#### TNO Symposium, 20 September 2023, Naturalis Leiden

- 1. Searching for synergistic effects of fibres and co-passengers. A new trend? Jan-Willem van der Kamp, TNO
- 2. Alignment of dietary fibers with gut bacteria for robust and predicted response. Bruce Hamaker and Thaisa Cantu-Jungles, Whistler Center for Carbohydrate Research, Purdue University, USA
- 3. No Guts No Glory project Lessons learned Femke Hoevenaars, TNO
- 4. Targeted microbiome modulation through dietary fibres: a new chapter in precision nutrition Frank Schuren, TNO
- 5. From a universal sugar replacement strategy towards unlocking the power of fibre-rich by-products Stefano Renzetti, Wageningen Food & Biobased Research
- 6. Strategies for increasing the fibre intake for low-income consumers Louise Dye, University of Leeds, UK
- 7. You are what you wheat. Impact of whole wheat and fibres on health and innovative ways for testing health effects Suzan Wopereis, TNO



## Searching for synergistic effects of fibres and co-passengers. A new trend?

TNO Willem van der Kamp

### Content

#### Food and health – studies and recommendations

Dietary recommendationsGeneric, food groups, categories of ingredientsHealth claims, Pre- and probiotics definitionsSpecific compounds, specific bacteriaTrends: Synergistic effects,Mixtures, bioactive compounds, food structure

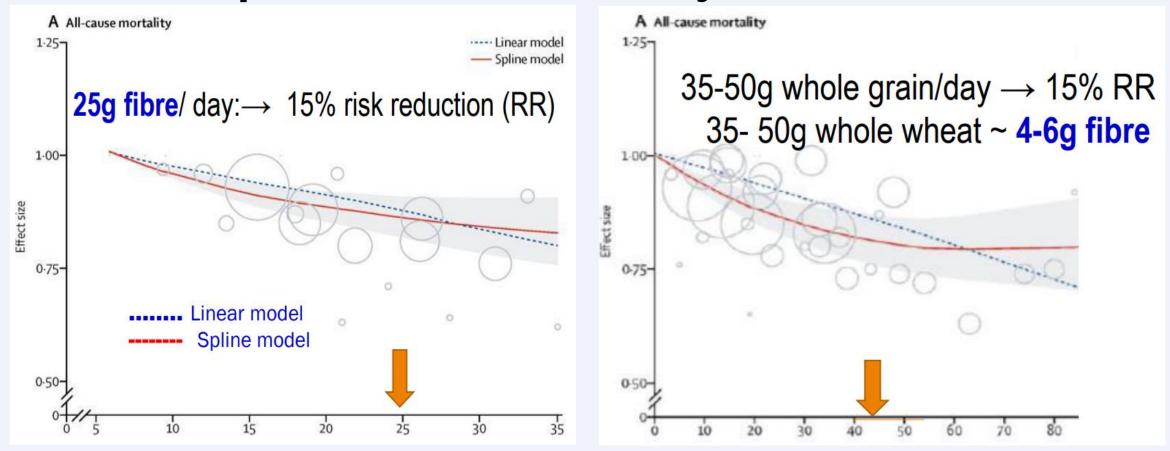
Synergistic effects of fibres and copassengers - examples

### This symposium – key points



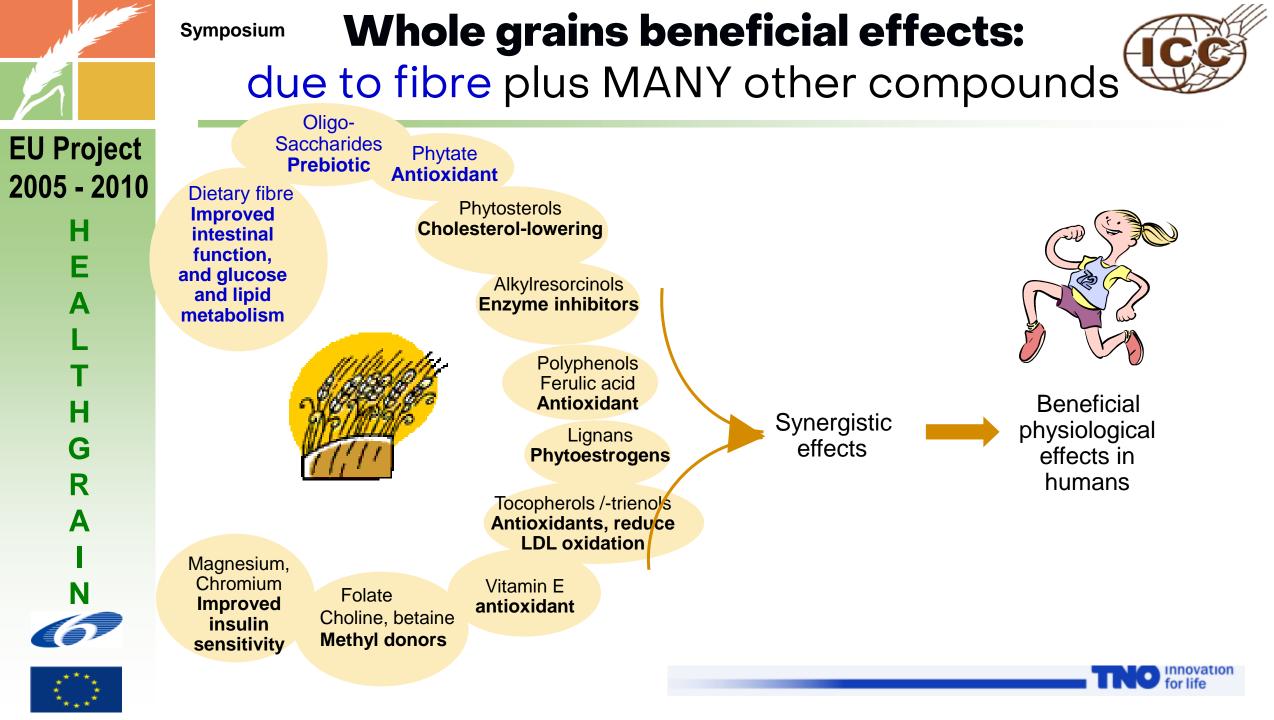
Symposium

### Whole grain – synergism of fibre and co-passengers Example: all-cause mortality – risk reduction



innovation

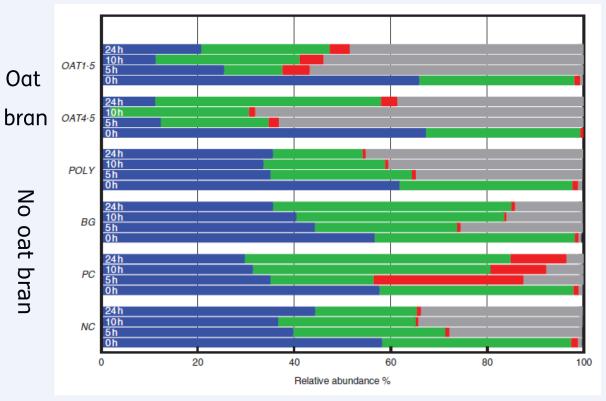
Reynolds A, Mann J, Cummings J, et al. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. *The Lancet* 2019;393(10170):434-45



### B-Glucans, polyphenols - synergistic matrix effects

KRISTEK, A., WIESE, M. et al. Oat bran, but not its isolated bioactive βglucans or polyphenols, have a bifidogenic effect in an in vitro fermentation model of the gut microbiota. *BJN*, **2019**, 121, 549-559

**Symposium** 



Jefferson A., Adolphus K. The Effects of Intact Cereal Grain Fibers, Including Wheat Bran on the Gut Microbiota Composition of Healthy Adults: A Systematic Review. Front. Nutr. 2019, 6:33.

- Intact cereal fiber consumption: increased microbiota diversity and/or abundance
- Hypothesis: Wheat bran (with non-fermentable and some fermentable fibers) could serve as an ideal "dinner table" for micro-organisms.

## Food Transition - Opportunities and challenges Food: plant-based, sugar, fat more fibre ealth: obesity pandemic - poor diets for poor people How to optimize composition and structur of food, fibres and co-passengers? For maximizing beneficial effects

Symposium

### **Optimizing food and fibre composition** The way forward

#### Strengthening insight – guidelines for studies

Insights in impact of structures of fibre for microbial health	Bruce Hamaker
Theoretical basis for optimizing product structure of high fibre products	Stefano Renzetti
and high-fibre by-products	

#### **Optimization of mixtures - Effective screening methods**

- Gut microbiome: High throughput predictive in vitro exposure methods
- Sensitive innovative phenotypic flexibility method for measuring health effects Suzan Wopereis

Strategies for reaching low-income consumers

Louise Dye

Femke Hoevenaars

Frank Schuren



Symposium

### My way forward

End of 2023 – departure from TNO

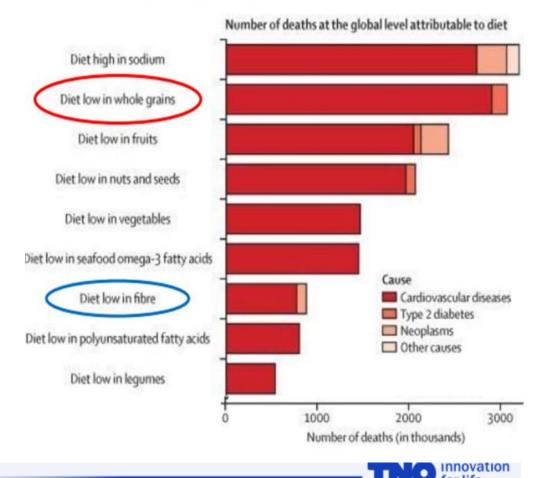
2023 – 2024 - ?? Active for Cereal Science, ICC and its Whole Grain Initiative

- Global Whole Grain Definitions Group chair
- ICC Cereals&Bread Congress, Nantes, April 2024
- WGI Food Policy Group Communication with WHO, FAO, EU, European Parliament Focus: highlighting importance of Whole Grain





#### Diet related mortality rates (Lancet, 2019)



### THANKS FOR YOUR ATTENTION!

## THANKS TO TNO, MANY TNO COLLEAGUES AND OTHERS FOR 38 GREAT YEARS

Jan Willem van der Kamp - TNO - 1985 - 2023

#### **PURDUE** UNIVERSITY

WHISTLER CENTER

for Carbohydrate Research

Food Science

Alignment of dietary fibers with gut bacteria for robust and predicted response

Bruce Hamaker and Thaisa Cantu-Jungles

Disclosure: RiteCarbs LLC (start-up)

WHISTLER CENTER FOR CARBOHYDRATE RESEARCH

Concept: Fermentable fiber structures align with gut bacteria and can be used to support them

- Hundreds, perhaps thousands, of diverse chemical structures
- Different physical structure types
  - Cell wall matrices

RDUE | Food Science

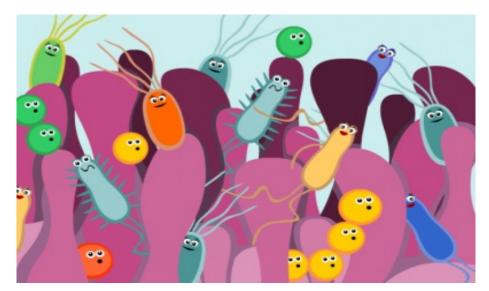
- Extracellular
   polysaccharides/biofilms
- Designed/modified physical structures



A Perspective on the Complexity of Dietary Fiber Structures and Their Potential Effect on the Gut Microbiota

### Variety of fermentable dietary fibers







### Matching fiber structures to specific gut bacteria

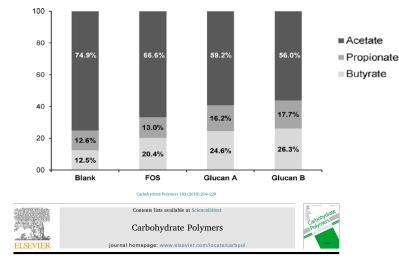
Matching fibers to preferentially support probiotic-type bacteria holds the promise of:

- Predictable and precise response for prebiotics
- Consistent response for population benefit



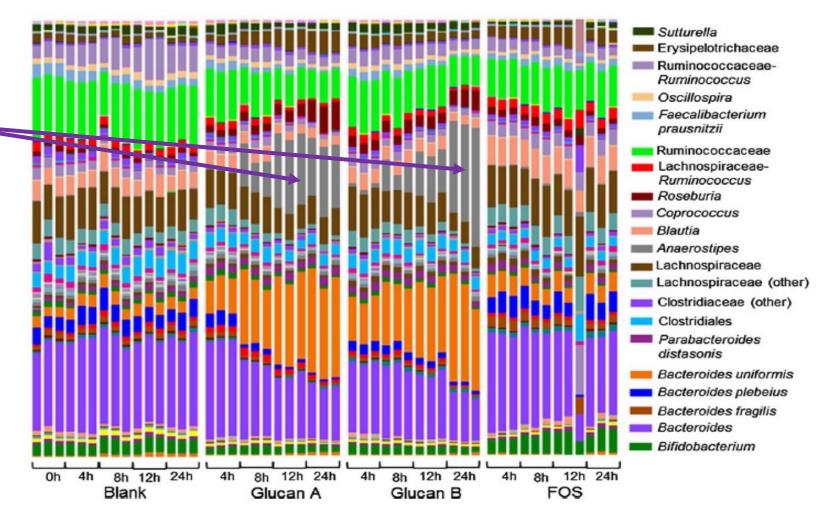
### Aligning structure to a butyrogenic genus

- Highly specific alignment of a fungal glucan to Anaerostipes, a butyrate producer in Clostridium cluster XIVa
- Substantial increase in butyrate production



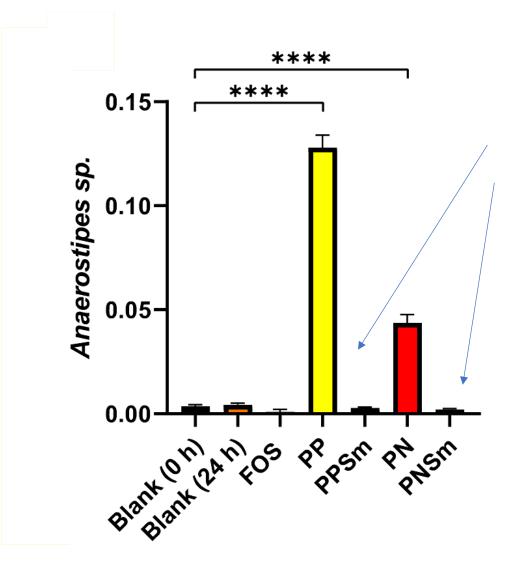
*In vitro* fermentation of *Cookeina speciosa* glucans stimulates the growth of the butyrogenic *Clostridium* cluster XIVa in a targeted way

Thaisa Moro Cantu-Jungles<sup>6,b</sup>, Andrea Caroline Ruthes<sup>6,c,d</sup>, Marwa El-Hindawy<sup>b</sup>, Roberta Barbara Moreno<sup>\*</sup>, Xiaowei Zhang<sup>b</sup>, Lucimara M.C. Cordeiro<sup>6,\*</sup>, Bruce R. Hamaker<sup>b,\*\*</sup>, Marcello Iacomini<sup>a</sup>





### **Relevance of fine structural alignment**



## Removal of β-D-glucan branches prevent *Anaerostipes sp.* promotion

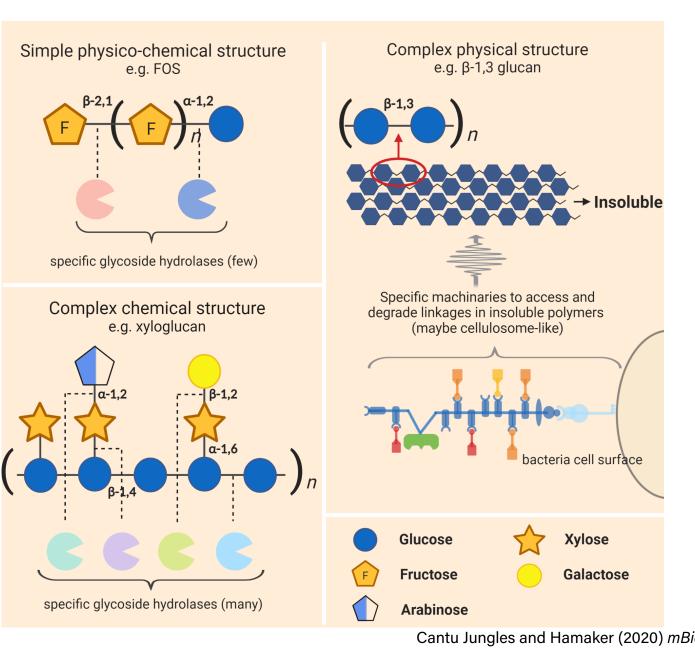
PP (branched insoluble β-D-glucan)
PN (branched soluble β-D-glucan)
PPSm (debranched β-D-glucan PP)
PNSm (debranched β-D-glucan PN)

In review, Carbohydr Polym

### Alignment of fiber structures to gut bacteria

Physico-structural variation of dietary fibers

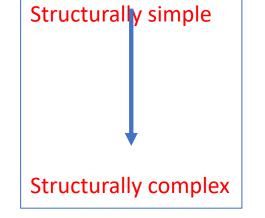
- Chemical structure
  - Monosaccharide composition
  - Polymer size
  - Branching distribution
  - Linkage types
- Physical structure/properties
  - Tri-dimensional arrangements (e.g., cell wall matrices)
  - Solubility degree
  - Viscosity





# Non-digestible oligosaccharides and mid-sized saccharides - examples

- Fructooligosaccharides
- Inulin
- Galactooligosaccharides
- Resistant maltodextrins
- Arabinoxylooligosaccharides



#### **Common starch-based material**

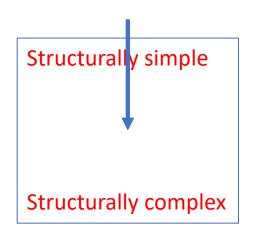
• Resistant starch (RS2 & RS3)

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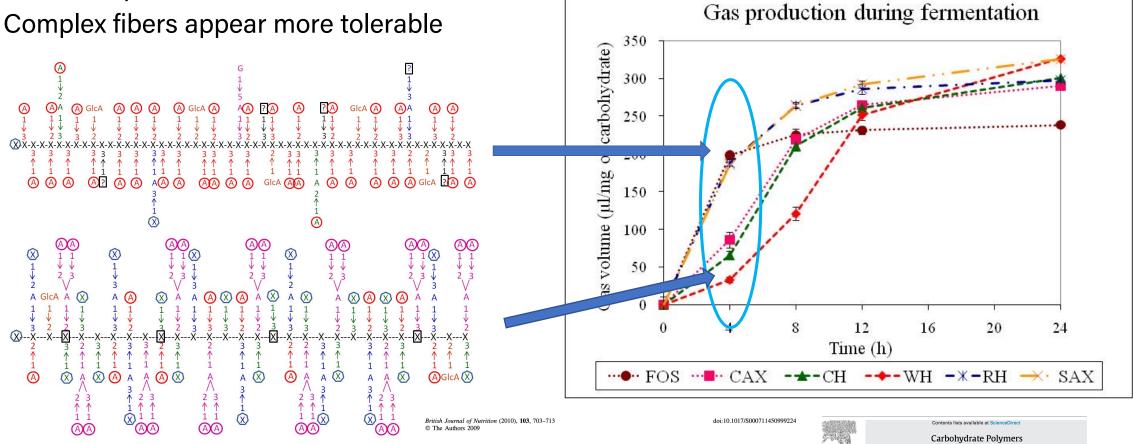
# Common non-starch polysaccharides (NSP)

- Cellulose
- β-Glucan
- Pectin
- Arabinoxylans



## **Tolerability**

Wheat AXOS (10 g) are tolerable (Cloetens et al., 2010)



Tolerance of arabinoxylan-oligosaccharides and their prebiotic activity in healthy subjects: a randomised, placebo-controlled cross-over study

Lieselotte Cloetens<sup>1</sup>, Willem F. Broekaert<sup>2</sup>, Yasmine Delaedt<sup>3</sup>, Frans Ollevier<sup>3</sup>, Christophe M. Courtin<sup>2</sup>, Jan A. Delcour<sup>2</sup>, Paul Rutgeerts<sup>1</sup> and Kristin Verbeke<sup>1</sup>\*

