

Fibre-based nutritional strategies for microbiome modulation and improved human health

Microbiome: Mastering the Market

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Faculty of Medicine & Dentistry



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Conflicts of Interest

- Anissa Armet and Jens Walter hold a trademark associated with the NiMe Diet.
- Anissa Armet completed a paid internship with Société des Produits Nestlé S.A. to receive training in microbiome data analysis for work presented today, and received conference travel support from Nestlé Health Sciences for work not discussed in this presentation.



↑ **Dietary Fibre**

↓ **Risk of chronic diseases**

Dietary Fiber Intake Reduces Risk for Colorectal Adenoma: A Meta-analysis

Gastroenterology 2014;146:689–699

Qiwen Ben,¹ Yunwei Sun,¹ Rui Chai,² Aihua Qian,¹ Bin Xu,¹ and Yaozong Yuan¹

Dietary fiber intake and risk of type 2 diabetes: a dose–response analysis of prospective studies

Eur J Epidemiol (2014) 29:79–88

DOI 10.1007/s10654-013-9876-x

Baodong Yao · Hong Fang · Wanghong Xu ·
Yujie Yan · Huilin Xu · Yinan Liu ·
Miao Mo · Hua Zhang · Yanping Zhao

Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis

OPEN ACCESS

BMJ 2013;347:f6879 doi: 10.1136/bmj.f6879 (Published 19 December 2013)

Diane E Threapleton *doctoral student*¹, Darren C Greenwood *senior lecturer in biostatistics*²,
Charlotte E L Evans *lecturer in nutritional epidemiology*¹, Christine L Cleghorn *research fellow*¹,
Camilla Nykjaer *research assistant*¹, Charlotte Woodhead *research assistant*¹, Janet E Cade
*professor of nutritional epidemiology group*¹, Christopher P Gale *associate professor of cardiovascular
health sciences*², Victoria J Burley *senior lecturer in nutritional epidemiology*¹

Dietary fiber and health outcomes: an umbrella review of systematic reviews and meta-analyses

Am J Clin Nutr 2018;107:436–444.

Nicola Veronese,^{1,2} Marco Solmi,³ Maria Gabriella Caruso,² Gianluigi Giannelli,² Alberto R Osella,²
Evangelos Evangelou,^{4,5} Stefania Maggi,¹ Luigi Fontana,^{7,8,9} Brendon Stubbs,^{10,11,12} and Ioanna Tzoulaki^{4,5,6}

Carbohydrate quality and human health: a series of systematic reviews and meta-analyses

Andrew Reynolds, Jim Mann, John Cummings, Nicola Winter, Evelyn Mete, Lisa Te Morenga *Lancet* 2019; 393: 434–45

