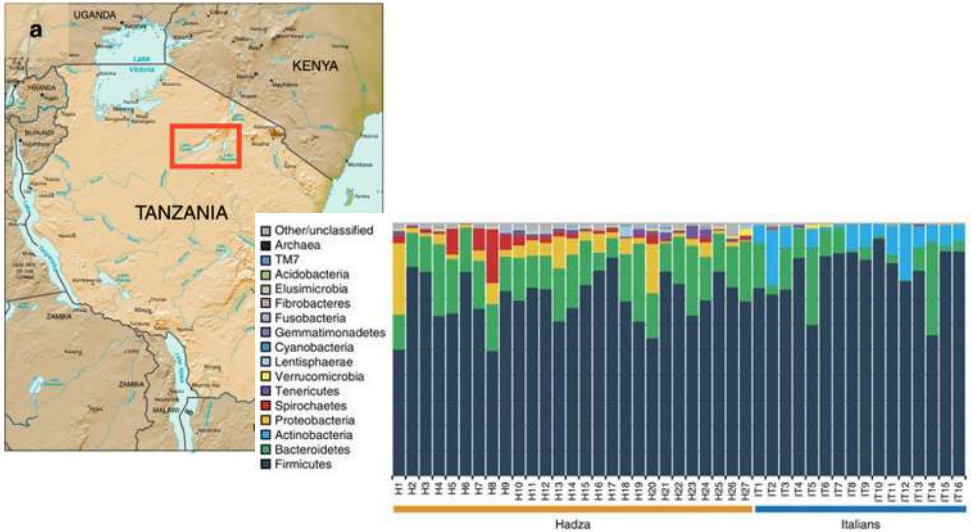
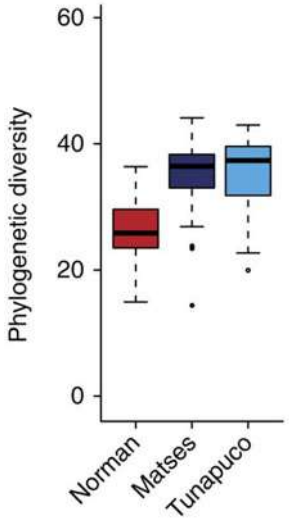
Hadza community of hunter-gatherers

- wild foods (meat, honey, baobab, berries and tubers)
- High fibre



Schnorr *et al.* (2014). Nat Communications, 5:3654

- **Matses |** remote hunter-gatherer population from the Peruvian Amazon **| tubers, plantain, fish, limited game**
- **Tunapuco |** traditional agricultural community from the Andean highlands **| stem tubers (potatoes, oka, mashua), fruit, meat**
- **Norman, Oklahoma, US |** typical US urban-industrialized lifestyle **| processed foods, bread and prepackaged meals**



Matses and Tunapuco are enriched in genus *Treponema*, an efficient carbohydrate metaboliser

Obregon-Tito *et al.* (2015). Nat Communications, 6:6505

Can the gut microbiome modulate response to diet?

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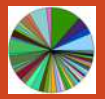
Indirect evidence

- Obese individuals show decreased bacterial diversity and gene richness
- Composition of the gut microbiota has the potential to affect energy harvest (capacity for fibre-utilization)
- Secretion of hormones affecting appetite (gut-brain axis)

How can we use information on gut microbiota to understand WHICH foods are doing WHAT to WHOM?

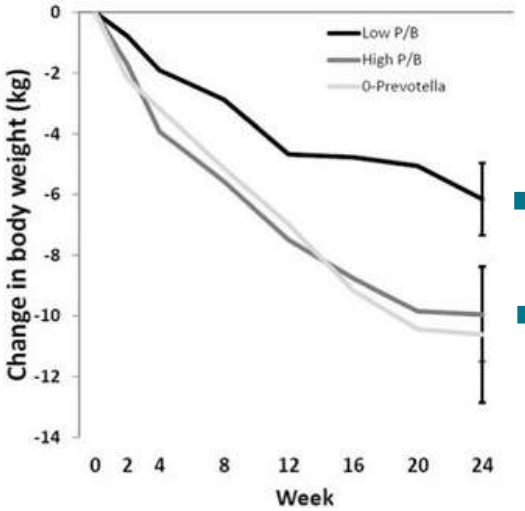
New sequencing technologies are revolutionising the field