Structural features of soluble cereal arabinoxylan fibers associated with a slow rate of *in vitro* fermentation by human fecal microbiota

journal homepage: www.elsevier.com/locate/carbpol

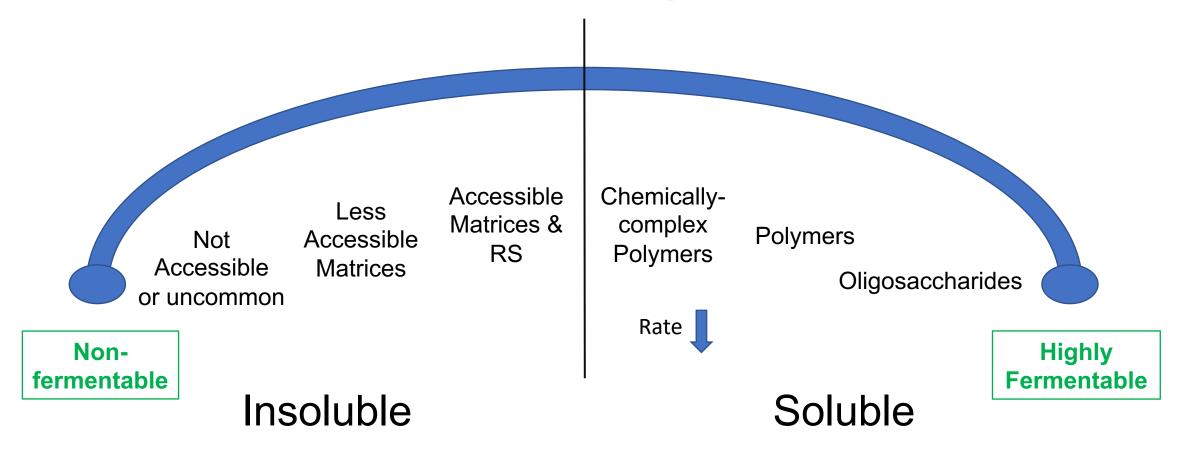
Pinthip Rumpagaporn<sup>a,1</sup>, Brad L. Reuhs<sup>a</sup>, Amandeep Kaur<sup>a</sup>, John A. Patterson<sup>b</sup>, Ali Keshavarzian<sup>c</sup>, Bruce R. Hamaker<sup>a,\*</sup>



### **Classifying dietary fibers for gut health**

- Soluble vs insoluble
- Fermentable vs non-fermentable
- Prebiotic vs non-prebiotic

### **Fiber Fermentability Spectrum**





# **Strategies to find alignment of fibers to bacteria**

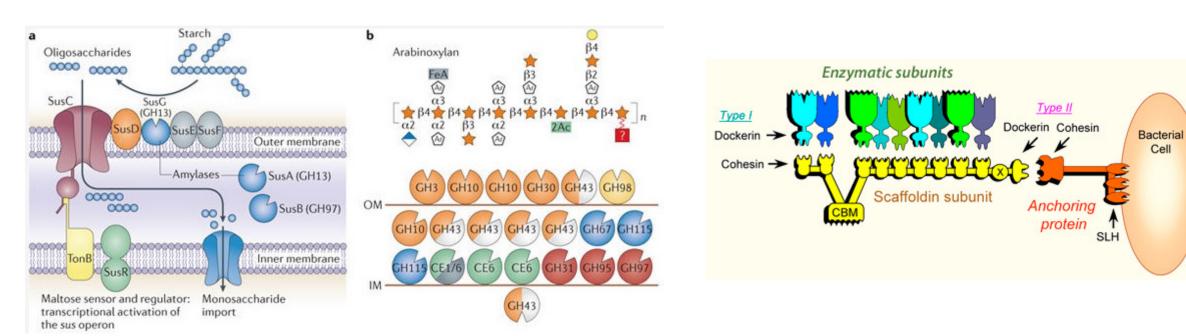
#### Alignment of chemical structures

- Look at the ability that different bacteria have to **degrade** fiber CHOs
  - The genomic presence of Carbohydrate-Active Enzymes, which are specific to the sugar moiety and linkage type in the molecule

#### Understanding chemical and physical matrix alignment

- Look at the machinery that different bacteria have to **access** fiber CHOs
  - Some have to physically bind to substrates (e.g. SUS-like systems, gram (-) bacteria, such as Bacteroides spp.)
  - Some have long appendages (cellulosomes) with enzymes attached to "reach in" and get CHOs from insoluble fiber matrices (e.g. Clostridia, such as *Ruminococcus spp.*)
  - Some have ports that directly and efficiently take in oligosaccharides (e.g. *Bifidobacterium spp.*)





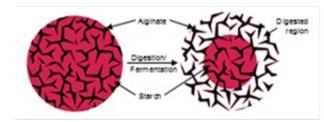
#### SUS-like

Source: CAZypedia

Cellulosomes

Koropatkin et al., Nat Rev Microbiol 10, 323-335, 2012

### **Aligning physical structure to butyrogenic Firmicutes**

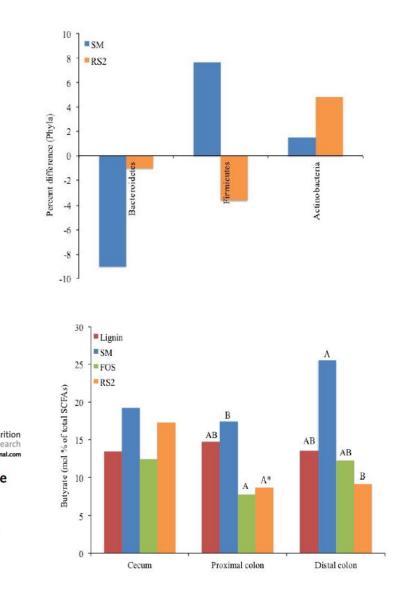


- Mouse study 2 types resistant starch - physically accessible (RS2) and inaccessible (starch microspheres, SM)
  - Phyla shift to Firmicutes
  - >2x mol% butyrate for SM group in distal colon

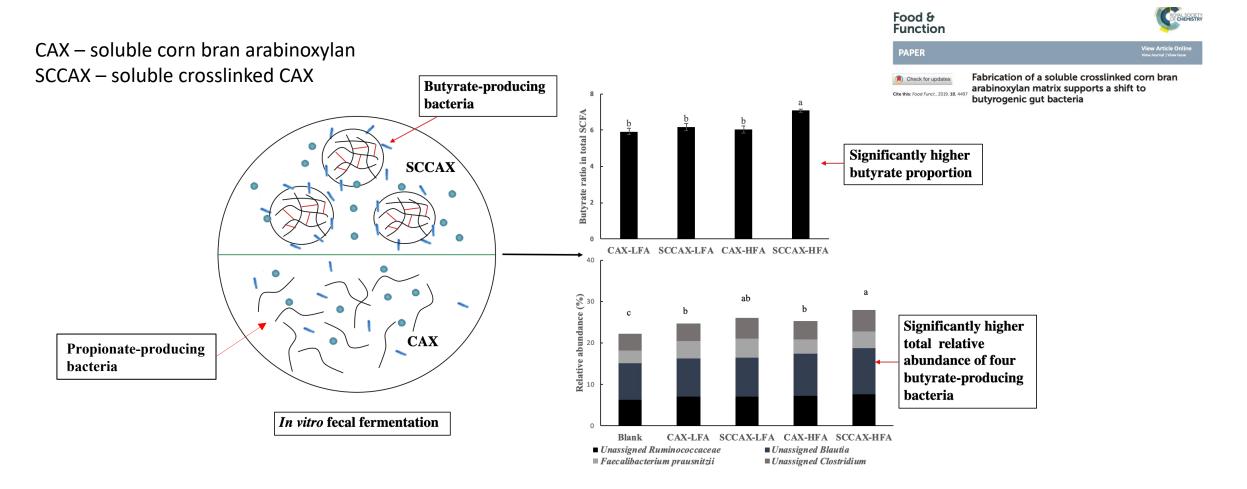
RESEARCH ARTICLE	Molecular Nutri Food Rese
Fiber and Gut Microbiota	www.mnf-journa

Physical Inaccessibility of a Resistant Starch Shifts Mouse Gut Microbiota to Butyrogenic Firmicutes

Amandeep Kaur, Tingting Chen, Stefan J. Green, Ece Mutlu, Berdine R. Martin, Pinthip Rumpagaporn, John A. Patterson, Ali Keshavarzian, and Bruce R. Hamaker\*



# Soluble crosslinked corn bran arabinoxylan matrix promotes butyrate proportion and butyrogenic bacteria

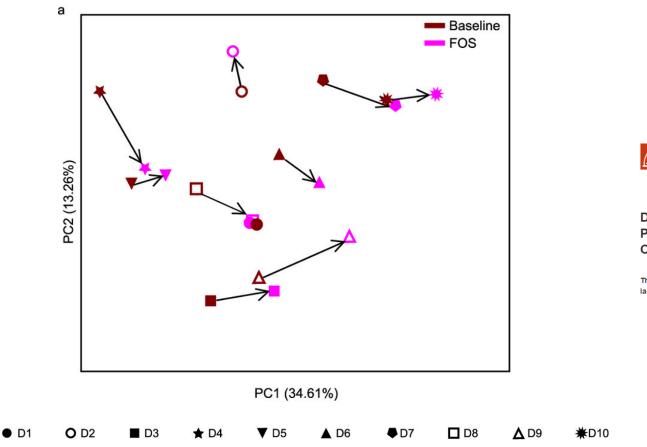


#### DIETARY FIBERS STRUCTURES CAN SUPPORT SPECIFIC GUT BACTERIA





#### USUALLY NO! DIFFERENT GUT MICROBIOTA COMMUNITIES RESPOND DIFFERENTLY TO FIBERS



Direction shifts in beta diversity (Weighted Unifrac) in 24 hours *in vitro* fecal fermentation of fructooligosaccharides (FOS)

RESEARCH ARTICLE May/June 2021 Volume 12 Issue 3 e01028-21 https://doi.org/10.1128/mBio.01028-21

Dietary Fiber Hierarchical Specificity: the Missing Link for Predictable and Strong Shifts in Gut Bacterial Communities

Thaisa M. Cantu-Jungles<sup>a</sup>, Nuseybe Bulut<sup>a</sup>, Eponine Chambry<sup>a</sup>, Andrea Ruthes<sup>b</sup>, Marcello lacomini<sup>b</sup>, Ali Keshavarzian<sup>c</sup>, Timothy A. Johnson<sup>d</sup>, and Bruce R. Hamaker 💿 <sup>a</sup>

Article | Open Access | Published: 01 June 2017

#### Fiber-utilizing capacity varies in Prevotella- versus **Bacteroides-dominated gut microbiota**

Tingting Chen, Wenmin Long, Chenhong Zhang, Shuang Liu, Liping Zhao 🖾 & Bruce R. Hamaker 🖾

Scientific Reports 7, Article number: 2594 (2017) Cite this article 10k Accesses | 265 Citations | 28 Altmetric | Metrics

#### JOURNAL ARTICLE

#### Interindividual variability in gut microbiota and host response to dietary interventions a

Genelle R Healey ⊠, Rinki Murphy, Louise Brough, Christine A Butts, Jane Coad

Nutrition Reviews, Volume 75, Issue 12, December 2017, Pages 1059–1080, https://doi.org/10.1093/nutrit/nux062

Published: 28 November 2017

#### Research Open Access Published: 19 August 2020

Gut microbiota modulation with long-chain corn bran arabinoxylan in adults with overweight and obesity is linked to an individualized temporal increase in fecal propionate

Nguyen K. Nguyen, Edward C. Deehan, Zhengxiao Zhang, Mingliang Jin, Nami Baskota, Maria Elisa Perez-Muñoz, Janis Cole, Yunus E. Tuncil, Benjamin Seethaler, Ting Wang, Martine Laville, Nathalie M. Delzenne Stephan C. Bischoff, Bruce R. Hamaker, Inés Martínez, Dan Knights, Jeffrey A. Bakal, Carla M. Prado & Jens Walter 🗠





8 | Author Video | Observation | 6 September 2016

in 🔛

Individualized Responses of Gut Microbiota to Dietary Intervention Modeled in Humanized Mice

#### **OPINION** article

Front. Public Health, 29 April 2020 Sec. Digital Public Health Volume 8 - 2020 | https://doi.org/10.3389/fpubh.2020.00144 This article is part of the Research Topic Creating Evidence from Real World Patient Digital Data View all 14 Articles )

#### The Need for Personalized Approaches to Microbiome Modulation

Nita Jain

Independent Researcher, Lilburn, GA, United States

#### Review Article | Published: 20 September 2019

#### Diet-microbiota interactions and personalized nutrition

#### Aleksandra A. Kolodziejczyk, Danping Zheng & Eran Elinav

Nature Reviews Microbiology 17, 742–753 (2019) Cite this article 45k Accesses | 378 Citations | 283 Altmetric | Metrics

#### JOURNAL ARTICLE

#### Perspective: Leveraging the Gut Microbiota to Predict Personalized Responses to Dietary, Prebiotic, and Probiotic Interventions 👌

Sean M Gibbons 🖾, Thomas Gurry, Johanna W Lampe, Anirikh Chakrabarti, Veerle Dam, Amandine Everard, Almudena Goas, Gabriele Gross, Michiel Kleerebezem, Jonathan Lane ... Show more

Advances in Nutrition, Volume 13, Issue 5, September 2022, Pages 1450–1461, https://doi.org/10.1093/advances/nmac075 Published: 01 July 2022 Article history •



#### 8 | Minireview | 29 September 2020

The Gut Microbiome and Individual-Specific Responses to Diet

Authors: Avner Leshem, Eran Segal, Eran Elinav 🙂

AUTHORS INFO & AFFILIATIONS

DOI: https://doi.org/10.1128/mSystems.00665-20 • (R) Check for updates • Special Series: Minireviews with Enhanced Videos

Article | Open Access | Published: 01 June 2017

#### Fiber-utilizing capacity varies in Prevotella- versus **Bacteroides-dominated gut microbiota**

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Scientific Reports 7, Article number: 2594 (2017) Cite this article 10k Accesses | 265 Citations | 28 Altmetric | Metrics

#### JOURNAL ARTICLE Interindivi host respo Genelle R Healey Nutrition Reviews. https://doi.org/10 Published: 28 No Research Open Access Gut microbiota arabinoxylan i linked to an in propionate Nguyen K. Nguyen, Edward C. Muñoz, Janis Cole, Yunus E. Tunci Stephan C. Bischoff, Bruce R. Hamaker, Inés Martínez, Dan Knights, Jeffrey A. Bakal, Carla M. Prado & Jens Walter 🗠 top-ranked journals

8 | Author Video | Observation | 6 September 2016

Individualized Responses of Gut Microbiota to Dietary Intervention Modeled in Humanized Mice

Authors: Samuel A. Smits, Angela Marcobal, Steven Higginbottom, Justin L. Sonnenburg, Purna C. Kashyap | AUTHORS INFO & AFFILIATIONS

#### **OPINION** article

Front. Public Health, 29 April 2020 Sec. Digital Public Health Volume 8 - 2020 | https://doi.org/10.3389/fpubh.2020.00144 This article is part of the Research Topic Creating Evidence from Real World Patient Digital Data View all 14 Articles >

The Need for Personalized Approaches to Microbiome Modulation

# Is there a way to have similar gut microbial responses to dietary fibers?

ut Microbiota to es to Dietary, ventions 👌 npe, Anirikh Chakrabarti, Veerle Dam, , Michiel Kleerebezem, Jonathan Lane

er 2022, Pages 1450–1461,

8 | Minireview | 29 September 2020

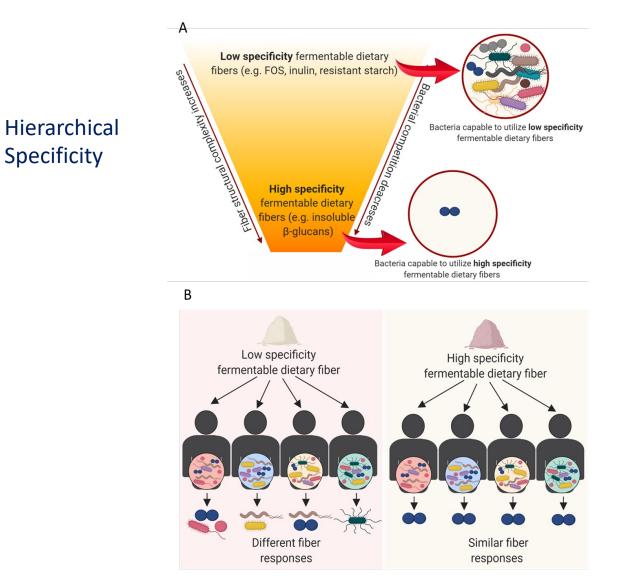
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The Gut Microbiome and Individual-Specific Responses to Diet

Authors: Avner Leshem, Eran Segal, Eran Elinav 💷 | AUTHORS INFO & AFFILIATIONS DOI: https://doi.org/10.1128/mSystems.00665-20 • 🔘 Check for updates • Special Series: Minireviews with Enhanced Videos 

### Using fiber alignment, potentially can gain common responses

Specificity







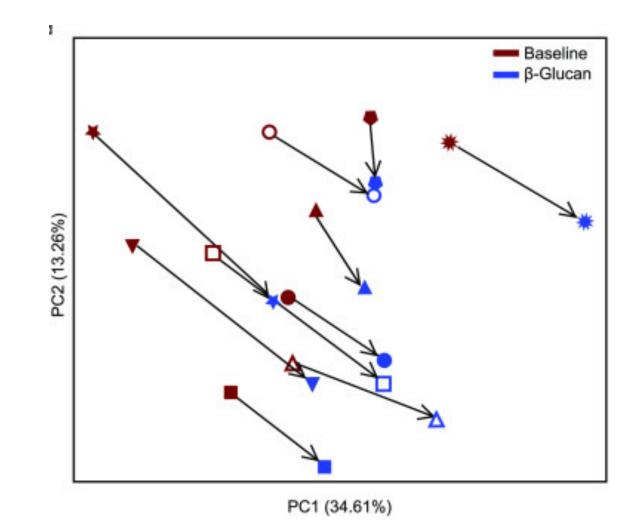
New View on Dietary Fiber Selection for Predictable Shifts in **Gut Microbiota** 

T. M. Cantu-Jungles,<sup>a</sup> 💿 B. R. Hamaker<sup>a</sup>

With this approach only specific beneficial bacteria are fed, and response is homogenous across people!



#### HERE, DIFFERENT GUT MICROBIOTA COMMUNITIES RESPOND THE SAME TO THE HIGHLY SPECIFIC FIBER





nigh specificity) *Versus* non BOHYDRATE RESEARCH

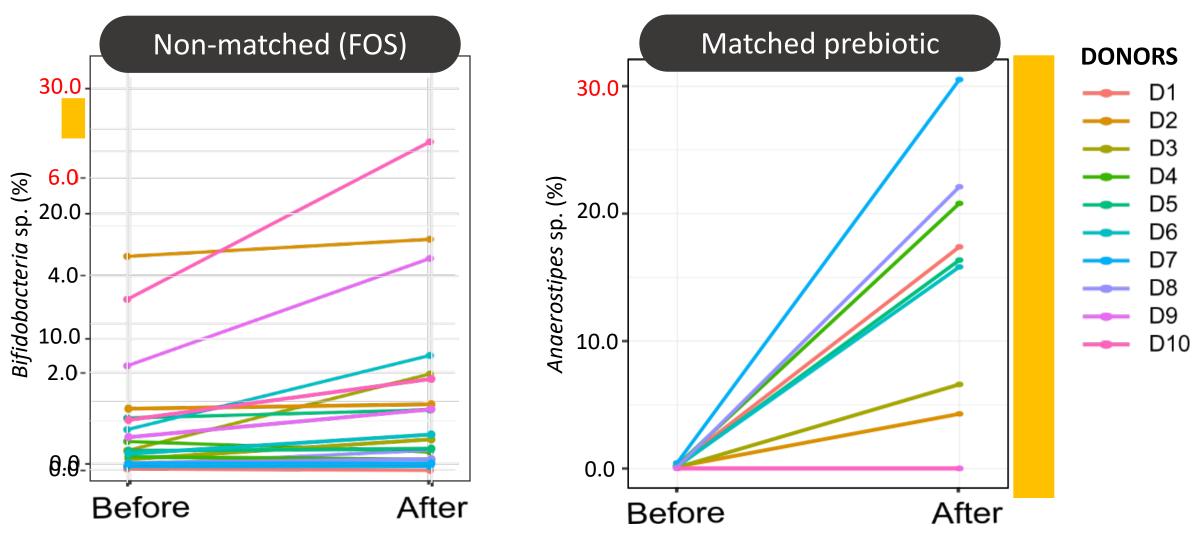
**Robust Responses** 

#### matched (low specificity)



Dietary Fiber Hierarchical Specificity: the Missing Link for Predictable and Strong Shifts in Gut Bacterial Communities