**Current
Intake:
12-20 g/day**

**Recommended
Intake:
25 g/day (females)
38 g/day (males)**

**Fibre
Gap**

**Ancestral Diet:
>100 g/day**

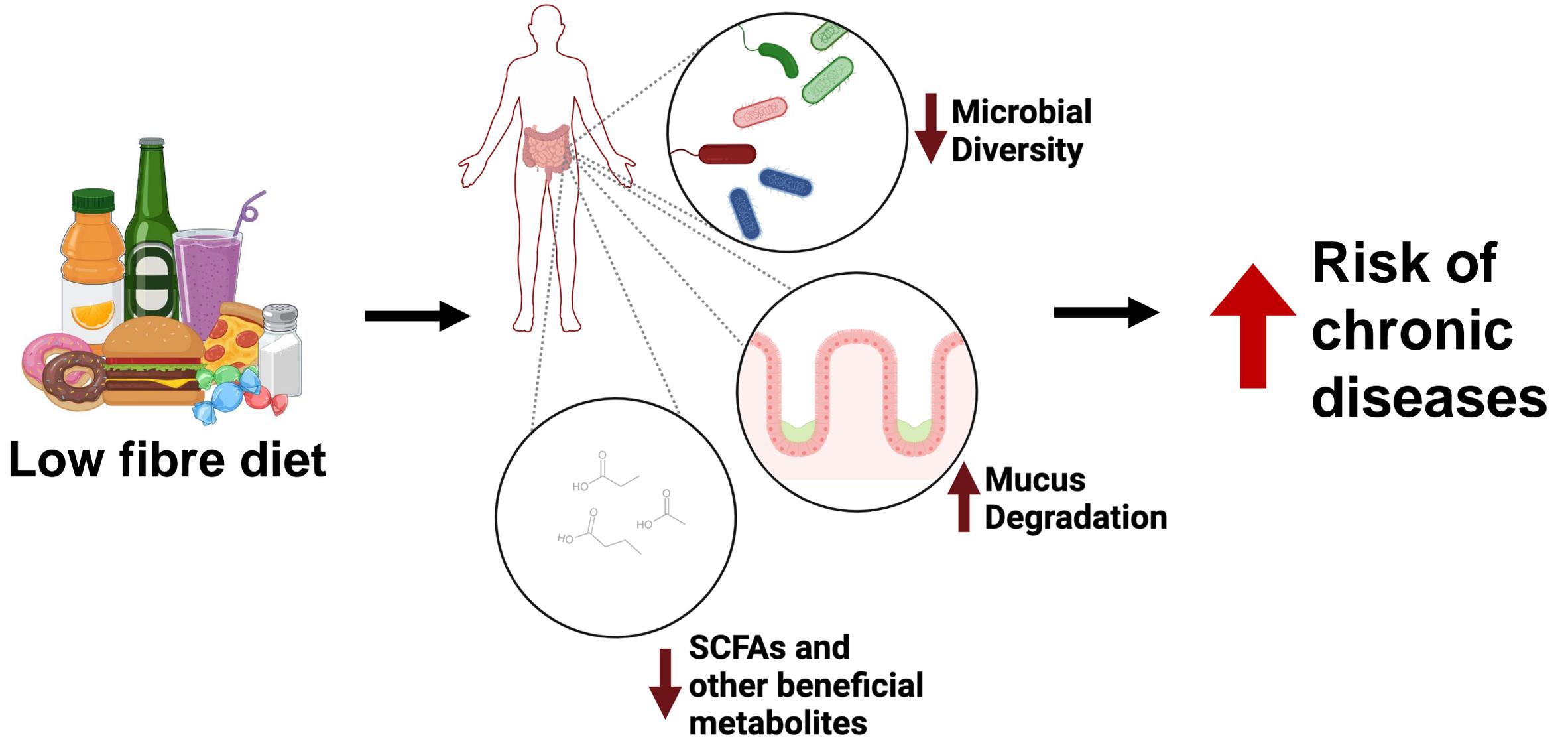


**Non-Industrialized Diet:
60-100 g/day**



Photos courtesy of Andrew Greenhill,
Federation University

Industrialization depletes the gut microbiome



Proposed solution: microbiome restoration using fibre-based nutritional strategies

