Delivering pre/probiotic health benefits and getting them to market by moving beyond the 'One Size Fits All' paradigm

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Probiotics (bugs) & Prebiotics (food for bugs)

“products that contain an adequate dose of live microbes that have been documented in target-host studies to confer a health benefit”

[Sanders. Clinical Infectious Diseases 46, 2008]

“a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits upon host wellbeing and health”

Gut microbiome in health and disease

Inflammatory bowel disease
Cancer
Metabolic disorders
Obesity
Diabetes
Cardiovascular disease
Psoriatic arthritis

[Valdes et al. BMJ 361, 2018]
Non-communicable disease (NCD) epidemic

- 60% of deaths worldwide
- 44% of premature deaths
- “In the next 10 years, China, India and the United Kingdom are projected to lose $558 billion, $237 billion and $33 billion, respectively [from NCD]”

[Daar et al. Nature 450, 2007]
Pre/Pro-biotics getting to market

- Consumers **want** health-promoting products
- However, regulators are **rejecting** probiotic health claims
- Limited evidence for probiotic health impacts, e.g.:
  - Reducing diarrhoea duration
  - Reducing constipation
  - Resisting respiratory or genito-urinary infections
  - Allergic rhinitis and asthma
- “So far, EFSA has rejected all submitted health claims for probiotics” [de Simone. Clinical Gastroenterology and Hepatology 17, 2019]; European Food Safety Authority

[Katan. Beneficial Microbes 3(2), 2012]
Regulation of probiotics

**Supplements:** evidence of general beneficial effects

**Drugs:** evidence of specific indications

**Medical food:** supported for the dietary management of a disease that has distinctive nutritional needs that cannot be met by normal diet alone

- **Live microbes (presence of a percentage of dead microbes):**
  - Food supplement
  - Medical food

- **Dead microbes (microbes inactivated by heat, radiation, etc):**
  - Drug

General health claims
- Low consumer interest
- Low evidence burden

Specific health claims
- High consumer interest
- High evidence burden

[de Simone. Clinical Gastroenterology and Hepatology 17, 2019]
Divergent responses to the same interventions

% *Ruminococcus* in whole community in overweight patients

Maintenance | Non-Starch Polysaccharide | Resistant Starch | Weight Loss

[Walker et al. ISME 5(2), 2011]

Participants vary in probiotic mucosal colonization during supplementation

(11 strains pooled)

[Zmora et al. Cell 174, 2018]
Prebiotics

Diversity in strain carbohydrate degradation capacity

Microbial systems are complex

[Bifidobacterium Animalis]

[Welch et al. PNAS 2017]
It’s not that pre/pro-biotics can’t work,

It’s that they don’t work the same way in all people.

So how do we characterize those individuals who would benefit?

In CAFE:
1. Harness clinical data to identify who.
2. Employ mechanism-level modelling to identify why.
[Slides containing unpublished data have been removed.]
Outlook

- Pre- & pro-biotics can benefit health
  - But not the same way for all people
- Regulatory impasse
  - General public/patients lose
  - Companies lose
- Can we (cheaply) identify who **will** benefit, and market to them?
- Requires input of clinical data (identify **who**)
- Requires input of experimental data (identify **why**