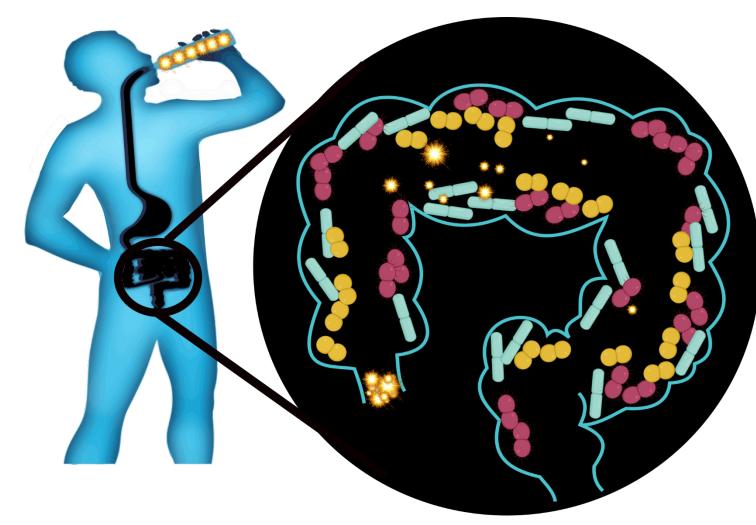
Thaisa M. Cantu-Jungles<sup>a</sup>, Nuseybe Bulut<sup>a</sup>, Eponine Chambry<sup>a</sup>, Andrea Ruthes<sup>b</sup>, Marcello Iacomini<sup>b</sup>, Ali Keshavarzian<sup>c</sup>, Timothy A. Johnson<sup>d</sup>, and Bruce R. Hamaker 😰 <sup>a</sup>





## Can we match a fiber to any bacteria?

# Prebiotic "matching technology"



Prebiotic fibers that promote gut bacteria in a targeted way

- Promotes specific gut microbes or key groups
- Consistent response across different individuals
- Allows promotion of bacteria that are difficult to cultivate outside the body



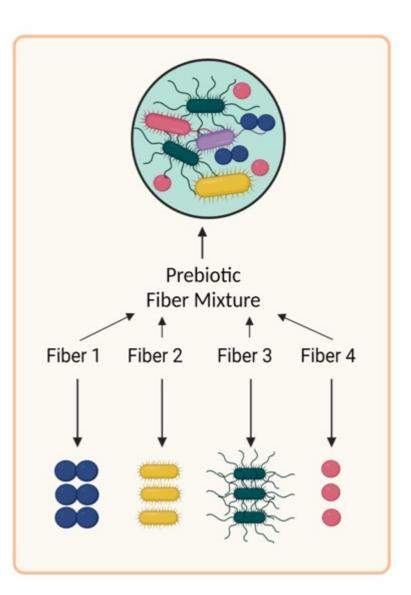
### Potential of aligned or "precision" prebiotics

- Target specific microbial taxa or groups of microbes
- Robust promotion of target bacteria and related health responses
- Works with oral probiotics, as well as gut-resident probiotics
- More consistent results in different individuals
  - Circumvent the need for individualized testing of gut microbiota responses to fiber
  - ✓ Effective at population levels

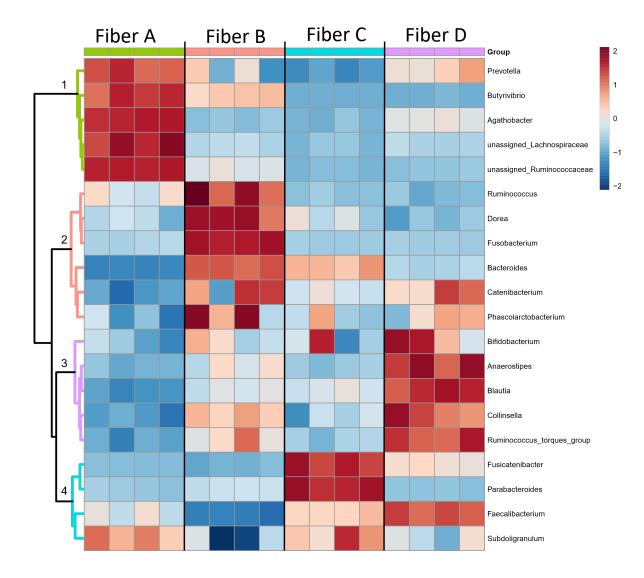
# Same approach of alignment towards groups led to prebiotic fiber mixtures for gut health

To support the core microbiome:

• Mix fibers that align to important healthrelated gut bacteria



### Core gut microbiota support – Parkinson disease



# Complementary groups of bacteria are promoted with our designed fiber mixture



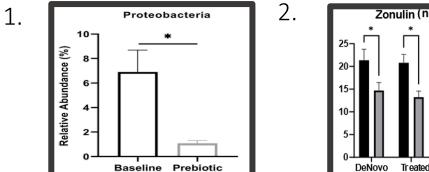
Nat Commun. 2023; 14: 926. Published online 2023 Feb 18. doi: <u>10.1038/s41467-023-36497-x</u> PMCID: PMC9938693 PMID: <u>36801916</u>

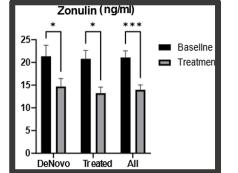
An open label, non-randomized study assessing a prebiotic fiber intervention in a small cohort of Parkinson's disease participants

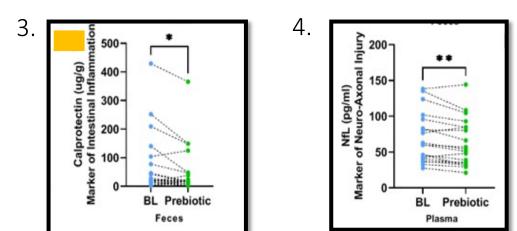
Deborah A. Hall,<sup>#1</sup> Robin M. Voigt,<sup>#2,3,4</sup> Thaisa M. Cantu-Jungles,<sup>3,5</sup> Bruce Hamaker,<sup>3,5</sup> Phillip A. Engen,<sup>3</sup> Maliha Shaikh,<sup>3</sup> Shohreh Raeisi,<sup>3</sup> Stefan J. Green,<sup>2,3,6</sup> Ankur Nagib,<sup>3,4</sup> Christopher B. Forsyth,<sup>2,3,4</sup> Tingting Chen,<sup>5,7</sup> Richard Manfready,<sup>2</sup> Bichun Ouyang,<sup>1</sup> Heather E. Rasmussen,<sup>3,8</sup> Shahriar Sedghi,<sup>9</sup> Christopher G. Goetz,<sup>1</sup> and Ali Keshavarzian<sup>82,3,4,10</sup>

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### Core gut microbiota support – Parkinson disease







✓ Highly tolerable<sup>1</sup>

✓ Effective<sup>1</sup> in only 10 days to:

- 1. Promote a healthier balance of bacteria in the gut
- 2. Increase gut epithelial health
- 3. Reduce intestinal inflammation
- 4. Reduce brain injury

<sup>1</sup> Based on a Clinical trial with 20 Parkinson Disease patients, consuming 20g/day of the fiber mixture for 10 days



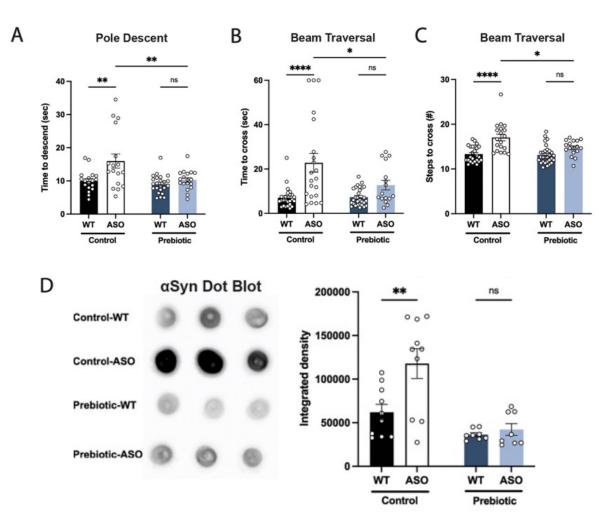
Nat Commun, 2023; 14: 926. Published online 2023 Feb 18. doi: <u>10.1038/s41467-023-36497-x</u> PMCID: PMC9938693 PMID: <u>36801916</u>

An open label, non-randomized study assessing a prebiotic fiber intervention in a small cohort of Parkinson's disease participants

Deborah A. Hall,<sup>#1</sup> Robin M. Voigt,<sup>#2,3,4</sup> Thaisa M. Cantu-Jungles,<sup>3,5</sup> Bruce Hamaker,<sup>3,5</sup> Phillip A. Engen,<sup>3</sup> Maliha Shaikh,<sup>3</sup> Shohreh Raeisi,<sup>3</sup> Stefan J. Green,<sup>2,3,6</sup> Ankur Nagib,<sup>3,4</sup> Christopher B. Forsyth,<sup>2,3,4</sup> Tingting Chen,<sup>5,7</sup> Richard Manfready,<sup>2</sup> Bichun Ouyang,<sup>1</sup> Heather E. Rasmussen,<sup>3,8</sup> Shahriar Sedghi,<sup>9</sup> Christopher G. Goetz,<sup>1</sup> and Ali Keshavarzian<sup>32,3,4,10</sup>

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### Fiber mixture on mice model Parkinson disease

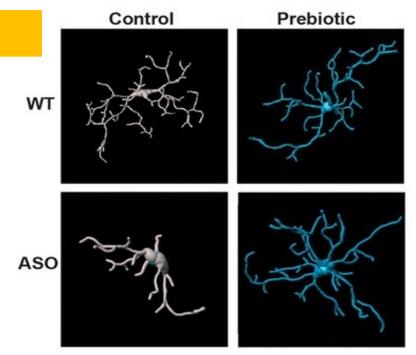


Prebiotic diet improves some of the motor deficits in ASO mice (A,B and C) and reduced  $\alpha$ -synuclein expression (D).

> Elife. 2022 Nov 8;11:e81453. doi: 10.7554/eLife.81453.

#### A prebiotic diet modulates microglial states and motor deficits in α-synuclein overexpressing mice

Reem Abdel-Haq <sup>1</sup><sup>2</sup>, Johannes C M Schlachetzki <sup>3</sup>, Joseph C Boktor <sup>1</sup>, Thaisa M Cantu-Jungles <sup>4</sup>, Taren Thron <sup>1</sup>, Mengying Zhang <sup>1</sup>, John W Bostick <sup>1</sup>, Tahmineh Khazaei <sup>1</sup>, Sujatha Chilakala <sup>5</sup>, Livia H Morais <sup>1</sup>, Greg Humphrey <sup>6</sup>, Ali Keshavarzian <sup>7</sup><sup>8</sup>, Jonathan E Katz <sup>5</sup>, Matthew Thomson <sup>1</sup>, Rob Knight <sup>6</sup> <sup>9</sup> <sup>10</sup> <sup>11</sup>, Viviana Gradinaru <sup>1</sup><sup>2</sup>, Bruce R Hamaker <sup>4</sup>, Christopher K Glass <sup>3</sup>, Sarkis K Mazmanian <sup>1</sup><sup>2</sup>



Prebiotic diet alters microglia morphology and reactivity status in ASO mice -Representative 3D reconstructions of microglia imaged at 40 X magnification.



### **OPPORTUNITIES IN THE DESIGN OF PREBIOTICS**

Fibers for targeted, predicted, common response across individuals

Mixture of fibers aligned to resident health-related microbial groups to support the core community and promote overall health

Blends of fibers designed to support marginalized bacterial groups in specific disease states towards disease treatment and prevention

From material side, use of processing techniques to make a new generation of fiber prebiotics

#### WHISTLER CENTER for Carbohydrate Research

Purdue University Whistler Center for Carbohydrate Research 745 Agriculture Mall Drive West Lafayette, IN 47907-2009 whistlercenter@purdue.edu www.whistlercenter.purdue.edu

# **QUESTIONS?**



Food Science

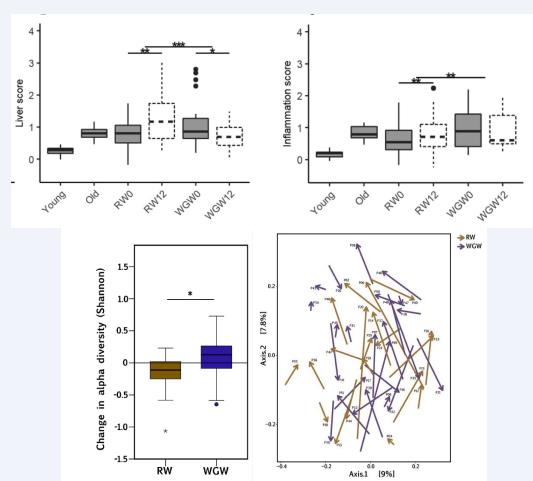
### **No Guts No Glory** Metabolic phenotyping and Microbiome Lessons Learned

Femke Hoevenaars, PhD. | MSB, HLW



# Introduction

• **Objective:** The health impact of WGW consumption was investigated by quantification of the body's resilience, which was defined as the "ability to adapt to a standardized challenge".



The Journal of Nutrition **Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions** 

#### Whole Grain Wheat Consumption Affects Postprandial Inflammatory Response in a Randomized Controlled Trial in Overweight and Obese Adults with Mild Hypercholesterolemia in the Graandioos Study

Femke PM Hoevenaars,<sup>1</sup> Diederik Esser,<sup>2</sup> Sophie Schutte,<sup>2</sup> Marion G Priebe,<sup>3</sup> Roel J Vonk,<sup>3</sup> Willem J van den Brink,<sup>1</sup> Jan-Willem van der Kamp,<sup>1</sup> Johanna HM Stroeve,<sup>1</sup> Lydia A Afman,<sup>2</sup> and Suzan Wopereis<sup>1</sup>

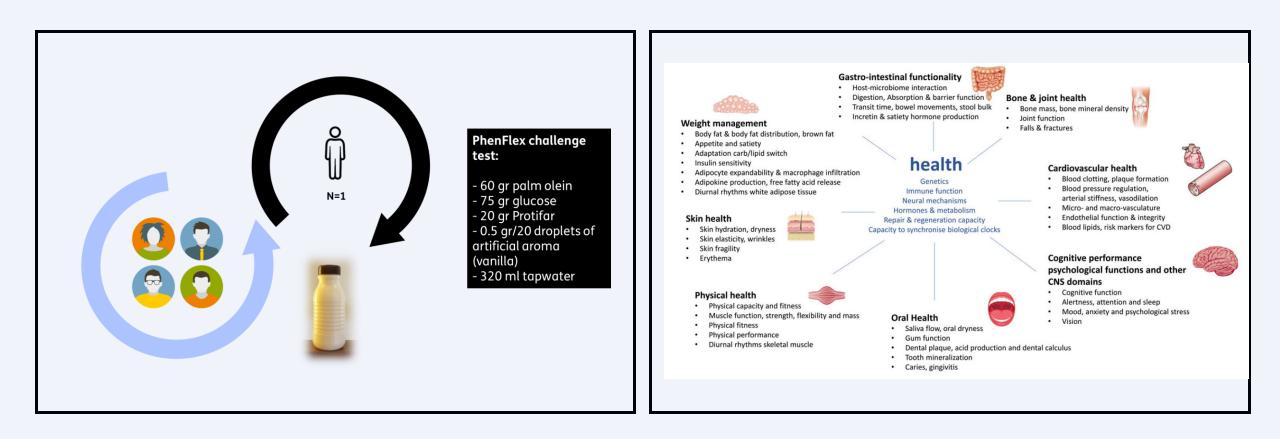
<sup>1</sup>TNO, Netherlands Organization for Applied Scientific Research, Zeist, Netherlands; <sup>2</sup>Wageningen University, Division of Human Nutrition, Wageningen, Netherlands; and <sup>3</sup>University Medical Center Groningen, University of Groningen, Center for Medical Biomics, Groningen, Netherlands

Fiber consumption				
Refined	2.5 g fibres/day			
Whole grain	10.3 g fibres/day			

many changes in individual variation at baseline, makes drawing conclusions difficult with n=25 per group

From: Stroeve et al. Genes Nutr. 2015; 10:13 From: Wopereis S, Proc Nutr Soc. 2022:1-13.

# **Metabolic Phenotyping**

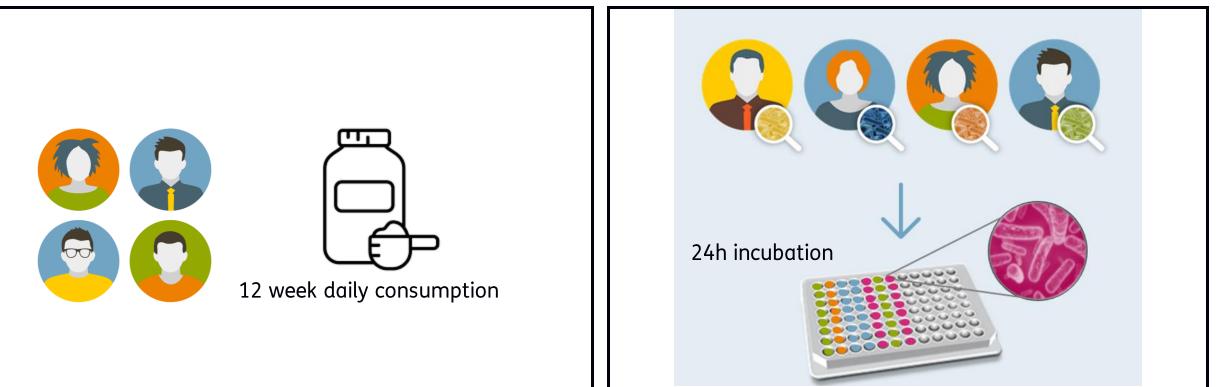




### A fiber intervention for microbiome modulation

# in vivo

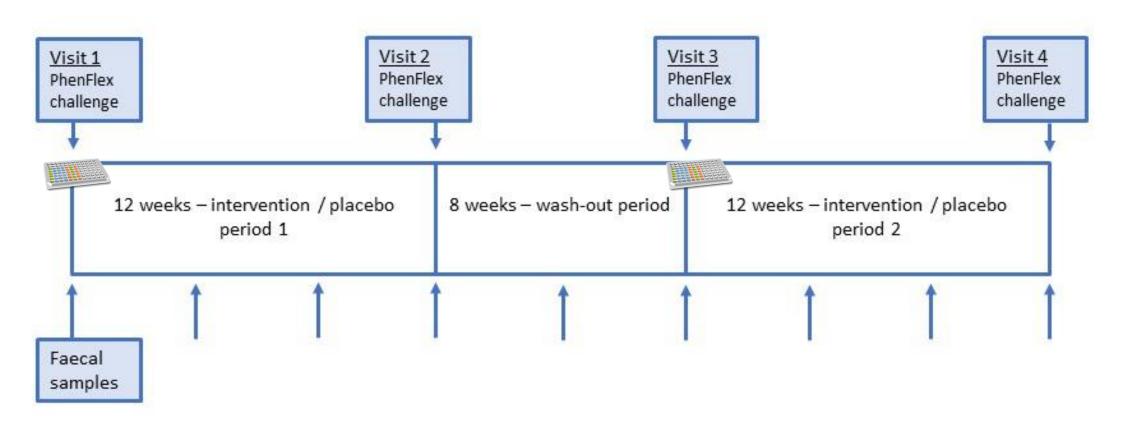
# in vitro



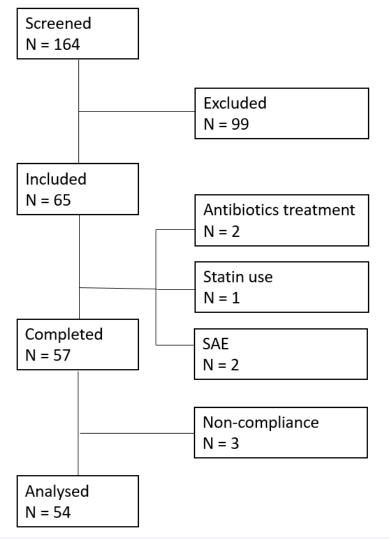
# Study design in vivo

#### Study population

- 54 subjects, males (29) and post menopausal females (25)
- 45-70 years
- BMI 25-30kg/m2
- Low fiber intake
- No medication influencing metabolism such as statins or metformin
- No recent antibiotic usage



# **Baseline Characteristics**



	Entire cohort (N=54)	Males (N=29)	Females (N=25)
Gender (N, %)	N/A	29,53.7%	25,46.3%
Age, years (mean ±SD)	57.9±5.8	60.0±6.1	55.7±4.9
BMI, kg/m² -(mean, SD)	27.3±1.4	27.3±1.4	27.3±1.3



# **Microbiome modulation**



# Two clusters discernable in Phenflex biomarker response



# Take home message

Microbiome modulation

• The fiber mixture was able to modulate the microbiome after 4 weeks of ingestion

#### Metabolic phenotyping

• Clustering on postprandial metabolism indicates a subset of metabolic responding participants

In vivo versus in vitro outcomes

• More to come...



# Acknowledgements

The collaboration project is co-funded by the PPP Allowance made available by Top Sector Agri & Food to stimulate public-private partnerships.