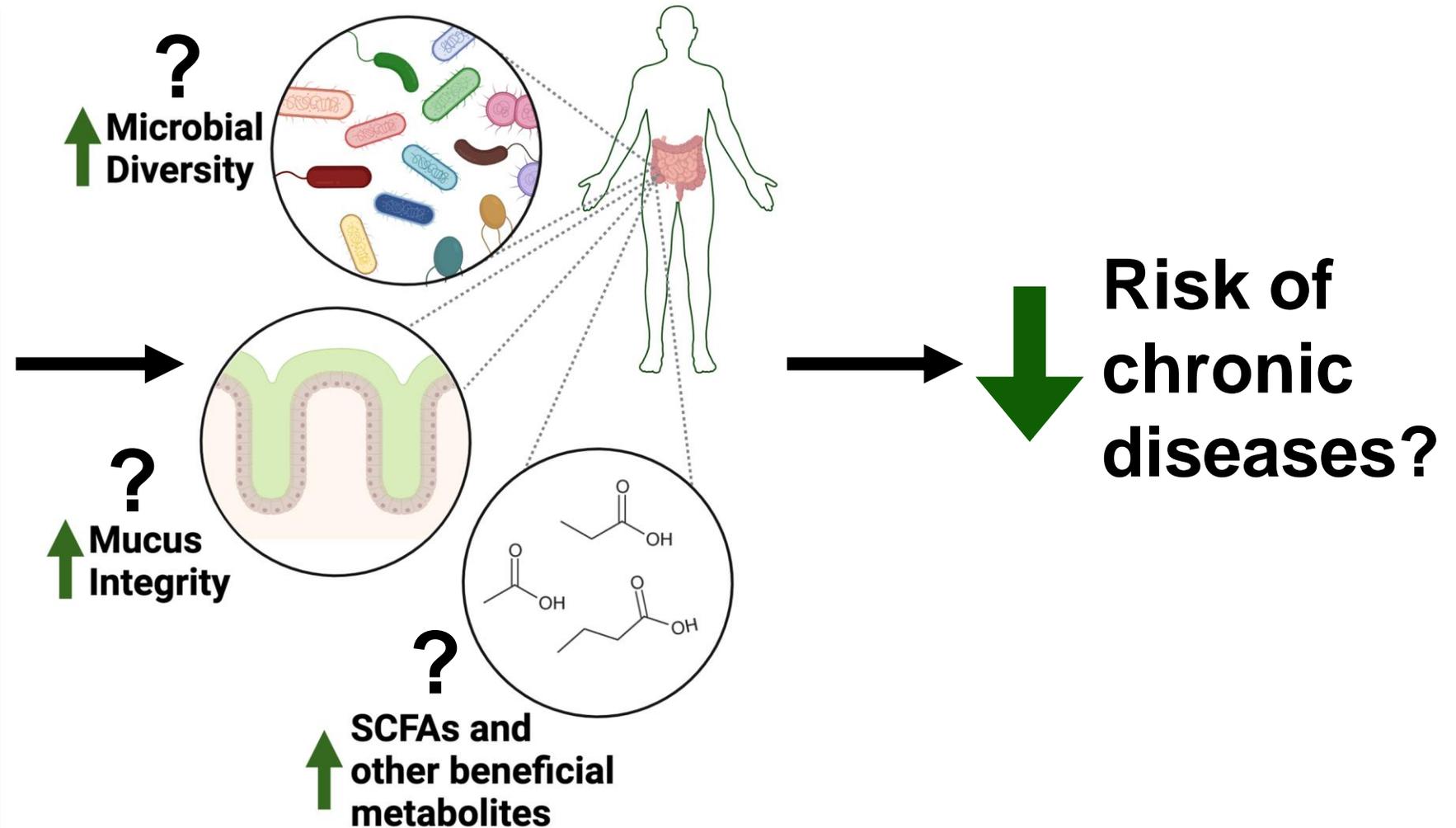
High fibre diet



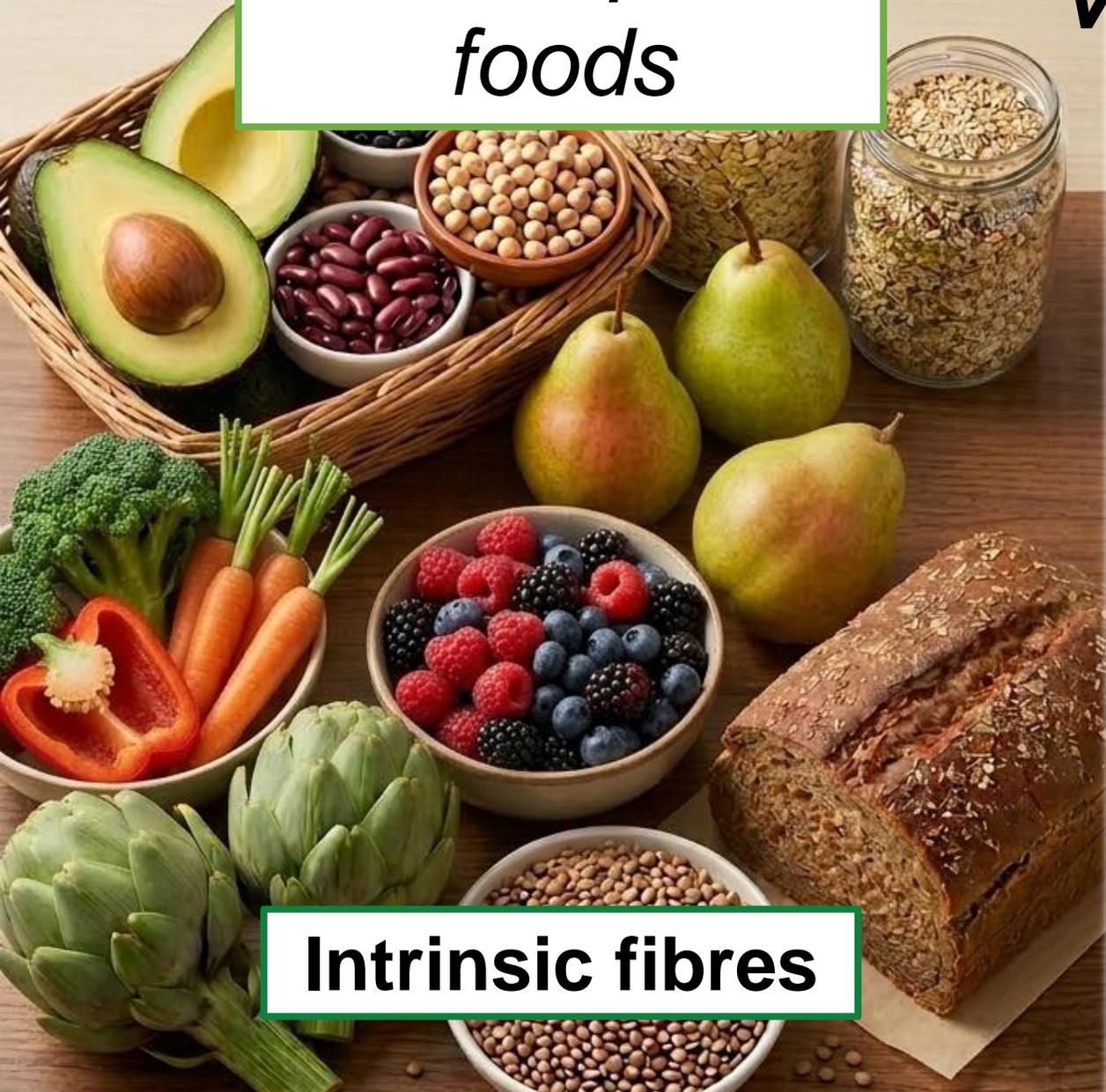
Fibre-enriched foods



Fibre supplements



Whole-plant foods



Intrinsic fibres

vs.

Fibre-enriched foods and supplements



Functional fibres

Dietary Fiber Intake Reduces Risk for Colorectal Adenoma: A Meta-analysis

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Qiwen Ben,¹ Yunwei Sun,¹ Rui Chai,² Aihua Qian,¹ Bin Xu,¹ and Yaozong Yuan¹

Dietary fiber intake and risk of type 2 diabetes: a dose-response analysis of prospective studies

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Dietary fibre intake and risk of cardiovascular disease: a systematic review and meta-analysis

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Diane E Threapleton *doctoral student*
Charlotte E L Evans *lecturer*
Camilla Nykjaer *researcher*
professor of nutrition
health sciences

Intrinsic fibres

Dietary fibre intake and risk of cardiovascular disease: an umbrella review of systematic reviews and meta-analyses

Am J Clin Nutr 2018;107:436-444.