Evidence from human studies (RCTs) – Taxonomic information

Obese individuals stratified by **Prevotella–to–Bacteroides (P/B)** ratio (n=52) on low calorie diets (500 kcal/d) for 24w

- **Prevotella |** high CHO and fibre diets
- **Bacteroides |** high protein and animal fat



High fibre >30g

8.3 kg more

3.2 kg more

Hjorth *et al.* (2019). Int. J. Obesity, 43:149-157

Using taxonomic AND functional information
Not just what is present but what they are doing

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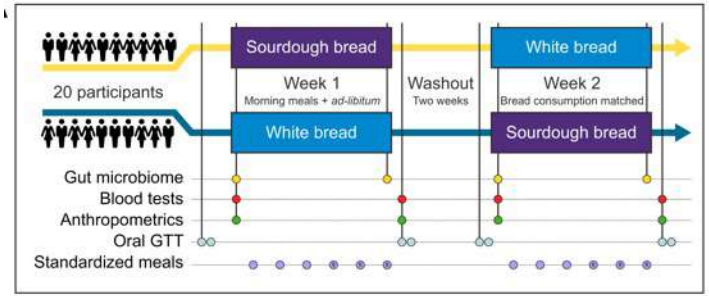
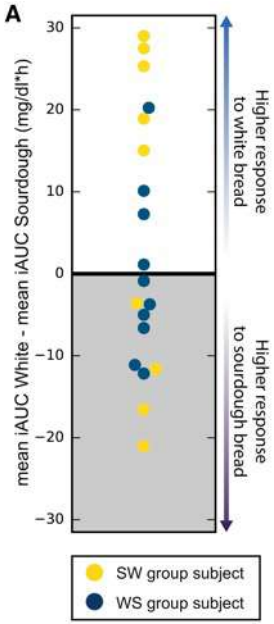
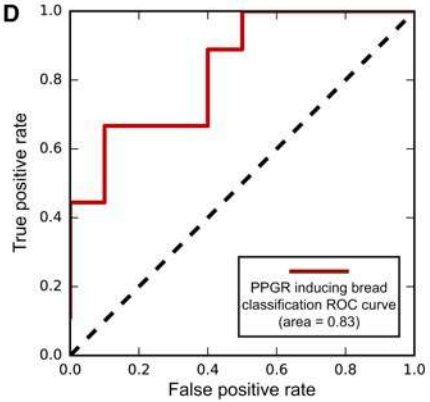
In healthy (n=20) **no difference** in metabolic or clinical parameters





When only gut microbiota were used in a classification algorithm they could predict the bread that induced lower glycemic response



Korem *et al.* (2017). Cell Metabolism, 25: 1243-1253

Challenges for integrating gut microbiome in PN solutions

- Requires individuals to be engaged
- Multiple sample collection and analyses is costly
- RCTs are necessary to show efficacy above and beyond a existing personalised interventions (eg with a professional) – **REPRODUCIBILITY**
- Healthy vs diseased
- Evidence for sustained effect is yet to be demonstrated
- Requires multidisciplinary approaches – **DATA CONNECTIVITY**