### dsm-firmenich 👄

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- Remon Dulos
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# TNO innovation for life

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  - Margreet Heerikhuisen →
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- Nicole Plomp
- Angelique Kreikamp
- Femke Schaafsma\*
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Elwin Verheij

**Birol** Usta

Petra

- Matthijs van Moerland
- > Boukje Eveleens Maarse
- Bas van Kraaij





# NL Health~Holland



### THANK YOU FOR YOUR TIME

Dr. Femke Hoevenaars Senior Scientist Nutritional Physiology and Metabolism Microbiology & Systems Biology

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#### Targeted microbiome modulation through dietary fibres: a new chapter in precision nutrition

Frank Schuren, PhD. | MSB, HLW TNO

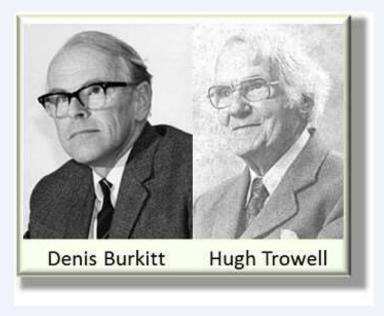


### **Fibres historically**

The history of dietary fibre goes all the way back to ancient Greece. However, although it has been known since then that wheat bran<sup>\*1</sup> is good for preventing constipation, dietary fibre was thought to be food waste that was not absorbed by the intestines, and was even thought to cause the excretion of essential nutrients.

#### 1970s Dietary Fibres Hypothesis

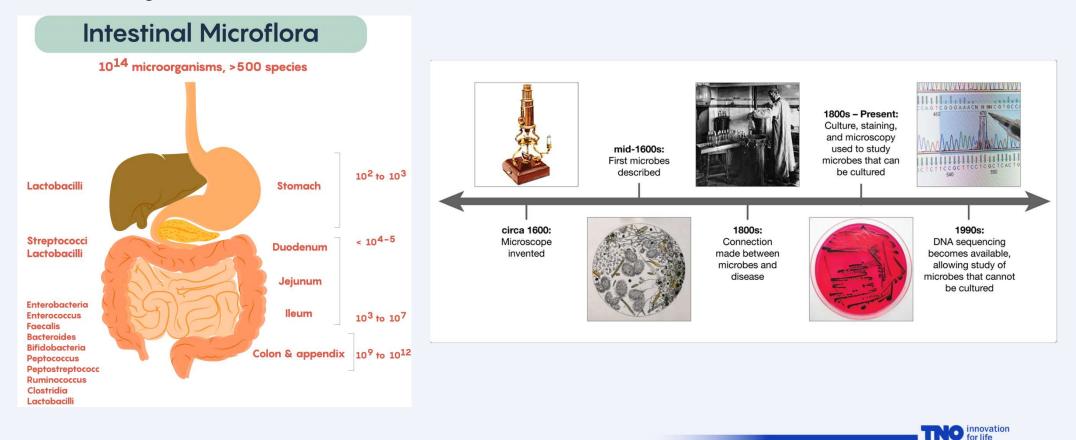
The role of dietary fibres in human health and its relation to Western diseases





### History of the human gut microbiome

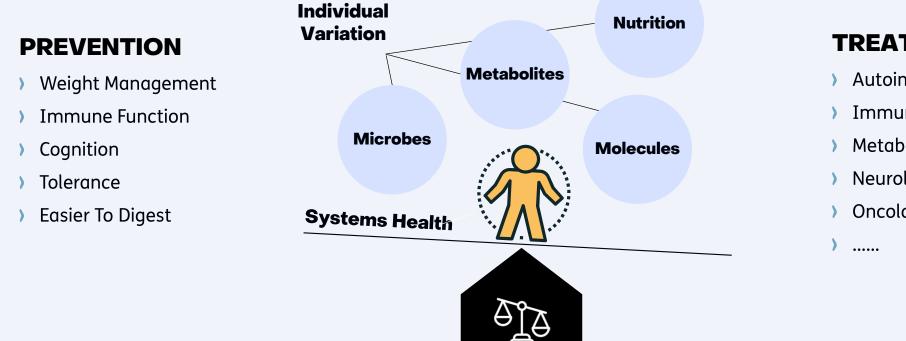
• Around year 2000



#### Human microbiome revolution

- Year 2000: TNO management saying: why should we study these beasts (=microbes), we study humans!
- Much happened since then: we now suffer from a microbiome hype
- However, it has become clear that the human microbiome is an integral part of the human body and system and plays important roles in health and diseases
- The current challenge is how to modulate the microbiome in order to stimulate health and prevent disease
- And that is where fibres com into play

### Human microbiome and systems health



#### TREATMENT

- Autoimmune
- Immuno-inflammatory
- Metabolic
- Neurological
- Oncology



#### Fiber

- Fiber driven microbiome effects
- Many prebiotic fibers show bifidogenic effect, but not all
- Induction SCFA production



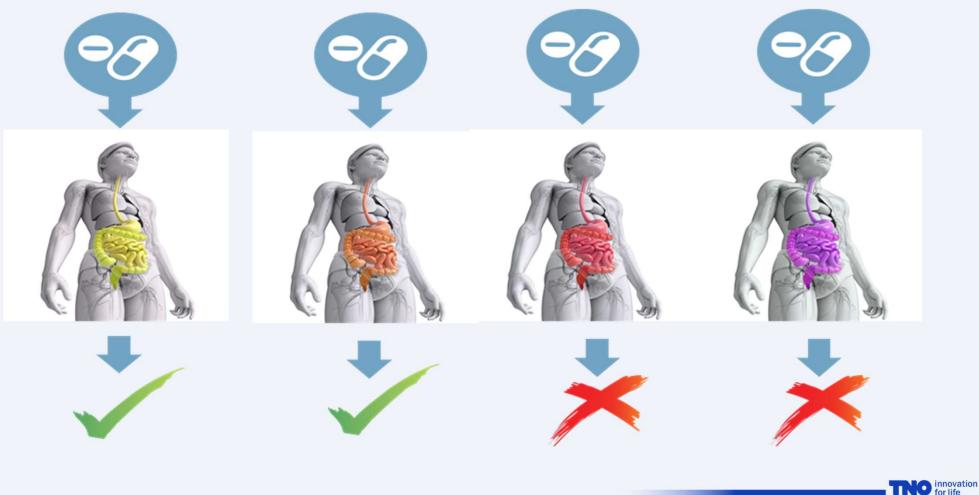
		ACETATE	PROPIONATE	N-BUTYRATE
untreated	0	51.4	8.4	8.0
FOS	4	55.2	11.4	13.5
inulin	4	83.2	10.8	14.7
alpha-GOS	4	77.1	6.5	14.3
beta-GOS	4	66.5	6.0	12.7
XOS-C	4	84.4	7.9	16.4
XOS-S	4	81.9	9.4	9.7
beta-glucan	4	<mark>80.2</mark>	<mark>31.0</mark>	<mark>19.2</mark>



Int J Mol Sci. 2018 Oct 10;19(10). In Vitro Fermentation of Selected Prebiotics and Their Effects on the Composition and Activity of the Adult Gut Microbiota. Fehlbaum S, Prudence K, Kieboom J, Heerikhuisen M, van den Broek T, Schuren FHJ, Steinert RE, Raederstorff D.

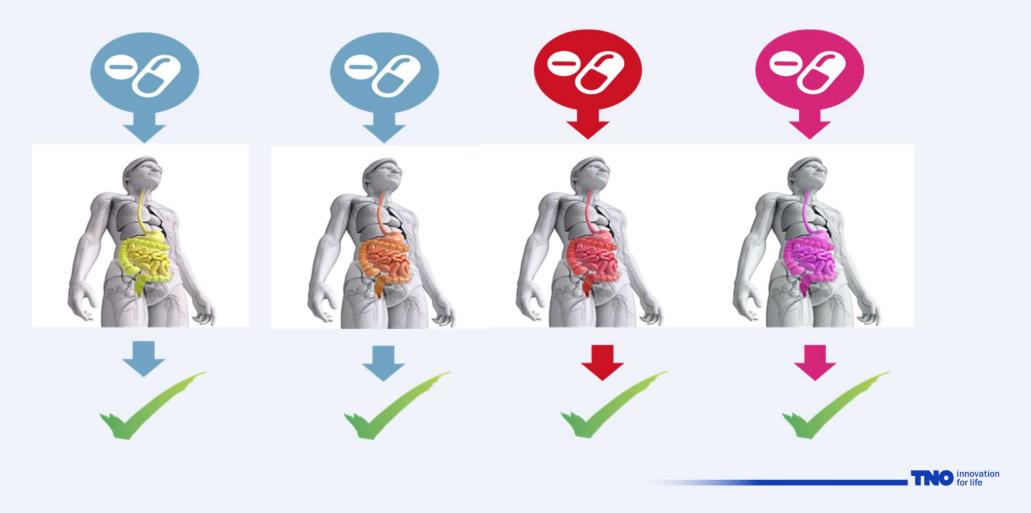
NGNG project

#### One size fits all does not work for microbiome

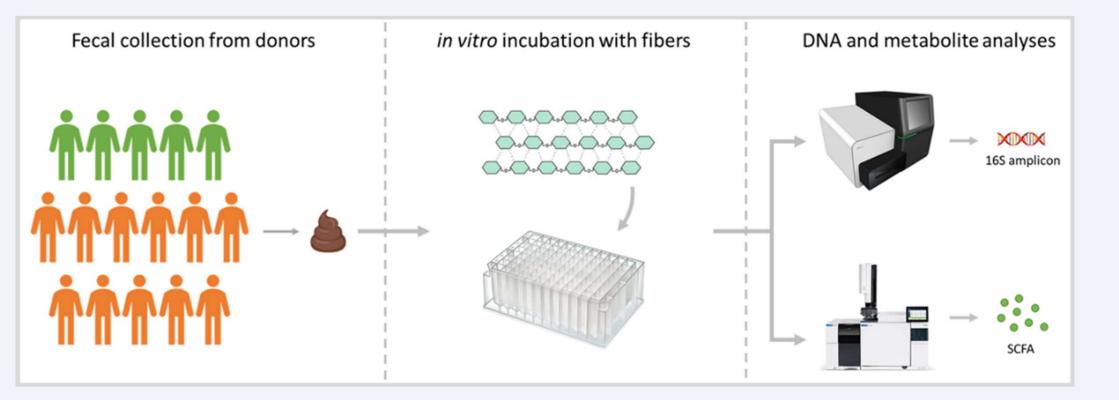


NGNG project

#### Novel personalized approaches are needed

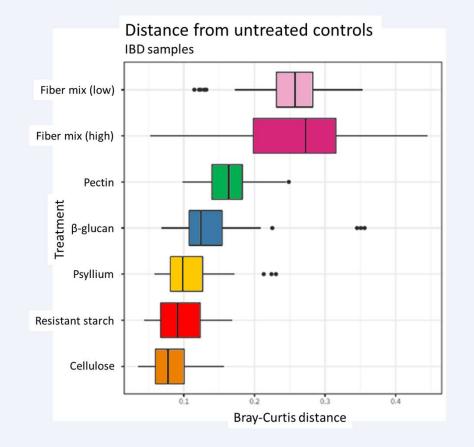


### **OUR ANALYTICAL APPROACH**





#### **EFFECT SIZE ON MICROBIOTA COMPOSITION**

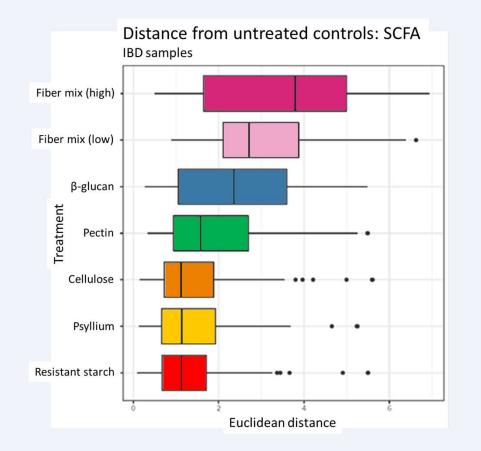


The fiber mixes have a stronger effect on microbiota composition than the individual fibers

Agamennone et al 2023

TNO innovation for life

#### **Fiber Effect on SCFA production**



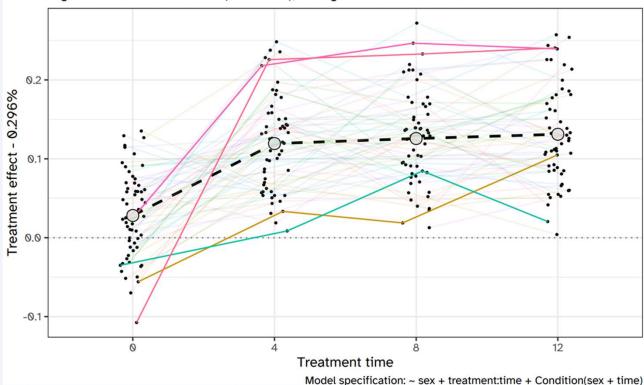
The fiber mixes have a stronger effect on SCFA production than the individual fibers



Agamennone et al 2023

### **Microbiome modulation results in humans**

Principal Response Curve analysis Includes taxa representing 95% of all classified reads Centre-log-ratio transformed Significant treatment effect (P < 0.001), no significant treatment:time interaction



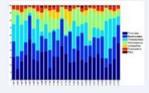
- Treatment effect for each participant is corrected for its placebo effect
- Mean treatment effect is significant, but not all subjects respond equally: large individual variation!

innovation

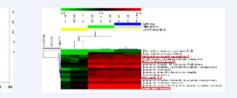
### Human intervention mimick in vitro in i-screen

- Microtiter plate platform for high throughput human gut fermentations
  - Colon (infants, children, teenagers, adults, obese)
  - > Pooled versus individual microbiome
- > Fully anaerobic culture conditions
- > Dedicated set-up for stabilizing high density gut microbiota
- Multiple read-outs

#### PCR DETECTION – GENUS LEVEL



#### METABOLOMICS

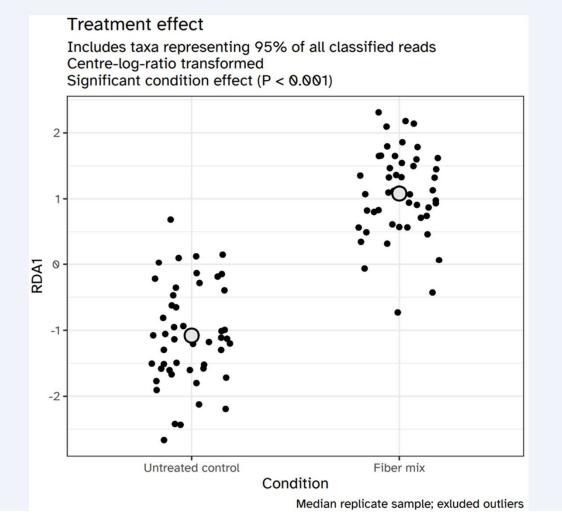


TRANSCRIPTOMICS



NGNG - Study ClinicalTrials.gov: NCT04829396

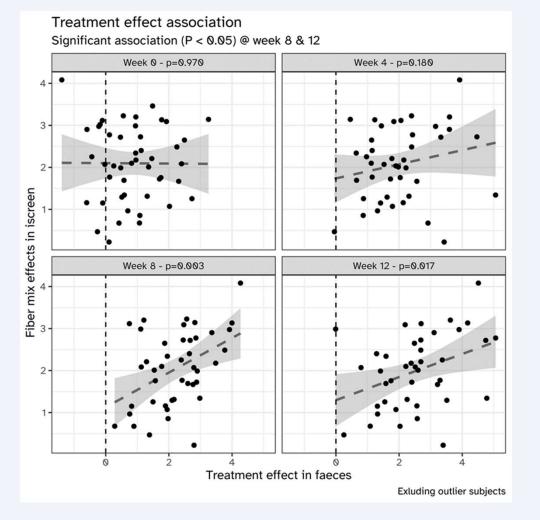
#### **Microbiome treatment effects in vitro**



 Mean treatment effect on βdiversity is significant, but not all subjects respond equally: large individual variation



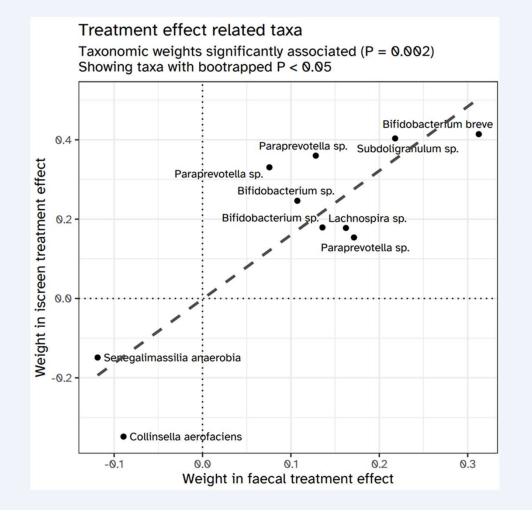
### **Comparison in vitro in vivo treatment effects**



- Treatment effect: within-subject difference between treatment and control situation
- Correlation of effect between in-vivo & in-vitro
  - Principal response curve analysis
  - Significant association at week 8 & 12



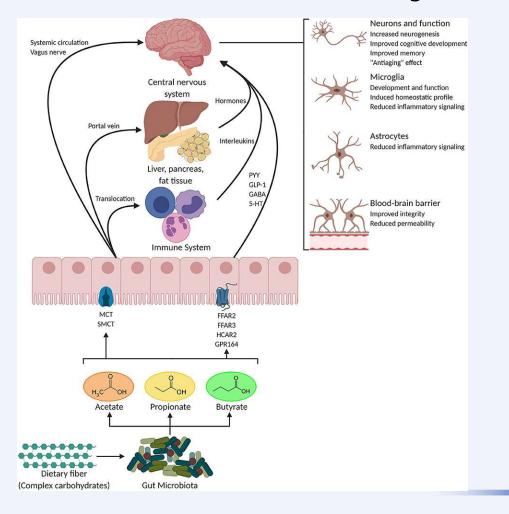
#### Taxa responding to treatment in vitro and in vivo



- Overlap in treatment-associated microbial taxa between in-vivo & in-vitro results
- This learns us in vitro results can be predictive for human effects

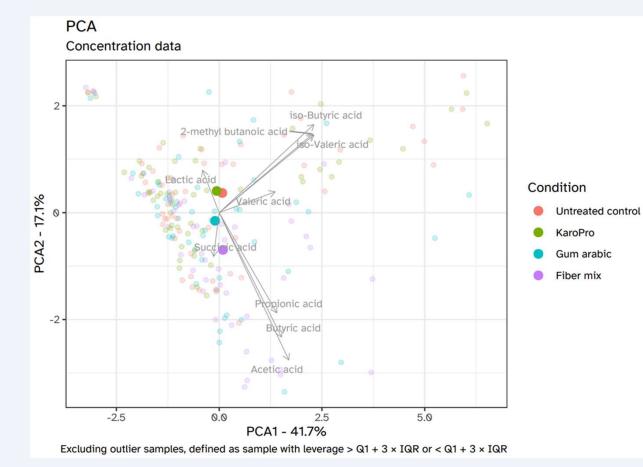


#### How do gut microbes influence systemic health?





#### **SCFA** results in vitro

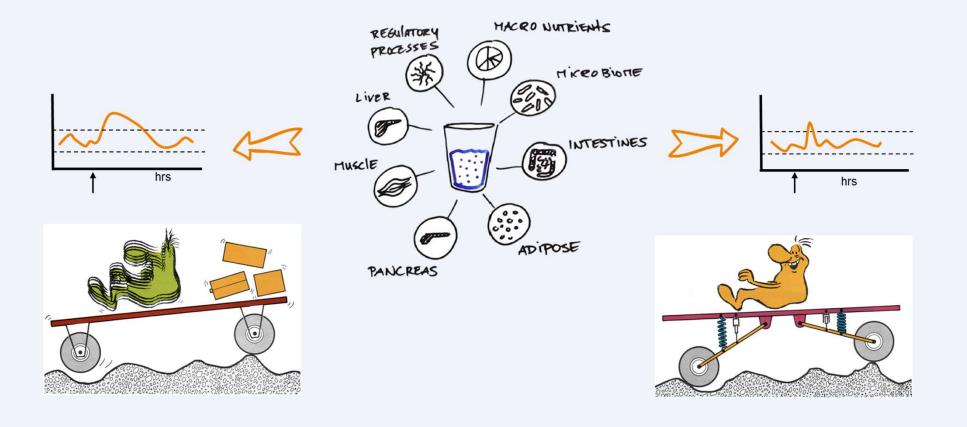


 Gum Arabic and Fiber mix significantly induce production of acetate, propionate and butyrate