Nicola Veronese,^{1,2} Maria Carla Caruso,² Gianluigi Giannelli,² Alberto R Osella,² Evangelos Evangelou,^{4,5} Gianluca Fontana,^{7,8,9} Brendon Stubbs,^{10,11,12} and Ioanna Tzoulaki^{4,5,6}

Carbohydrate quality and human health: a series of systematic reviews and meta-analyses

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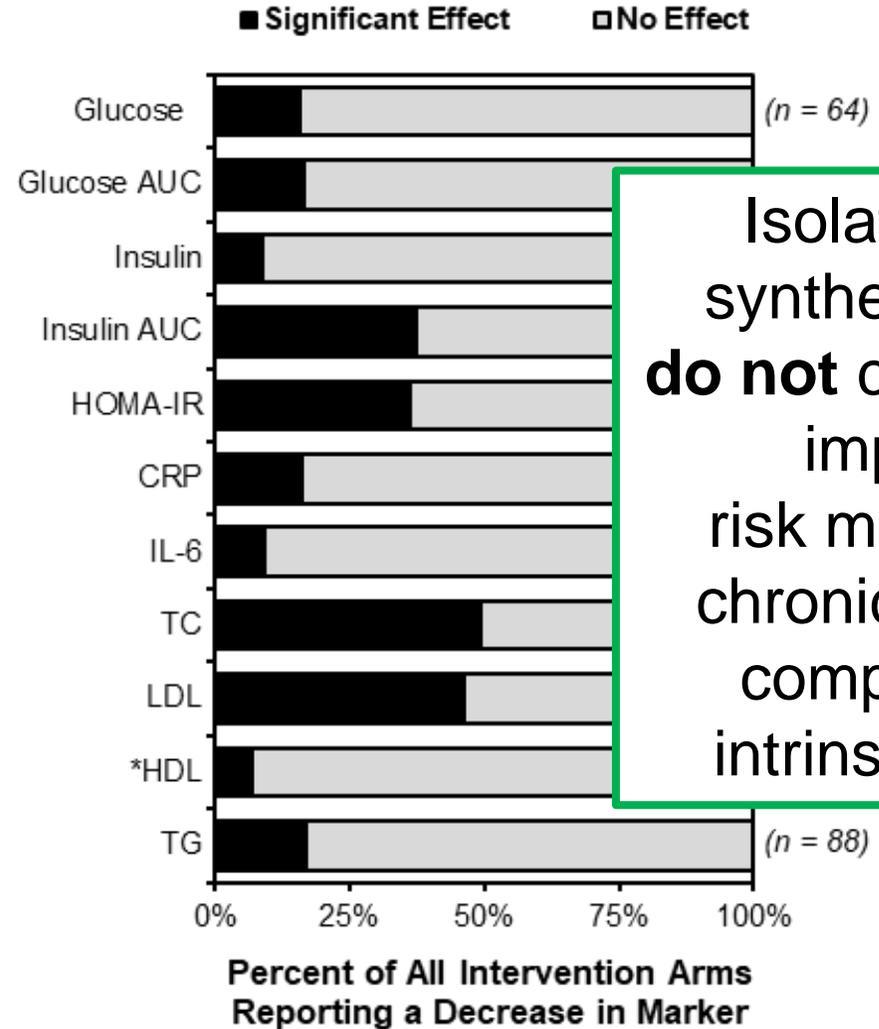
↑ Dietary Fibre