…just because we can measure all doesn't mean we should…

Clinical nutrition, big data and digital Health for PN

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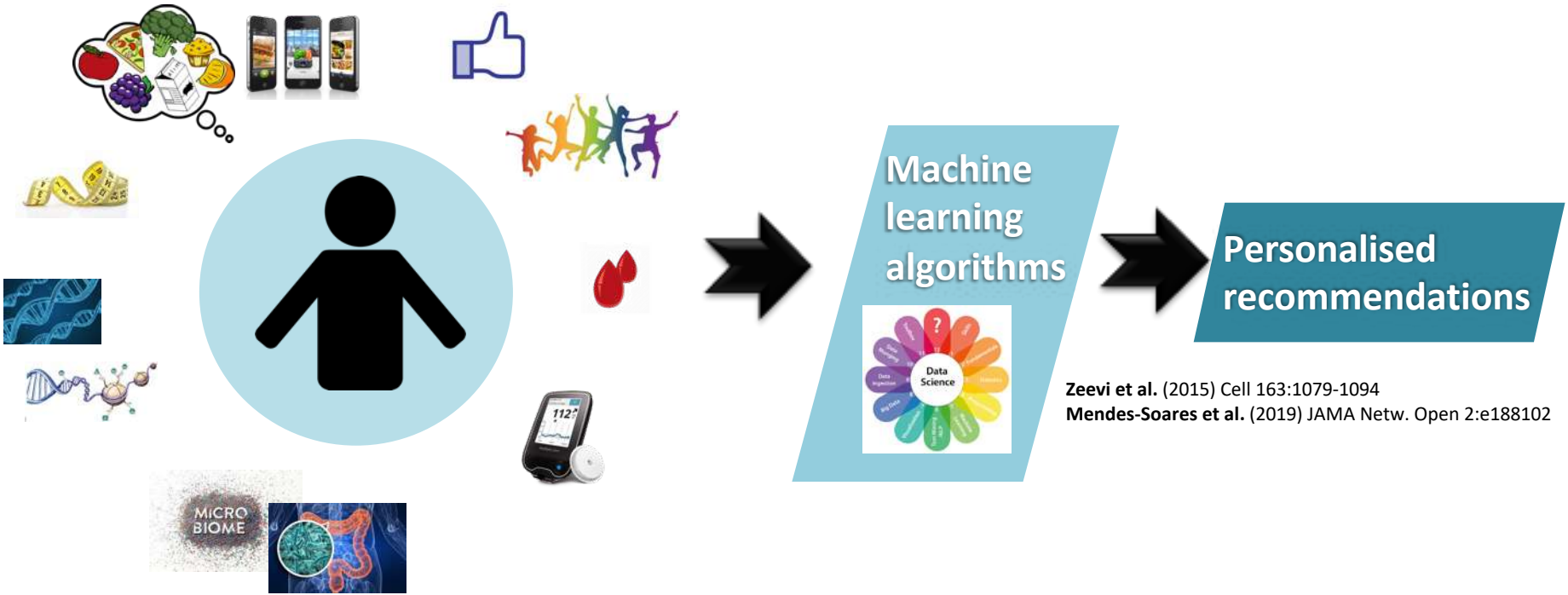
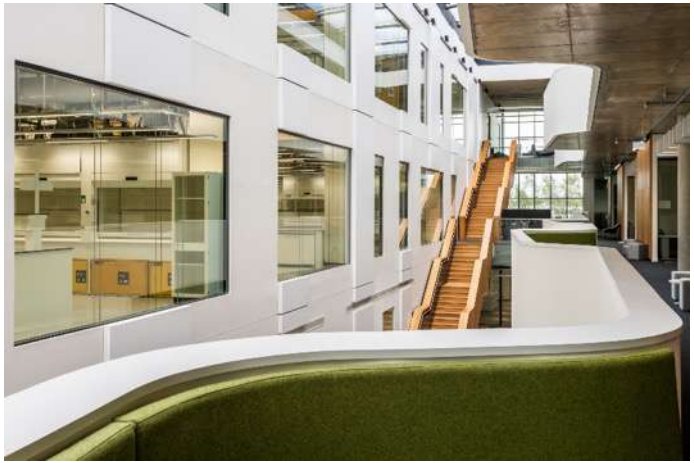


Zeevi et al. (2015) Cell 163:1079-1094
Mendes-Soares et al. (2019) JAMA Netw. Open 2:e188102

Opportunities for academia – industry collaborations



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Science Health Food Innovation

UEA
University of East Anglia

NHS
Norfolk and Norwich University Hospitals
NHS Foundation Trust

BBSRC
bioscience for the future

Thank you for listening….

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Science Health Food Innovation

FOOD DATABANKS

Paul Finglas

Jenny Plumb

Hannah Pinchen

Daniela Segovia Lizano

Talk to me about opportunities to join us and the Quadram Institute…