• This may be an indication of systemic health effects

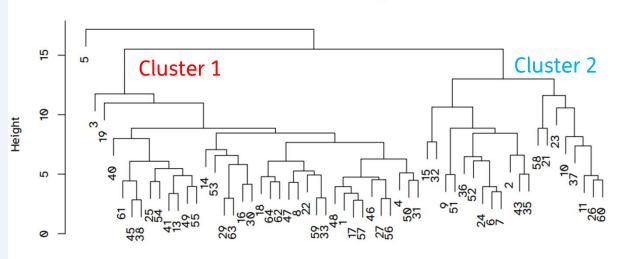


#### **PhenFlex challenge**





#### Two clusters discernable in Phenflex biomarker response



**Cluster Dendrogram** 

Based on metabolic features

Goal: indentification metabolic responders vs non-responders

Clustering of subjects by magnitude of change in metabolic features

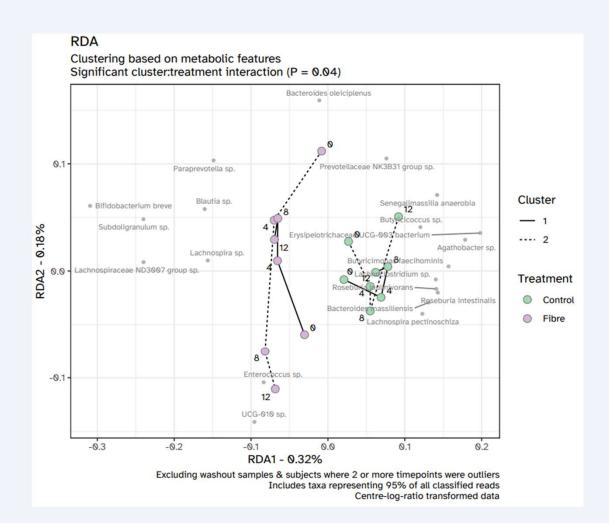
- Glucose
- Insulin
- Triglycerides
- Total cholesterol
- HDL cholestserol
- NEFA

Change is defined as difference between Placebo and Fibre condition at week 12

Clusters are independent of gender and fibre intake

#### **Metabolic phenotyping and Microbiome modulation**

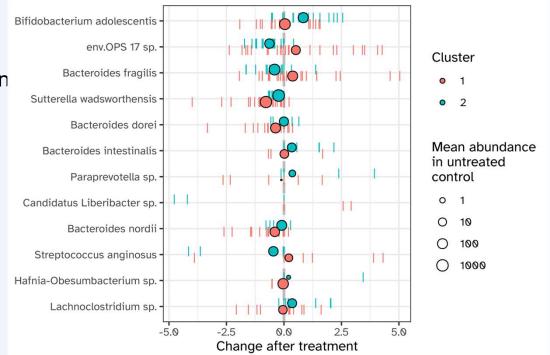
- Both clusters show a difference between control and treatment.
- There is a significant cluster treatment interaction indicating that clusters 1 and 2 show statistically significant differences in microbiome composition



No Guts No Glory - Confidential

#### **I-screen as a predictor for metabolic response**

- Elastic-net model for classification
  - Predicts responder/non-response
  - Using treatment induced change in i-screen
- Taxa ordered by importance in model
- Accuracy: 91.5%
  - Specificity: 100%
  - Sensitivity: 88.2%
  - 4 misclassified subjects



**Conclusion:** The *in vitro* i-screen results can predict with high accuracy whether a participant will be a PhenFlex reponder or non-responder



NGNG study

### **Ecological Momentary Assessment (EMA)**

(a.k.a. experience sampling methodology)

#### **Collecting everyday life data**

- Behavior (diet, social activity, etc)
- Mood, anxiety, stress, well-being
- Context (social, location, etc)
- Short and immediate questionnaires
- Repeated assessment, timing can be decided



Events (daily events, pleasant and/or unpleasant)

**Positive affect** (6 items: relaxed, energetic, enthusiastic, content, calm, and cheerful)

**Negative affect** (6 items: gloomy, anxious, nervous, irritable, dull, and tired)



#### NGNG study

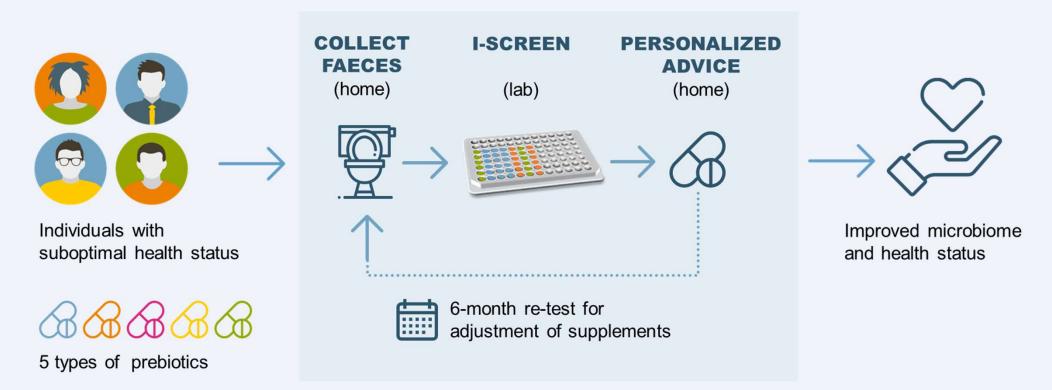
# **Prebiotic intervention improves daily mood in healthy adults**

- Negative affect: fibre treatment results in improvement in females
- Positive affect: fibre treatment causes improvement in both males and females
- Microbiome changes are somehow involved
- 12 weeks of fibre improved mood in daily life in healthy adults
- Some mood improvements were associated with increased microbial diversity
- Despite comprehensive biomarker analyses, underlying gut → brain mechanism remains unclear

	innovation for life
	for life

#### NGNG study

#### Human studies with personalized microbiome approach



#### New Public Private Partnership based on in vitro stratification of participants in preparation

innovation

#### Take home message

- Microbiome can influence human health systemically
- Dietary fibres can play an important role
- Personalized approaches are necessary to achieve the full potential
- Simple prescreening can predict and support showing human efficacy

#### **Future outlook**

- Dietary fibres are an important part of healthy diets and can certainly support the prevention of disease and support a healthy body system
- The future will learn if they also show potential in treating and maybe even curing diseases
- There are as an example first indications that fibres may support the efficacy of cancer immunotherapy, something no-one would have thought of 10-20 years ago

**TNO** innovation for life



# From a universal sugar replacement strategy towards unlocking the power of fibre-rich by-products

Stefano Renzetti Wageningen Food & Biobased Research *Optimising food and fibre composition* Leiden 20<sup>th</sup> September 2023







### Outline

□ Principles of sugar functionality: focus on bulking properties

□ Universal strategy for sugar replacement?

**□** Example on bakery applications

□ Valorization of fibre-rich by-products and ingredients

□ Conclusion





## Outline

#### Principles of sugar functionality: focus on bulking properties

- Universal strategy for sugar replacement?
  - **C** Example on bakery applications
- □ Valorization of fibre-rich by-products and ingredients
- □ Conclusion





3

# Sugar functionality: Central hypothesis

#### □ It is more than just sweetness

- Sweetness and color controlled independently of texture, e.g. via addition of minor ingredients:
  - -> reducing sugar-> natural sweetness enhancers
- □ **Texture** → controlled by multiple parameters, most challenging
- No single ingredient can mimic sugar
- □ First focus on texture in sugar replacement



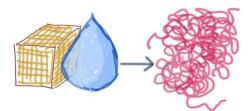


4



# Texturizing function: Two physical parameters

- Sugar acts as a humectant: it binds water as hygroscopic matter
  - → competes with biopolymers for water during mixing
    - $\rightarrow$  Described by water interaction parameter  $\chi_{eff}$
- Sugar acts as a plasticizer: softening texture/lowering viscosity
  - → works together with water to soften biopolymers
    - $\rightarrow$  Described by hydrogen bond density  $\Phi_{w,eff}$  (or  $n_{OH,eff}$ )

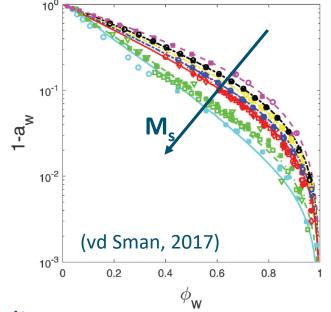






# Sugar as humectant: binds water

#### From sugar sorption properties...



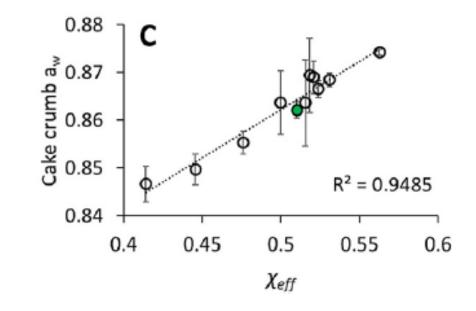
Water binding

 $\rightarrow$  well described by Flory-Huggins model

 $\rightarrow$  Related to water-interaction parameter  $\chi_{eff}$ 





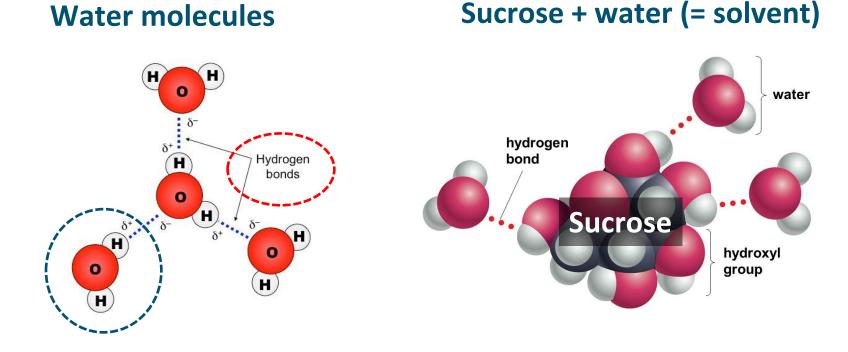


#### Application in cake

<u>Renzetti, Sman, 2022. Food Hyd.</u> https://doi.org/10.1016/j.foodhyd.2022.107795



### Sugar as plasticizer: works with water to soften polymers



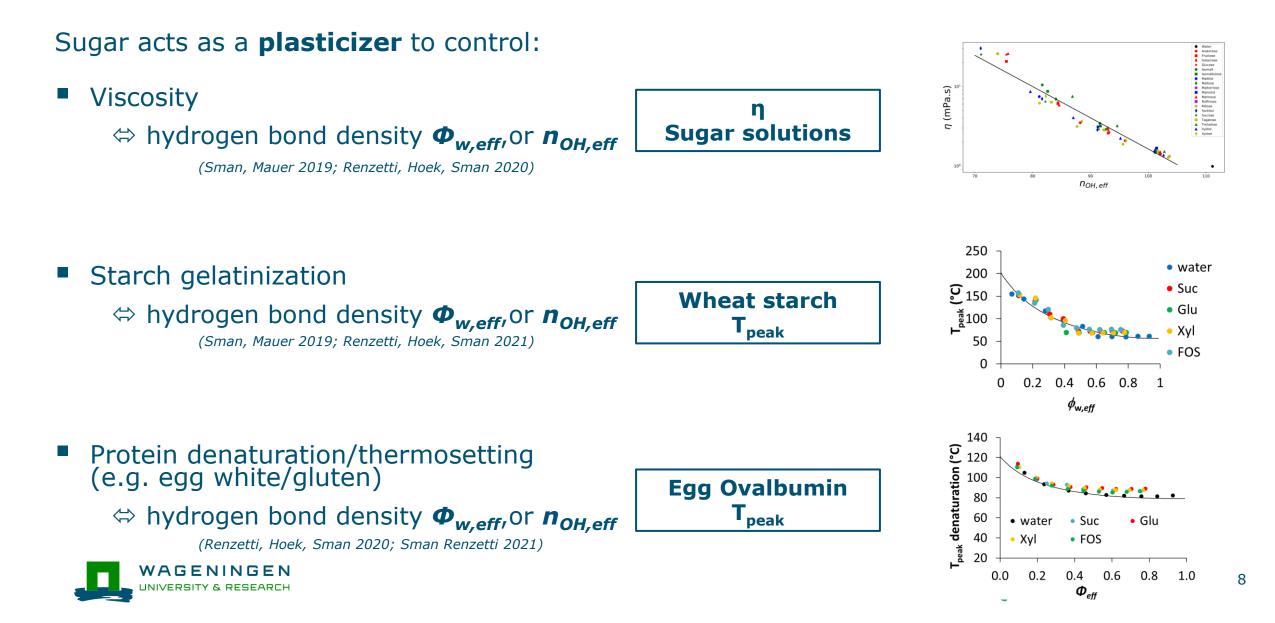
- Water, sugar and biopolymers (proteins, starches) interact via H-bonds
- For biopolymers it appears not to matter which molecule delivers H-bonds
- It is the volumetric density of H-bonds of the solution (solvent) what counts  $\rightarrow \Phi_{w,eff}$





7

### Sugar as plasticizer: works with water to soften polymers



## Outline

□ Principles of sugar functionality: focus on bulking properties

Universal strategy for sugar replacement?
 *Example on bakery applications*

Valorization of fibre-rich by-products and ingredients

□ Conclusion





### Sugar functionality in biscuit

- □ Humectant →  $\chi_{eff}$  □ Competes with flour for water
   □ Plasticizer →  $Φ_{w,eff}$ 
  - Provides viscosity
  - Controls gluten thermosetting
  - Prevents starch gelatinization

Sman, Renzetti 2022. Food Hydr. 10.1016/j.foodhyd.2022.107966



#### Table 1

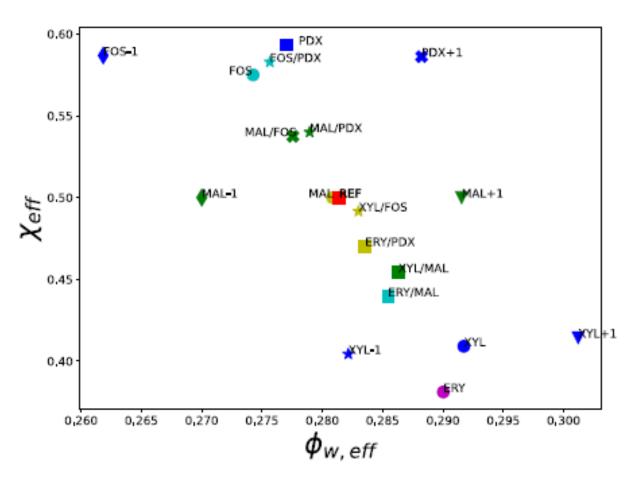
Sugar functionality for biscuit texture, with associated governing parameter.

Function during mixing	Parameter		
Sheared sugar crystals lead to abrasion of fat crystals, promoting air bubble stability	Xtal		
Stabilization of air bubbles via steric hindrance	Xtal		
Slow dissolution allows partial hydration of gluten	Xeff		
Dissolved sugar competes with gluten, arabinoxylans, and damaged starch for water	Xeff		
Together with fat it prevents full development of hydrated gluten network	Xeff		
Dissolved sugar provides viscosity to the dough	$\varphi_{w,eff}$		
Sugar syrup provides cohesion to the dough			
Function during baking			
Delays its own dissolution	Xtal, $\varphi_{w,eff}$		
Decrease of viscosity of dough by further dissolution	Xtal, $\varphi_{w,eff}$		
Promotes spreading (via decrease of viscosity and quantity of solvent)	φ <sub>w,eff</sub>		
Retards bubble growth via increase viscosity if moisture evaporates	$\varphi_{w,eff}$		
Regulates a <sub>w</sub> , rate of evaporation, steam pressure	Xeff		
Delay gluten denaturation at higher temperatures	$\varphi_{w,eff}$		
Prevents starch gelatinization	$\varphi_{w,eff}$		
Promote surface cracking via recrystallization	Xtal		
Sets biscuit into glassy state; renders crispiness	$\varphi_{w,eff}$		

10

### Working hypothesis

- □ Similar texture if values of  $\boldsymbol{\Phi}_{w,eff}$  and  $\boldsymbol{\chi}_{eff}$  matched with reference product
- □ Variations with 50% sugar replacement
- Sucrose replaced by mixtures of replacers
- □ (FOS, polydextrose, inulins, polyols)

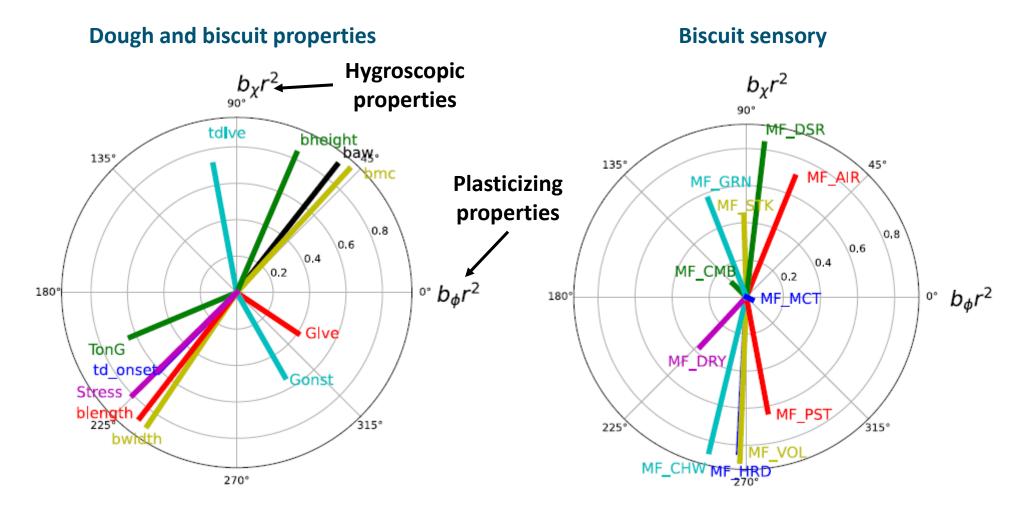




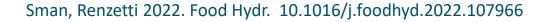
Sman, Renzetti 2022. Food Hydr. 10.1016/j.foodhyd.2022.107966



#### Experimental validation of hypothesis

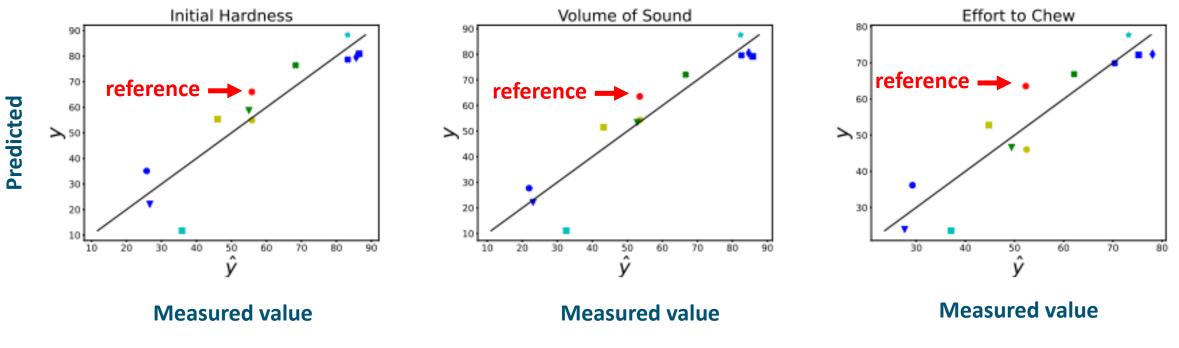








#### Predicting sensory



Sman, Renzetti 2022. Food Hydr. 10.1016/j.foodhyd.2022.107966

• Multiple solutions can be calculated for sugar replacement using  $\Phi_{w,eff}$  and  $\chi_{eff}$ , allowing room for optimization of the biscuit for other quality or nutritional traits

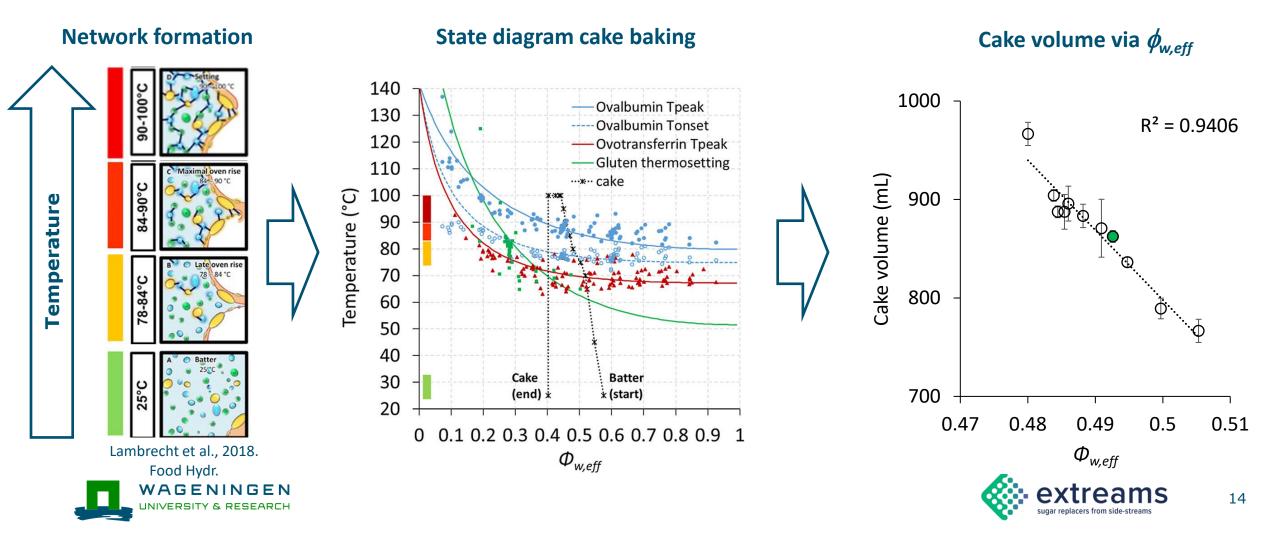




13

## Extension of principles to cake baking

• Illustrated in state diagram with  $\phi_{w,eff} \sim n_{OH,eff}$  (Renzetti et al., 2022. Food Hydr.)