↓ Risk of chronic diseases



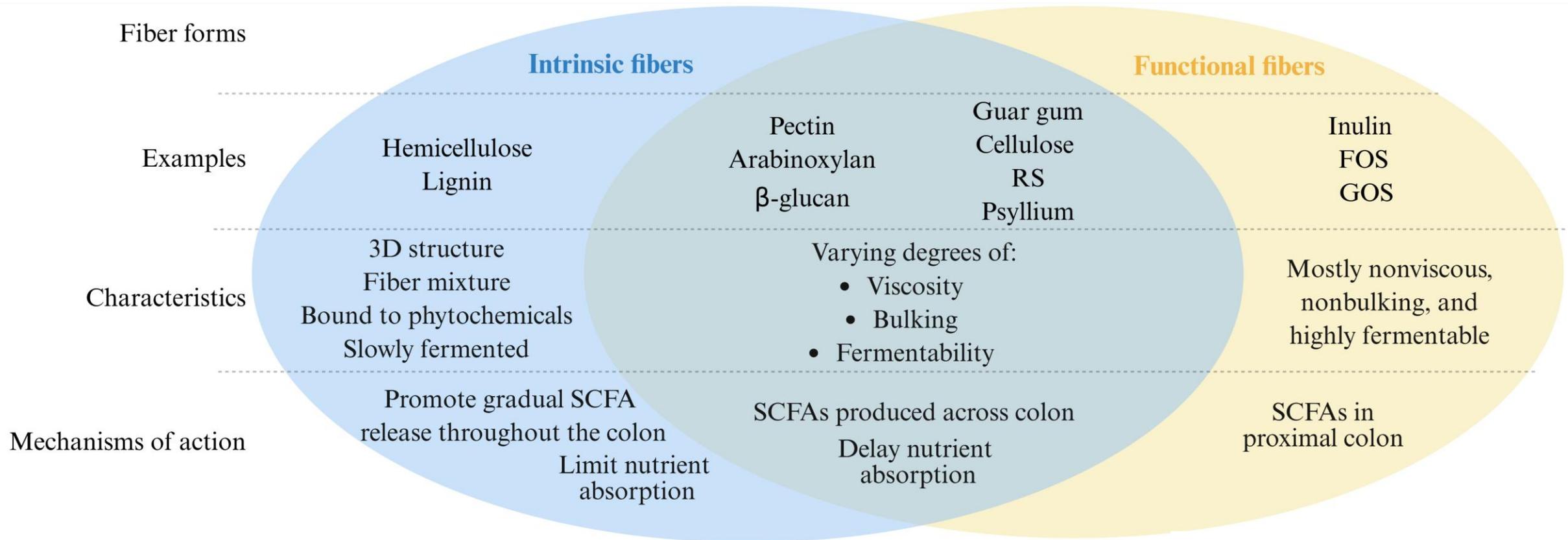
Do functional fibres similarly reduce risk of chronic diseases?

Risk markers of chronic disease



Isolated and synthetic fibres do not consistently improve risk markers of chronic disease compared to intrinsic fibres!