## Outline

□ Principles of sugar functionality: focus on bulking properties

□ Universal strategy for sugar replacement?

**□** Example on bakery applications

□ Valorization of fibre-rich by-products and ingredients

□ Conclusion



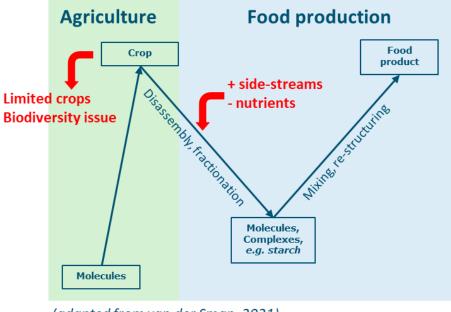


### Valorization of by-products

- Food loss & side-streams still rich in nutrients
- >700 millions people obese from calorie dense and nutrients poor diets

# If the principles for sugar functionality are universal:

#### **Food production & transformation**



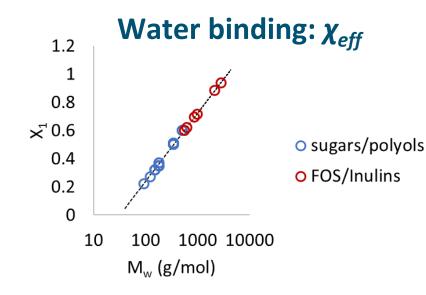
<sup>(</sup>adapted from van der Sman, 2021)

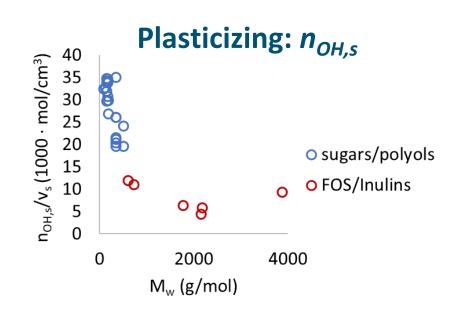
- □ Can we engineer sugar replacers from fibre-rich by-products?
- Can we use these principles towards a more flexible use of fibre-rich byproducts and ingredients?





# Engineering sugar replacers from by-products





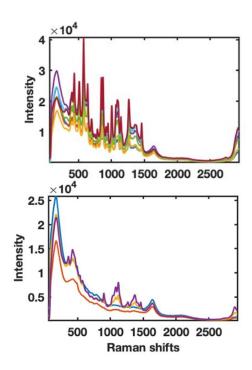
- For sugars, polyols, FOS/inulins
  - $\rightarrow \chi_{eff}$  largely controlled by  $M_w$
  - $\rightarrow n_{OH,s}$  depend on molecular structure (not just M<sub>w</sub>)
- Modify cell-wall fibres to optimally steer  $\chi_{eff}$  and  $n_{OH}$

- X can be screened with sorption measurements
- Develop spectroscopic techniques to screen for n<sub>OH,s</sub>

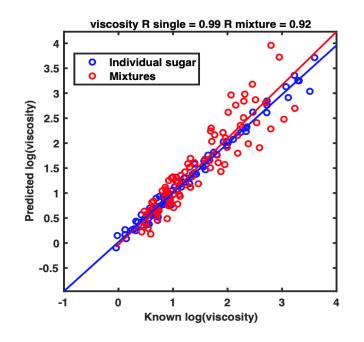


#### Raman spectroscopy as process monitoring?

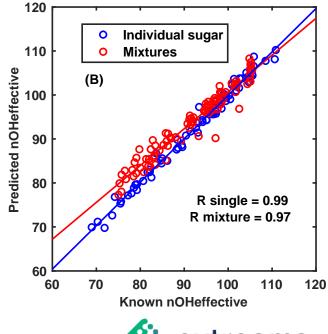
- Raman to allow characterization of physicochemical properties during processing
- Measure single sugar, oligos and build model to predict viscosity and n<sub>OH,eff</sub>
- Models tested on complex mixtures



#### Log(Viscosity)



#### **n**<sub>OH,eff</sub>

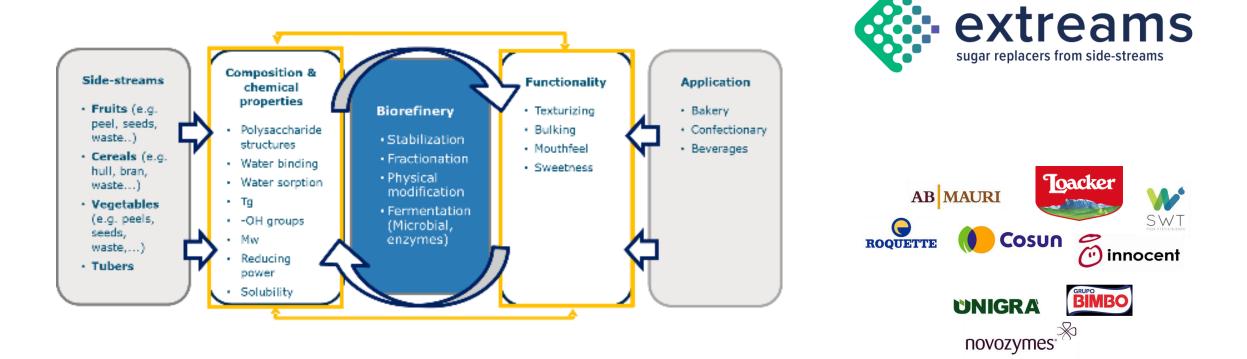






# Engineering sugar replacers from by-products

Designing fibre-rich sugar replacers from by-products



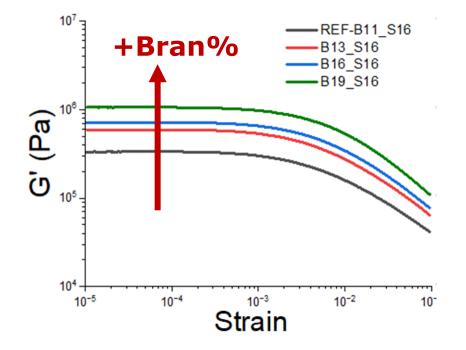




### Sugar replacement to allow more flexible use of bran?

Bran enrichment in biscuit has detrimental effects on:

- □ dough rheology  $\rightarrow$  stiffer dough
- □ biscuit texture  $\rightarrow$  harder biscuits



Can sugar replacement compensate negative effect of bran enrichment?



Renzetti & van der Sman 2024. *Food Hydr. https://doi.org/10.1016/j.foodhyd.2023.109226* 



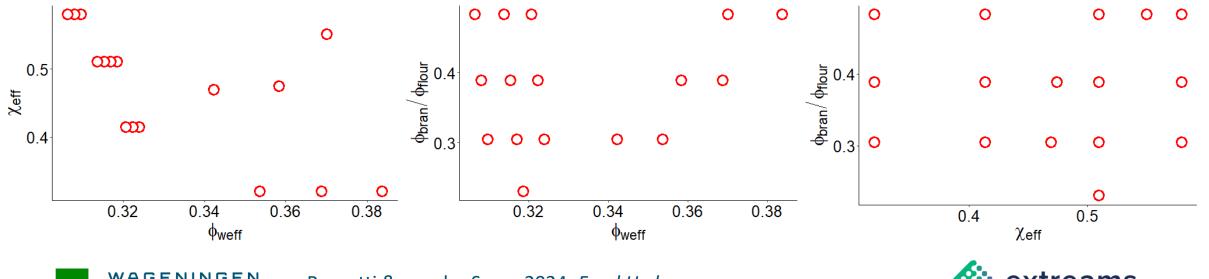
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### Working hypothesis

□ 3 main physicochemical parameters controls biscuit properties:

- $\Box \Phi_{w,eff}$  (plasticizing role water+sugars)
- $\Box \chi_{eff}$  (moisture binding sugars)
- $\Box \Phi_{\text{bran}}/\Phi_{\text{flour}}$  (ratio bran:flour)

Bran content from 11 to 19 g/100g dough Sugar reduced to 50 and 100%



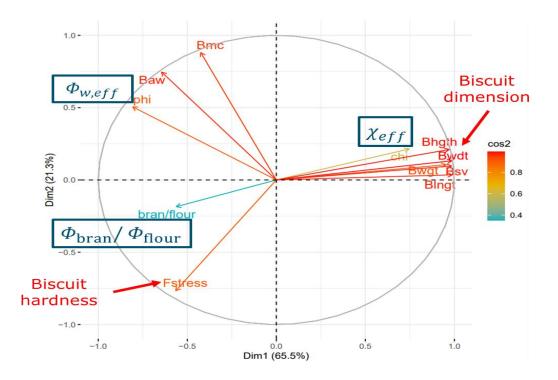


Renzetti & van der Sman 2024. Food Hydr. https://doi.org/10.1016/j.foodhyd.2023.109226



### Predicting biscuit quality

Symbols	Description	R <sup>2</sup>	bø	<mark>b</mark> ∗	Deranstlour
Dough rhe	ology				
Janset	Onset temperature	0.96	-1.00		
Garset	G' at onset	0.93	-0.27	-0.40	0.34
G <sub>90</sub>	G' at 90°C	0.86		-0.58	0.42
tdanset	tan (δ) at onset	0.96	-0.27	0.46	-0.28
td <sub>90</sub>	tan (δ) at 90°C	0.98	-0.20	0.53	-0.27
Biscuit pro	operties				
Bhath	Height	0.91		0.57	-0.43
Blogt	Length	0.93	-0.24	0.38	-0.39
Bsv	Specific volume	0.92	-0.20	0.41	-0.40
Estress	Fracture stress	0.76	-0.31	-0.40	0.29



□ Combination of  $\Phi_{w,eff}$ ,  $\chi_{eff}$  and  $\Phi_{bran}/\Phi_{flour}$  predict dough and biscuit properties

Possibility to decouple biscuit properties from nutritional composition



Renzetti & van der Sman 2024. Food Hydr. https://doi.org/10.1016/j.foodhyd.2023.109226

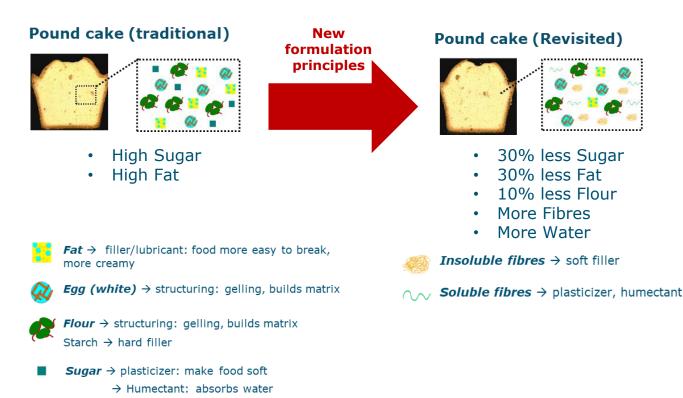


# A paradigm shift in bakery formulations

• Combined sugar reduction and fat reduction improves sensory perception of cakes

(Renzetti, van den Hoek, Stieger & van der Sman 2023. Food Hyd. In preparation)

- □ Using novel formulation approaches with holistic view of food matrices
- Decoupling texture from nutritional composition



#### Sensory with naïve consumers (n=51)

	REF	VAR 1	VAR 2	VAR 3	VAR 4	VAR 5
Liking	$49 \pm 22^{bc}$	47±21 <sup>b</sup>	53±20 <sup>bc</sup>	30±18 <sup>a</sup>	$47 \pm 20^{b}$	60±20 <sup>c</sup>
Softness	51±20 <sup>b</sup>	49±20 <sup>b</sup>	54±19 <sup>b</sup>	25±17 <sup>a</sup>	46±17 <sup>b</sup>	68±19 <sup>c</sup>
Dryness	$52\pm22^{bc}$	57±18 <sup>c</sup>	41±21 <sup>b</sup>	72±16 <sup>d</sup>	$55\pm20^{c}$	26±18 <sup>a</sup>
Sweetness	43±21 <sup>ab</sup>	46±19 <sup>bc</sup>	55±19 <sup>c</sup>	34±20 <sup>a</sup>	41±19 <sup>ab</sup>	57±19 <sup>c</sup>

## Outline

□ Principles of sugar functionality: focus on bulking properties

Universal strategy for sugar replacement?

**□** Example on bakery applications

□ Valorization of fibre-rich by-products and ingredients

#### □ Conclusion





# Conclusion

- Cell-wall materials could be a source of functional sugar replacers provided governing physical parameters can be matched with e.g. sucrose
- Screening methodologies can be developed to assess physical properties of cell-wall derived ingredients
  - → Allow to identify functional blends of cell-wall hydrolysates from various by-products (ongoing work)
- Innovative formulation principles open opportunities to:
  - $\rightarrow$  Enable a flexible use of by-products as nutrient-dense ingredients
  - → Provide multiple (or personalized) solutions to optimize texture and nutritional composition





# Thank you for your kind attention!

# Questions?Feel free to contact me



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#### Funding



#### Acknowledgments: Prof. Ruud van der Sman Dr. Puneet Mishra Dr. Lijiao Kan Irene van den Hoek Jolanda Henket Abigail Smith (Mondelez, biscuit sensory)

# Targeted initiatives to help bridge the fibre gap in lower socioeconomic groups

Healthy soil, Healthy food, and Healthy people (H3)

#### **Professor Louise Dye**

Chair in Nutrition & Behaviour



With thanks to Dr Katie Adolphus Postdoctoral Research Fellow Human Appetite Research Unit School of Psychology University of Leeds



School of Food Science and Nutrition University of Leeds

#### Outline

- 1. Healthy soil, Healthy food, and Healthy people (H3)
  - Overview and work packages
- 2. Fibre consumption in the UK
  - Focus on low SES groups
  - SES inequalities in diet
  - Health behaviour change in low SES groups
- 3. Fibre reformulation
  - Background and framework
  - Modelling study on what fibre reformulation could achieve
  - Communicating about fibre
- 4. The new H3 fibre work package
  - Co-designing interventions with industry



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**HEALTHY FOOD** 

**HEALTHY PEOPLE** 





#### Background

•

SACN 30g/day recommendation for adults

- Constipation, intestinal transit time, faecal mass
- LDL-cholesterol, cardiovascular diseases, colorectal cancer, T2DM.
- BNF simple dietary modelling on feasibility of the recommendation. Possible to consume 30g/day if:
  - Meals are based on starchy foods
  - High fibre snacks are selected
  - 8 portions F&V
- Not reflective of average diets in the UK
- Encourage greater consumption of fibre via public health campaigns and education
- Formulate foods with increasing levels of fibres via innovation and reformulation

## Replace pre-existing products

- Gradual and 'silent' reformulation
- Without significantly altering food choices

### Add to pre-existing versions

• Diversification of products

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- Adding food choices
- Marketing strategies may actively encourage consumers to switch





### **Transforming UK food systems for healthy people & a healthy environment**

- Transform the UK food system by placing healthy people & a healthy natural environment at its centre.
- Addressing questions around what we should eat, produce & manufacture & what we should import, taking into account the complex interactions between health, environment & socioeconomic factors.





#### HEALTHY SOIL HEALTHY FOOD HEALTHY PEOPLE



Hybrid farming



Regenerative agriculture



Biofortification to increase micro-nutrient profiles



Interventions to increase fibre access & intake

Novel growing techniques

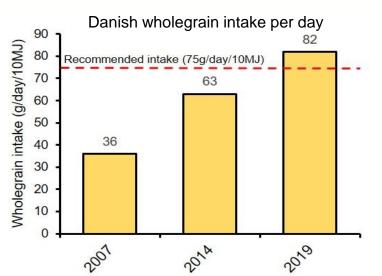
Transforming the UK food system 'from the ground up' with interventions at the lab, farm, landscape and consumer scale



Increasing food system resilience

### Learning from The Danish Wholegrain Partnership

- A multi stakeholder public-private partnership including government, health NGOs, and food industry
- Aim: increase WG intake, improve accessibility and awareness of WG products and health benefits
- Combination of scientific evidence, dietary guidelines, logo, product reformulation and innovation, communication and education
- WG intake and availability increased
- Not evenly distributed across SES
- Reaching low SES populations is critical to address dietrelated health disparities



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Danish market availability of food products branded with the DWP WG logo

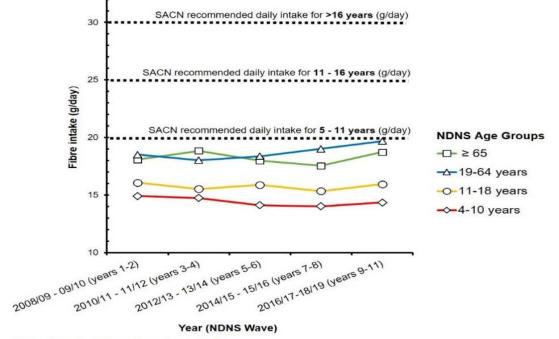






#### Fibre intakes in the UK

- Mean intake of fibre is below 30g/day for all age groups
- Adults (19-64 years): mean intake of fibre is 19.7g and 9% meet the recommendation.
- Fibre intakes are fairly stable overtime, but a small significant increase in fibre intake of 0.2 g/day per year for adults aged 19-64 years.
- Public health information campaigns and reformulation/innovation actions ineffective at increasing fibre intake in UK.



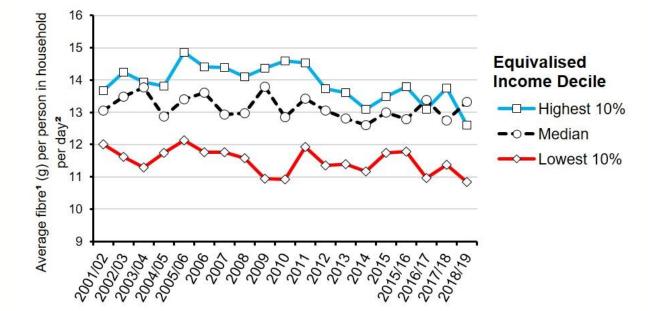
SACN: Scientific Advisory Committee on Nutrition

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# Socioeconomic differences in fibre intakes in the UK

Fibre intake increases with increasing income

- Female adults (19-64 years) showed a significant increase in fibre intake of 0.5g/day for every £10k increase in equivalised income.
- Intakes of most micronutrients also increases with income
- The average UK quantity of fibre purchased per person per day is lower for the lowest equivalised income deciles between 2001/02 2018/19



<sup>1</sup>Fibres non-starch polysaccharides.

<sup>2</sup> Intake estimated as average purchased available dietary fibre (in grams) divided by total number of household occupants

- NDNS Years 1 to 9 of the Rolling Programme (2008/2009 2016/2017): Time trend and income analyses
- DEFRA (2018/2019). Family food datasets: Equivalised income decile group, Household Nutrient Intakes: https://www.gov.uk/government/statistical-data-sets/family-food-datasets.
- DEFRA, Food Statistics in your Pocket. 2022.

### Socio-economic inequalities in diet Contribution of food expenditure

- Cost of food: less nutritious foods often cheaper and higher diet quality associated with higher diet cost (Rehm et al., 2015).
- Actual food expenditure, take-home food and beverage purchases (2010) obtained for 24,879 UK households stratified by occupational social class. Kantar WorldPanel UK household survey
- Purchases of (1) F&V and (2) less-healthy foods/beverages.





- Higher SES was significantly associated with greater actual food expenditure, which was in turn associated with healthier purchasing.
- Expenditure (cost) mediated 36% and 63% of the SES differences in F&V and less-healthy foods/beverages purchasing
- Actual and/or perceived cost of healthy diets is one factor driving SES differences in food purchasing choices.
- Food inflation, cost of living crisis, increasing food insecurity will drive further SES inequalities in fibre intake.

Mild food insecurity	Moderate for	od insecurity	Severe food insecurity
Worrying about ability to obtain food	Compromising quality and variety of food	Reducing quantities, skipping meals	Experiencing hunger



Pechey R, Monsivais P. Socioeconomic inequalities in the healthiness of food choices: Exploring the contributions of food expenditures. Prev Med. 2016 Jul;88:203-9.

### **Barriers to fibre consumption**

- Sensory profile
- Consumer perceptions: Starchy food associated with weight gain or digestion discomfort
  - Fattening/heavy/filling/bloating/sluggishness
- Cost
- Longer preparation and cooking time
- Lack of cooking skills or facilities
- Need to eat (and cook) separately often families do not eat together
- Lack of awareness of high fibre foods and health benefits
- Rapid abandonment of high fibre diets
  - GI symptoms, constipation, taste



# Health behaviour change in low income populations



- Lower SES groups have poorer health outcomes vs. high SES groups
- Behaviours linked to health (diet, PA, smoking) show a similar social gradient
- Targeting health behaviour change interventions at low SES groups is a means to reducing health inequalities but differential effects by SES.
- Effects are smaller in low SES vs. high SES groups. This may lead to intervention-generated inequalities and may even widen SES-related health inequalities.