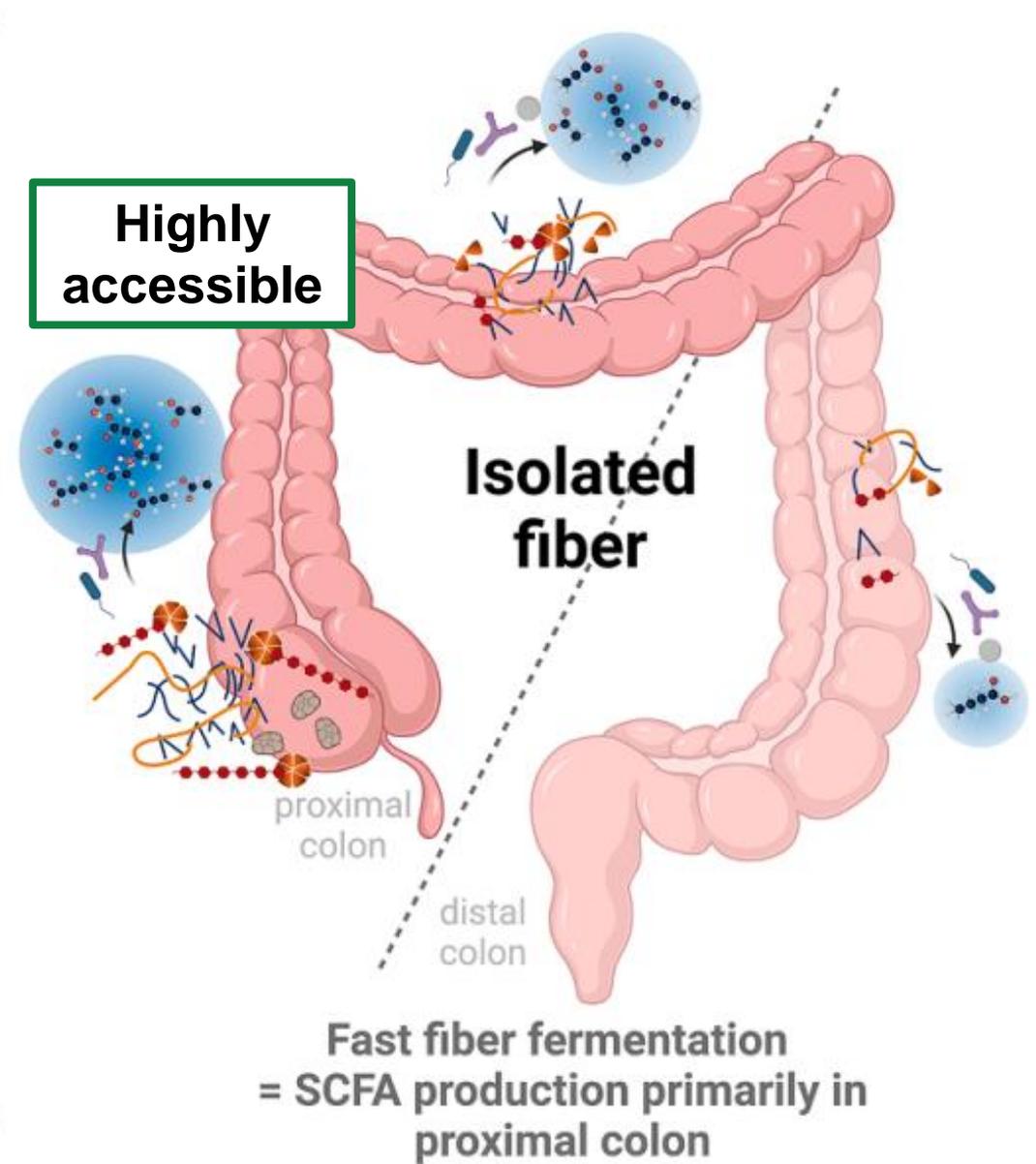
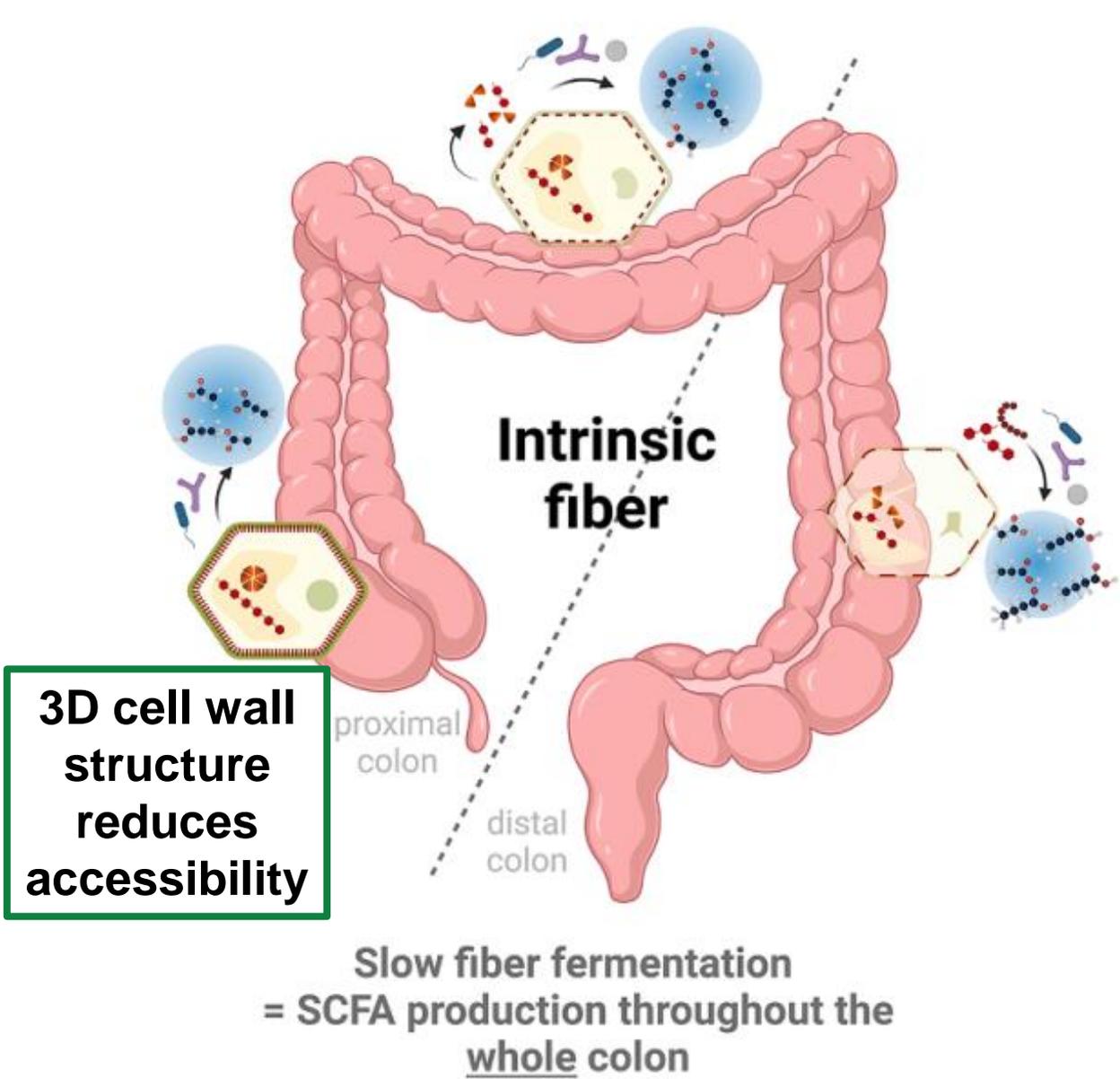
Intrinsic and functional fibres distinctly affect health due to differences in their characteristics