	Inte	erventio	n	Control		1	Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Parra-Medina 2011	-21.3	6.9	80	-26.8	7.3	71	4.0%	0.77 [0.44, 1.10]	
Chang 2010	6.33	3.42	28	4.73	3.41	42	2.1%	0.46 [-0.02, 0.95]	
Jackson 2011	0.44	1.6	134	-0.2	1.5	153	6.3%	0.41 [0.18, 0.65]	
Keyserling 2008	4	0.31	107	3.9	0.31	110	5.3%	0.32 [0.05, 0.59]	
Steptoe 2003	1.49	2.2	136	0.87	2.22	135	6.2%	0.28 [0.04, 0.52]	
Elder 2006 - Promotora	-43.1	19.65	107	-49.1	23.79	107	5.3%	0.27 [0.00, 0.54]	
Ahluwalia 2007	3.1	2.48	107	2.44	2.42	66	4.4%	0.27 [-0.04, 0.58]	
Auslander 2002	-32.1	13.37	138	-35.6	13.37	156	6.5%	0.26 [0.03, 0.49]	
Sanchez-Johnsen 2006	5.33	3.4	14	4.63	2.51	13	1.0%	0.23 [-0.53, 0.98]	
Emmons 2005	3.57	2	977	3.13	2	977	12.8%	0.22 [0.13, 0.31]	-
Gans 2009 - ST	0.92	2.92	454	0.42	2.51	150	8.1%	0.18 [-0.01, 0.36]	-
Nitzke 2007	4.9	2.35	571	4.6	2.45	684	11.7%	0.12 [0.01, 0.24]	
Gans 2009 - MT	0.72	2.55	462	0.42	2.51	151	8.2%	0.12 [-0.07, 0.30]	+
Tessaro 2007	3.74	2.11	131	3.55	2.24	131	6.1%	0.09 [-0.16, 0.33]	
Gans 2009 - MTI	0.36	2.58	474	0.42	2.51	150	8.2%	-0.02 [-0.21, 0.16]	
Elder 2006 – Tailored	-49.8	19.89	99	-49.1	23.79	53	3.9%	-0.03 [-0.37, 0.30]	
Total (95% CI)			4019			3149	100.0%	0.22 [0.14, 0.29]	•
Heterogeneity: Tau <sup>2</sup> = 0.0	01; Chi <sup>2</sup>	= 28.84	, df =	15 (P =	0.02);	$^{2} = 489$	6		-1 -0.5 0 0.5 1
Test for overall effect: Z =	= 5.51 (F	P < 0.00	001)						-1 -0.5 0 0.5 1 Favours control Favours experiment

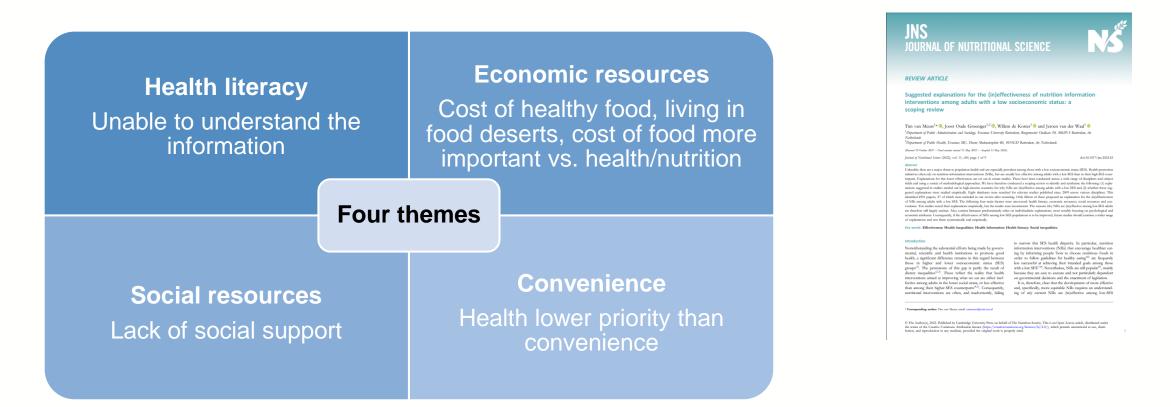
SR & MA of RCTs (35 studies; n=17000) on effectiveness of interventions for low-income groups in changing diet, PA, smoking demonstrated small positive effects.

- Effects positive but small for diet (n=16) SMD: 0.22.
- Equivalent to intervention groups eating just under half a portion of F&V more than controls a day.
- SRs in general populations tend to report larger effects for diet SMD 0.31.

Bull ER, Dombrowski SU, McCleary N, *et al* Are interventions for low-income groups effective in changing healthy eating, physical activity and smoking behaviours? A systematic review and meta-analysis *BMJ Open* 2014;**4**:e006046.

# Why are interventions less effective in low SES groups?

Review of 27 studies examining key explanations for ineffectiveness of nutrition interventions at achieving behavioural change among low SES adults



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# What reformulation could achieve in the UK



- Statistical modelling study on UK data: impact of a fibre reformulation intervention on intakes and health outcomes
- NDNS years 7 and 8 (2014/2015–2015/2016)
- A total of 915 food and beverages were deemed eligible for fibre enrichment

Foods included in the fibre enrichment intervention	Foods excluded from the fibre enrichment intervention
Bakery products	100 % fruit and vegetable juices, nectars, juice drinks and soft drinks
Flavoured dairy products such as yogurt drinks	Coffee, tea and infusions
Baked confectionery	Sugar confectionery
Canned soups and powdered soups and sauces to be reconstituted	Foods considered a traditional commodity such as milk, grains or cheese
Some beverages which could reasonably be enriched with fibre, such as fruit smoothies and malt-based powdered beverage drinks	Composite dishes (foods containing several ingredients) with a wide variety of ingredients unclear whether eligible for fibre enrichment

- Three fibre reformulation scenarios based on the EU legislation for nutrition claims:
  - 1. 0 g fibre/100 g- concentration was left at zero
  - 2. <3 g fibre/100g increased to 3 g/100g
  - 3.  $\geq$ 3 g fibre/100g, 3g of fibre added.
- Simple market share of 50% was used: 50% of the foods of interest consist of an altered fibre product

# What reformulation could achieve in the UK



- Nutritional composition changes were implemented and nutritional intake outcomes were assessed. Comparisons
  were made against the baseline diet (representing the market pre-reformulation)
- Algorithms sourced from literature were applied to the baseline and intervention intakes for fibre to estimate the
  effect of fibre reformulation on weight reduction, CVD, and T2DM risk reductions
- Fibre reformulation intervention demonstrated a 2.2 g/day increase from baseline in population aged 2-94 years.

Age (years)	% meeting recommendation at baseline	% meeting recommendation at intervention	% change
2–5	14.9	32.5	+218-1
6–10	10.6	22.4	+211.3
11–16	5.7	9-4	+164-9
17–94	8.0	12.2	+52.5

 5.9 % of ppts could achieve a weight reduction, 72.2 % a reduction in cardiovascular risk and 71.7 % a reduced risk of T2DM with fibre fortification (all Ps ≤ 0.05) under the modelled scenario.

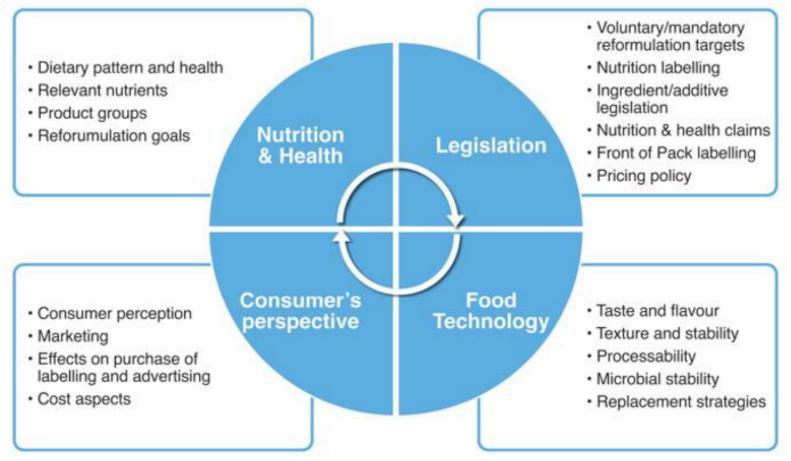


### **Reformulation and innovation**



# Framework for product reformulation

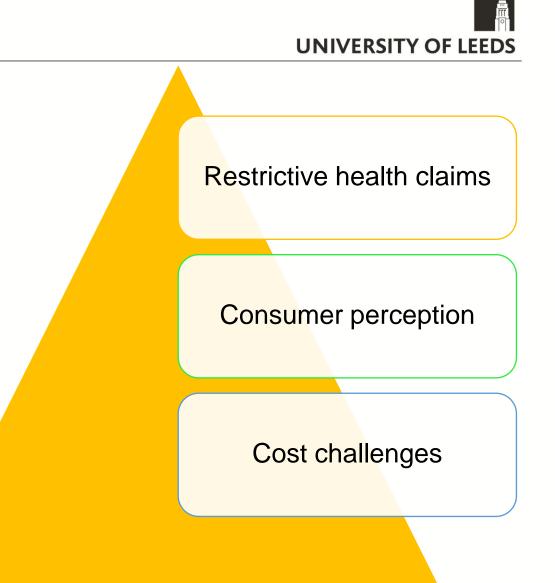
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van Gunst A, Roodenburg AJC, Steenhuis IHM. Reformulation as an Integrated Approach of Four Disciplines: A Qualitative Study with Food Companies. Foods. 2018 Apr 20;7(4):64. doi: 10.3390/foods7040064.;

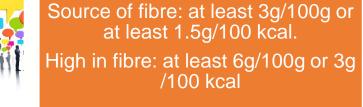
# Considering the barriers and motivations within the food industry

- UoL research 2022 (in prep)
- Aimed to understand the barriers and motivators for FR within industry
- Semi-structured interviews were carried out with food industry professionals employed throughout the supply chain from raw ingredient manufacturers to retailers



### **Communicating about fibre**

- Labelling and nutrition and health claim regulation pose challenges
  - Consumer awareness, marketing, commercial incentive.
- Fibre is not included in the list of mandatory BOP nutrients and FOP declaration (TL labelling in UK).
- No Reference Intake for fibre.
- For companies keen to capitalise on fibre content, developing products that meet nutrition and health claims is important.



Authorised health claims on specific fibre types and intestinal transit time, faecal bulk, normal bowel function, reduction of the blood glucose rise after meal, cholesterol levels.





Need particular type of fibre and meet CoU to bear claim.

Communication of the wider health benefits of fibre potentially difficult.



### New H3 work package on fibre

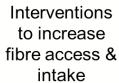
HEALTHY SOIL HEALTHY FOOD HEALTHY PEOPLE

#### How can we most effectively increase fibre intake in low SES populations?

- Reformulation and innovation and promotion products to increase fibre/WG (health by stealth)
- Community interventions with low-income consumers
- School meals and school breakfast programme in schools with high deprivation
- Demonstrate improved functionality: slower energy release/nutrient absorption (in vitro digestion), appetite & palatability
- Rollout reformulated products to schools/community interventions for longer term evaluation (taste panels, repeated exposure studies)



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### Collaborate to bridge the fibre gap

- The effects of fibre reformulation or innovation on
  - Consumer acceptance, satisfaction, palatability
  - Fibre intake, appetite, digestion, and wellbeing
- Outcomes:
  - Develop foods that are a source of/high in fibre, which are also affordable and appealing
  - Better understanding of people's preferences of reformulated or new higher fibre products through testing and trials to ensure that product is driven by consumer perception
  - Increase awareness and accessibility of higher fibre products
- Fully funded by UKRI
  - Co-design of protocol so that they align with both parties' objectives.
  - Products
- April 2022-Dec 2024



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To be involved or for more information contact: Louise Dye (I.dye@leeds.ac.uk)

AB Mauri UK & Ireland



## Thank you

Further information

Contact: Louise Dye (<u>I.dye@leeds.ac.uk</u>)

Watch the H3 project film: <a href="https://www.youtube.com/watch?v=4q26FkaVjtY">https://www.youtube.com/watch?v=4q26FkaVjtY</a>

Visit the H3 website: <u>https://www.h3.ac.uk/</u>

Read an outline of the project in Nutrition Bulletin (2021): https://doi.org/10.1111/nbu.12531





# You are what you wheat.

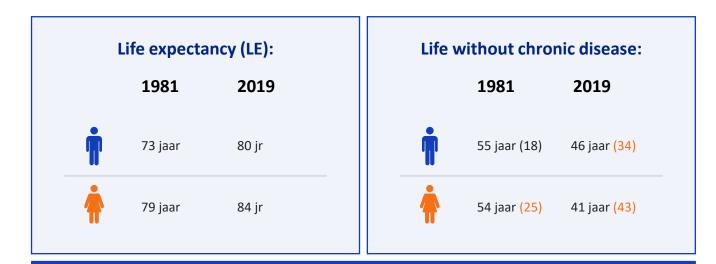
Impact of whole wheat and fibres on health – and innovative ways for testing health effects

Dr. Suzan Wopereis, Principal scientist, TNO



### Ambition "adding health to life"

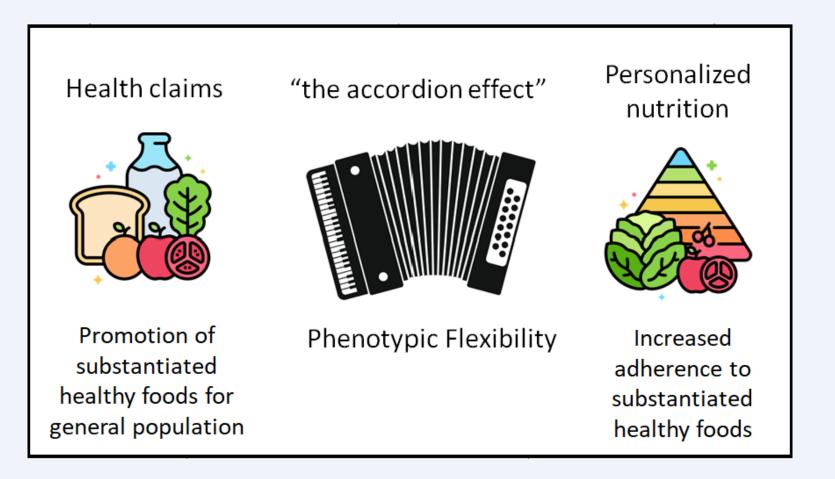
Going from lifespan to healthspan by bringing evidence based lifestyle solutions to the public.



We live longer (+ 6 years of life expectancy), but with less healthy years (+17 years of life expectancy <u>with</u> chronic disease)



### How in the context of food & nutrition?



Adapted From: Wopereis S, Proc Nutr Soc. 2022:1-13

3

innovation



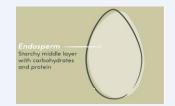




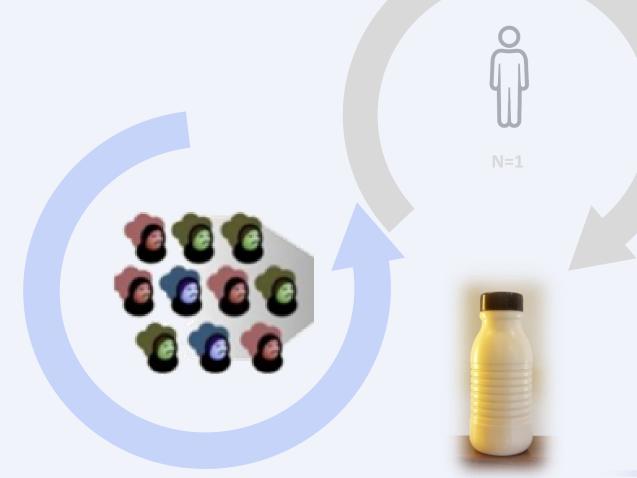
#### PhenFlex challenge test:

- 60 gr palm olein
- 75 gr glucose
- 20 gr Protifar
- 0.5 gr/20 droplets of
- artificial aroma (vanilla)
- 320 ml tapwater





#### The PhenFlex mixed-meal challenge test drink A new standardized method to quantify health and intervention effects

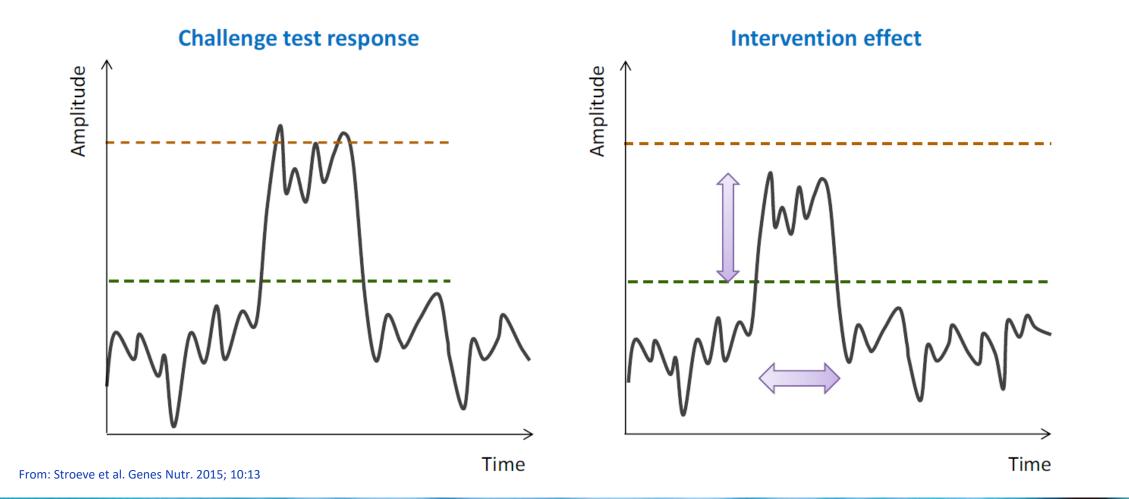


PhenFlex challenge test:

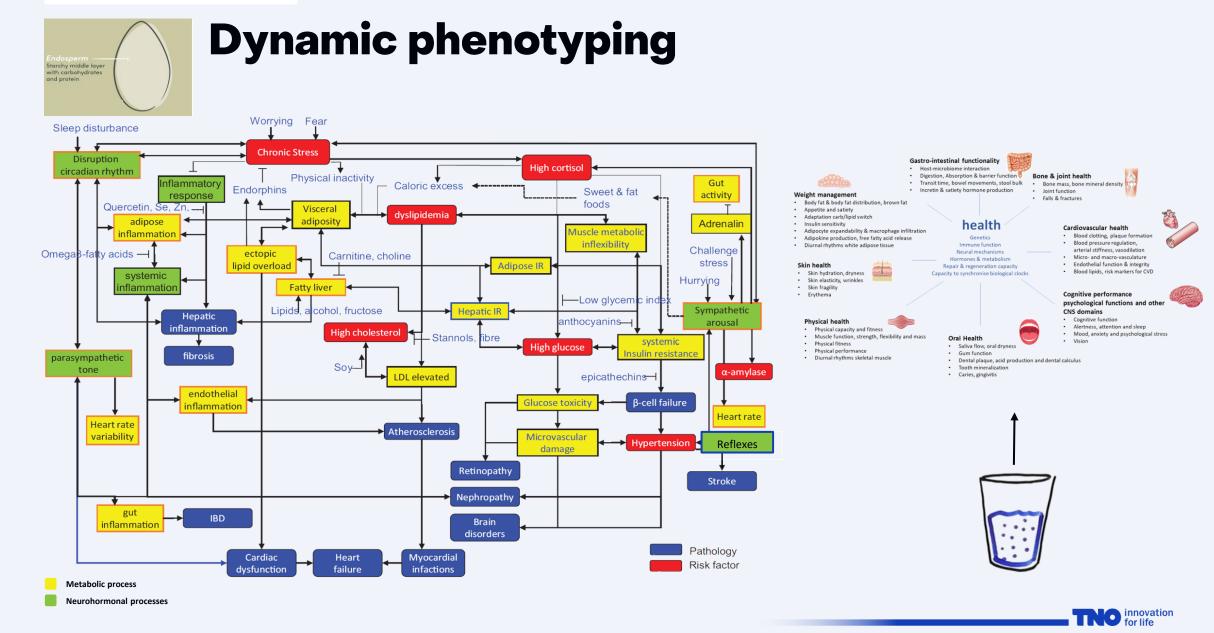
- 60 gr palm olein
- 75 gr glucose
- 20 gr Protifar
- 0.5 gr/20 droplets of
- artificial aroma (vanilla)
- 320 ml tapwater



## The challenge concept: Study and quantification of the stress response curve



Phenotypic flexibility as a measurement for health





Health effects from whole grain vs refined wheat



## The Resilience project

Kennis- en adviescentrun voor de bakkerii

#### Towards health claim substantiation for whole grain wheat products



INIVERSITY & RESEARCH

Innovation

200

W12

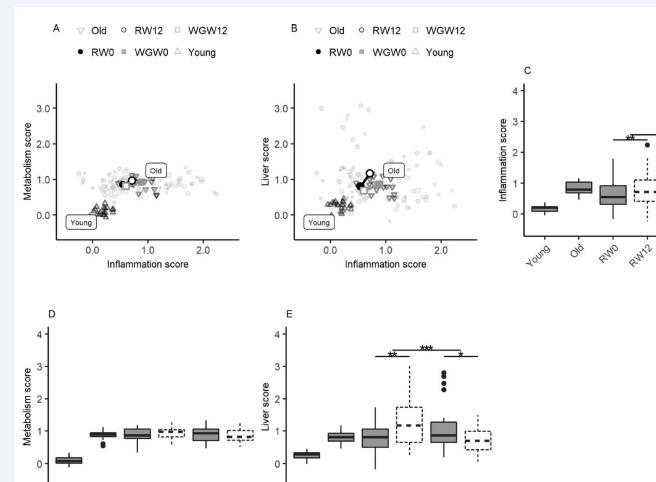
GNO



#### Health space analysis for interpretation of the health effect

NGNO

MGNNY



2200

10

2412

NGNO

NONN



Health space analysis may help to do an interpretation of multiple dynamic challenge responses related to separate health domains (i.e. using prior information) as a result from a nutritional intervention.

innovation

q

From: Hoevenaars et al. JoN 2019,149(12):2133-2144

Fiber-filled outer layer wi vitamin B and minerals

### **"YOU ARE WHAT YOU WHEAT."**

See corresponding editorial on page 1162.

#### A 12-wk whole-grain wheat intervention protects against hepatic fat: the Graandioos study, a randomized trial in overweight subjects

Sophie Schutte, <sup>1</sup> Diederik Esser, <sup>1</sup> Femke PM Hoevenaars, <sup>2</sup> Guido JEJ Hooiveld, <sup>1</sup> Marion G Priebe, <sup>3</sup> Roel J Vonk, <sup>3</sup> Suzan Wopereis,<sup>2</sup> and Lydia A Afman<sup>1</sup>

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#### ABSTRACT

Background: Whole-grain wheat (WGW) is described as nutri-NCT( tionally superior to refined wheat (RW) and thus advocated as the healthy choice, although evidence from intervention studies is often Keyw inconsistent. The liver, as the central organ in energy metabolism, whole might be an important target organ for WGW interventions. challe Objective: The aim of this study was to investigate the potential benefits of WGW consumption compared with RW consumption on liver health and associated parameters. INTR Design: We performed a double-blind, parallel trial in which W 50 overweight 45 to 70 v old men and postmenopausal women

liver

#### You are what you wheat: effects of a whole-wheat diet compared with a refined-wheat diet on hepatic steatosis

Vignan Manne and Kris V Kowdley

Liver Care Network, Swedish Medical Center, Seattle, WA

An estimated 24% of the population worldwide have some form of nonalcoholic fatty liver disease (NAFLD), ranging from steatosis to nonalcoholic steatohepatitis and nonalcoholic steatohepatitis cirrhosis (1). NAFLD/nonalcoholic steatohepatitis has become a leading cause of chronic liver disease and is one of the most common indications for liver transplant (1). The rise of NAFLD has mirrored the rise of metabolic diseases

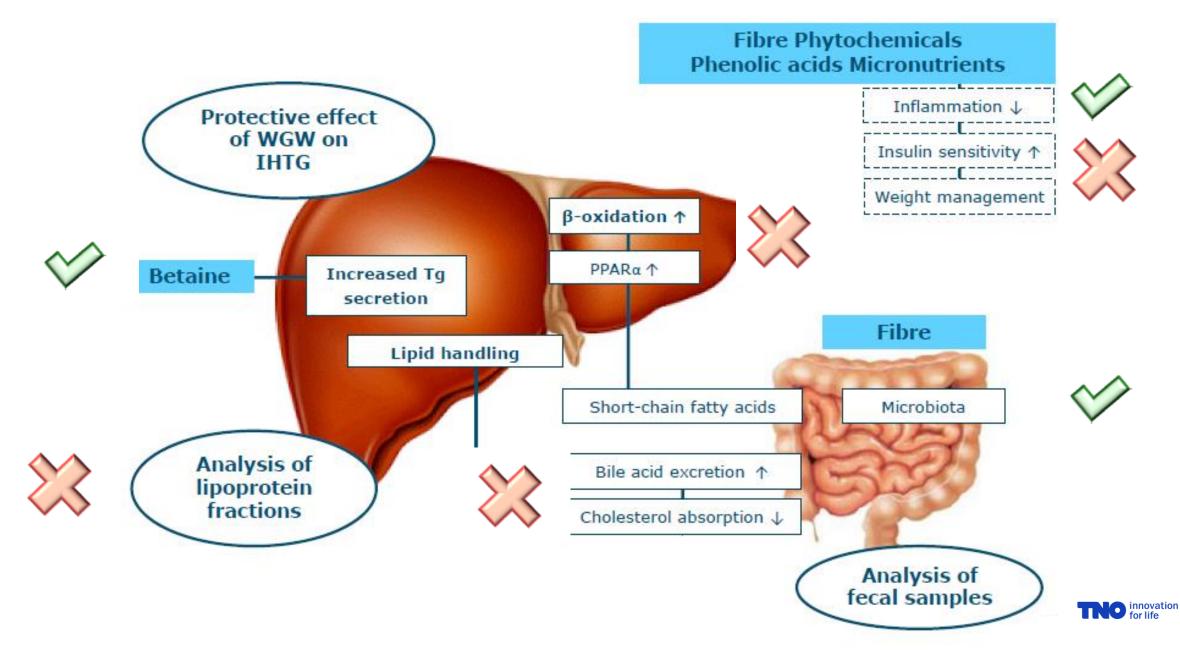
In this issue of the Journal, Schutte et al. (8) present a randomized, double-blind, parallel study of 50 overweight subjects on a 12-wk wholegrain-wheat (WGW) diet or refined-wheat (RW) diet. Subjects were included if they were 45-70 y old, were overweight, and had mild elevations in serum total cholesterol but were not on medication. Subjects were excluded if they had large changes in weight (>5 kg) a month before screening





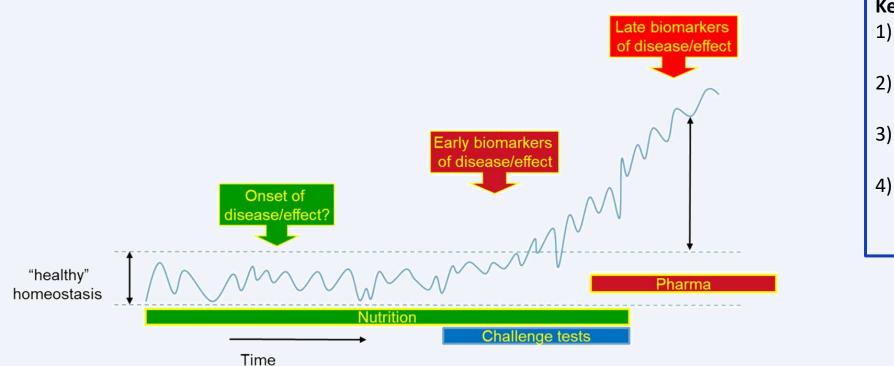
See corresponding article on page 1264.

#### **Mode of action**





#### **Could phenotypic flexibility deliver next generation health claims?**

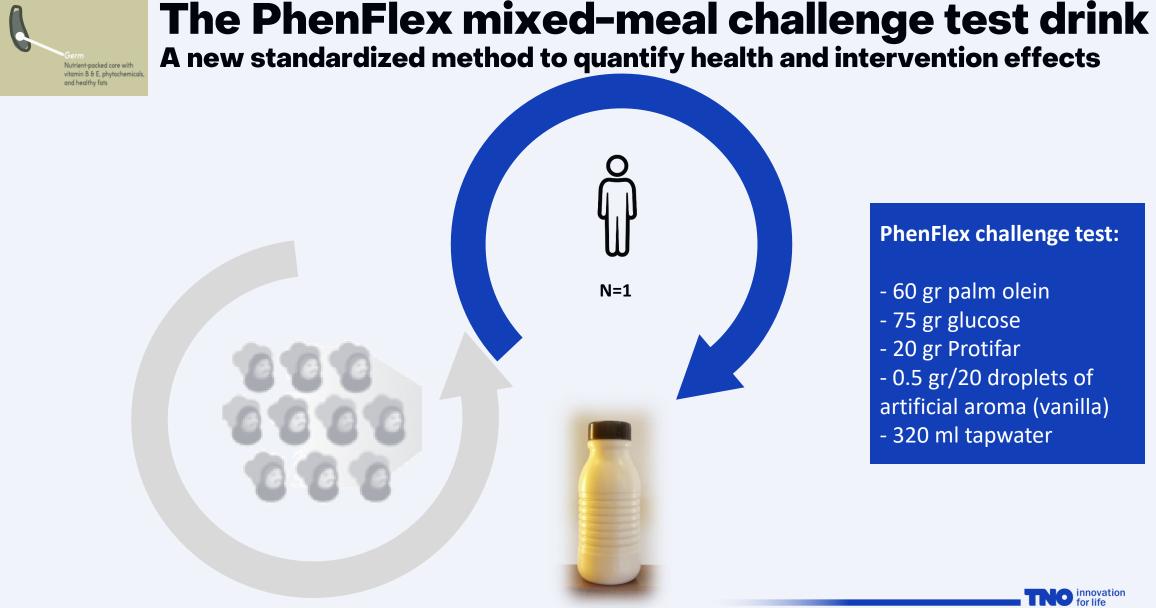


#### Key developments needed:

- Defined standardised challenge test
- Defined markers representing benefit area
- 3) Defined model (i.e. health space) for interpretation
- Determination of clinical relevance of significant effect

Good news:

In 2017 the EFSA Scientific Committee proposes "increased resilience to a challenge" as a beneficial nutritional health effect



#### **PhenFlex challenge test:**

- 60 gr palm olein
- 75 gr glucose
- 20 gr Protifar
- 0.5 gr/20 droplets of
- artificial aroma (vanilla)
- 320 ml tapwater

13

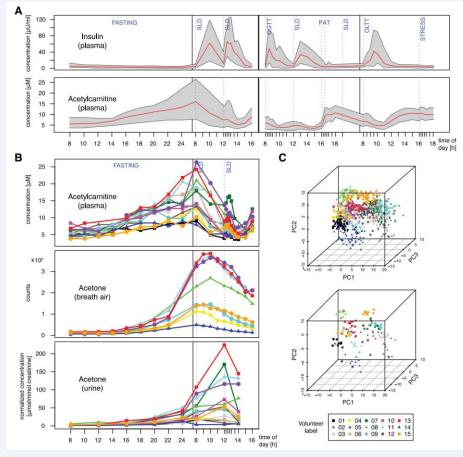
Optimising food and fibre composition



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# Challenge tests can be a starting point for personalised nutrition

N=15 healthy male Caucasians within narrow BMI and age range



"Interindividual variation can be extended and compressed by metabolic challenges: the accordion effect"

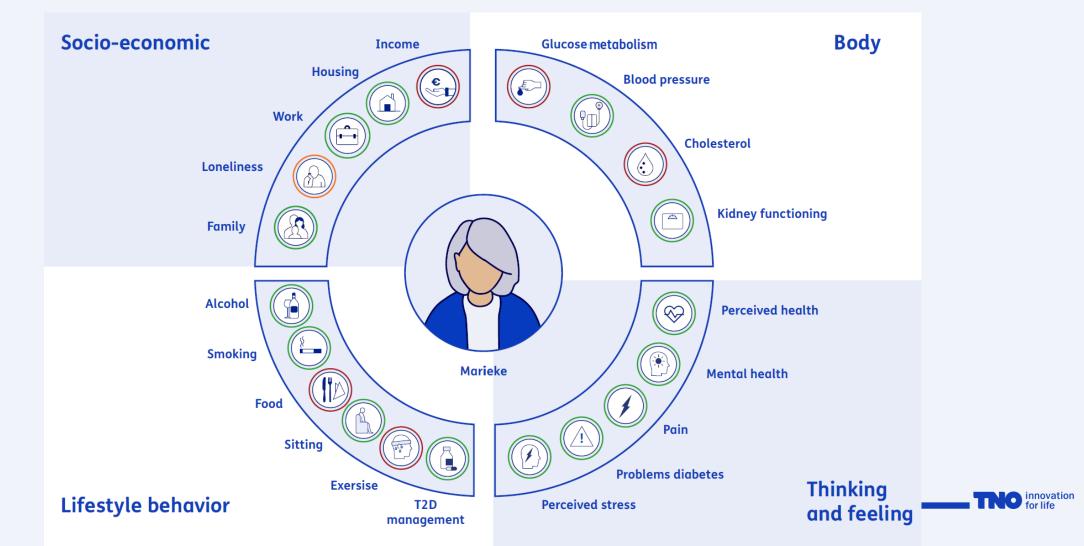






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## **Especially when combined with behaviour**





## **Goal-setting improves whole grain intake!**





check for

up date s

#### Article

**Evaluation of Food-Intake Behavior in a Healthy Population: Personalized vs. One-Size-Fits-All** 

Femke P. M. Hoevenaars<sup>1</sup>, Charlotte M. M. Berendsen<sup>1</sup>, Wilrike J. Pasman<sup>1</sup>, Tim J. van den Broek<sup>1</sup>, Emmanuel Barrat<sup>2</sup>, Iris M. de Hoogh<sup>1</sup> and Suzan Wopereis<sup>1,\*</sup>

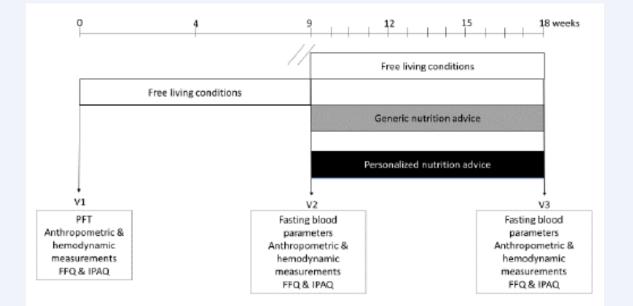
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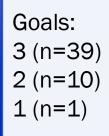
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Personalised nutrition advice improved intake for fruits, whole grains, unsalted nuts, fish, sugarsweetened beverages, added salt and less unhealthy choices, but no health effect observed.



Goal-setting significantly improved food intake vs not goal-setting. From 120 goals set, only 8 were not significantly improved. Goal-setters for whole grain and unsalted nuts decreased LDLcholesterol!



innovation



### **Goal-setting improves whole grain intake!**



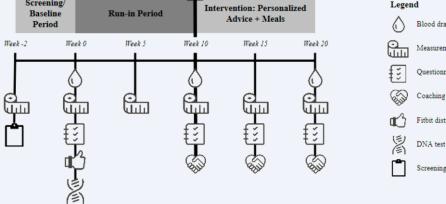


Article

A Novel Personalized Systems Nutrition Program Improves Dietary Patterns, Lifestyle Behaviors and Health-Related **Outcomes: Results from the Habit Study** 

Iris M. de Hoogh <sup>1</sup><sup>(D)</sup>, Barbara L. Winters <sup>2</sup>, Kristin M. Nieman <sup>3</sup><sup>(D)</sup>, Sabina Bijlsma <sup>1</sup>, Tanja Krone <sup>1</sup>, Tim J. van den Broek<sup>1</sup>, Barbara D. Anderson<sup>4</sup>, Martien P. M. Caspers<sup>1</sup>, Joshua C. Anthonv<sup>5,6,†</sup> and Suzan Wopereis 1,\*0





Blood draw Measurements Ouestionnaire Coaching Fitbit distribution

Screening questionnaire

"This study shows that a Personalised Systems Nutrition program in a workforce improves lifestyle habits and reduces body weight, BMI and other health-related outcomes. Health improvement was most pronounced in the compromised phenotypic flexibility subgroup, which indicates that Personalised Systems Nutrition program may be effective in targeting behavior change in healthcompromised target groups"





## The personalised systems nutrition program

Advice category	Personalized Advice	Personalization factor	Personalization based on SNP
Personalized Diet types & SNP-based	Protein intake	Glucose tolerance, disposition index, BP	FTO
macronutrient advice	Carbohydrate intake	WC, 2-h glucose	FTO, ADAMTS9, GCKR
	Fiber intake	Fasting glucose, 2-h glucose, LDL cholesterol, BP, WC	ADAMTS9, TCF7L2
Micronutrient advice	MUFA intake	Disposition index, LDL, BP, fasting and postprandial TG	-
	Omega-3 intake	BP, fasting and postprandial TG, n-3 index	FADS1









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### **Personalised nutrition & wholegrain**

Journal of Cereal Science 107 (2022) 103505         Contents lists available at ScienceDirect         Journal of Cereal Science         journal homepage: www.elsevier.com/locate/jcs					
The potential of personalized nutrition for improving wholegrain consumption Iris M. de Hoogh <sup>*</sup> , Jan-Willem van der Kamp, Suzan Wopereis					
A R T I C L E I N F O Keywords: Personalized nutrition Behavior change Personalized advice system Health benefits					
<ol> <li>Introduction         Despite several public here     </li> </ol>	alth efforts promoting intake of whole-	environment. These interindividual d long-term responses to food (Blanco-R 2016), as well as differential acute effe	lojo et al., 2016; Kirwan et al.,		

1. Introduction	env lon
Despite several public health efforts promoting intake of whole- grains, worldwide in most countries intakes are below recommended levels (Meynier et al., 2020; Seal et al., 2016; Marquart et al., 2003). However, wholegrain consumption has multiple health benefits, including a beneficial effect on body weight, blood lipid levels and in- flammatory parameters (Munch Roager et al., 2019; Reynolds et al., 2020). Additionally, in the long term, wholegrain consumption may contribute to a lower risk for cardiovascular disease, diabetes and several types of cancer (Slavin et al., 2001). Therefore, to increase wholegrain consumption, alternative wholegrain promoting strategies	201 vari nuti can tent con aliz app will
may be required. Recent research shows that a personalized nutritional approach may be more effective in achieving dietary behavior change as	2.

riable glycemic response to foods (Zeevi et al., 2015). In personalized trition all these interindividual differences as well as personal drivers n be taken into account. This short communication evaluates the pontial of personalized nutrition specifically focusing on wholegrain nsumption. It will first explain in more detail the concept of personized nutrition followed by what is known in literature in terms of plying personalized nutrition to stimulate wholegrain consumption. It ill finish with some conclusions and future considerations.

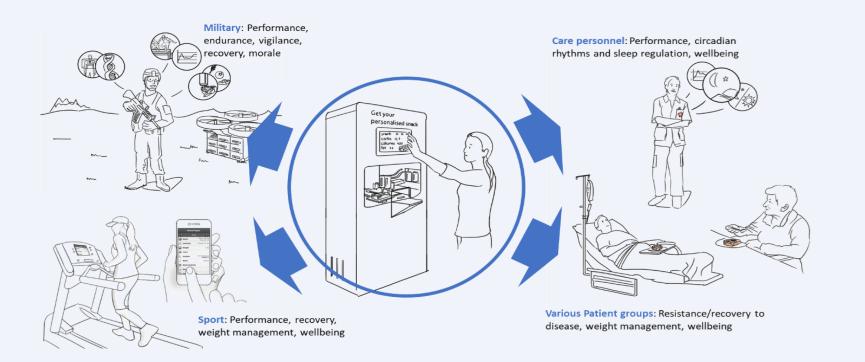
Personalized nutrition applied to wholegrain consumption

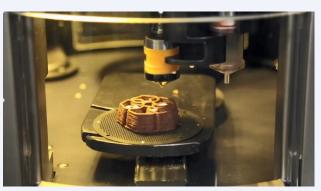
Personalized products or services	Example application for wholegrain
Dietary recommendation systems, which provide for instance individualized recommendations for calorie intake, macro- and micronutrients or whole foods. Personalized meal plans or recipes, which translate personalized advice into fitting recipes or at home-delivered meal plans.	Portal providing personalized recommendations based on health status and current wholegrain consumption, including tips for increasing wholegrain consumption. Personalized recipes for wholegrain lunch or dinner options.
Personalized supplements and functional	Enriched bread for specific individuals
foods.	or target groups.
Personalized food production, e.g. with 3D food printing a personalized food product can be produced with personalized macro- and micronutrients fitting an individual's activity pattern, time of day and chronotype.	Personalized wholegrain products for breakfast, lunch and dinner, taking int account an individual's energy needs and insulin sensitivity throughout the day.
Personalized behavior change support, for instance via a live or digital coach, entailing helping the consumer to implement the (personalized) dietary recommendations into daily life in a personalized way. Especially, personal drivers and barriers and personality aspects are taken into account	Mobile application enabling consumer to set dietary intake goals for wholegrain and which provides personalized support in goal monitoring, maintaining motivation and solving barriers.

19



## **IMAGINE: personalised food production**









#### Optimising food & fibre composition

## **Questions?**

Suzan Wopereis