Annual Review of Food Science and Technology



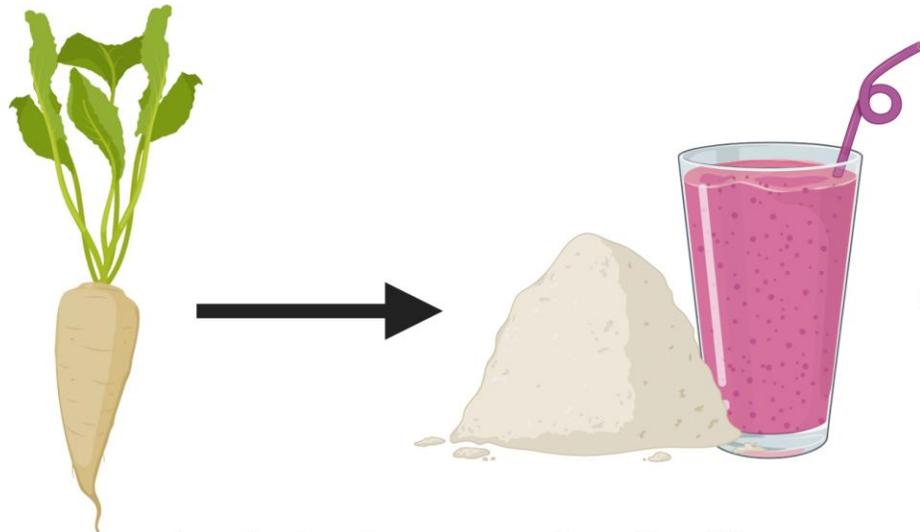
Optimizing Dietary Fiber Intake: Strategies for Human Nutrition and Food Science





Fibre-rich whole-plant foods

Diversity of fibre structures with different physicochemical properties



Isolated or synthetic fibres

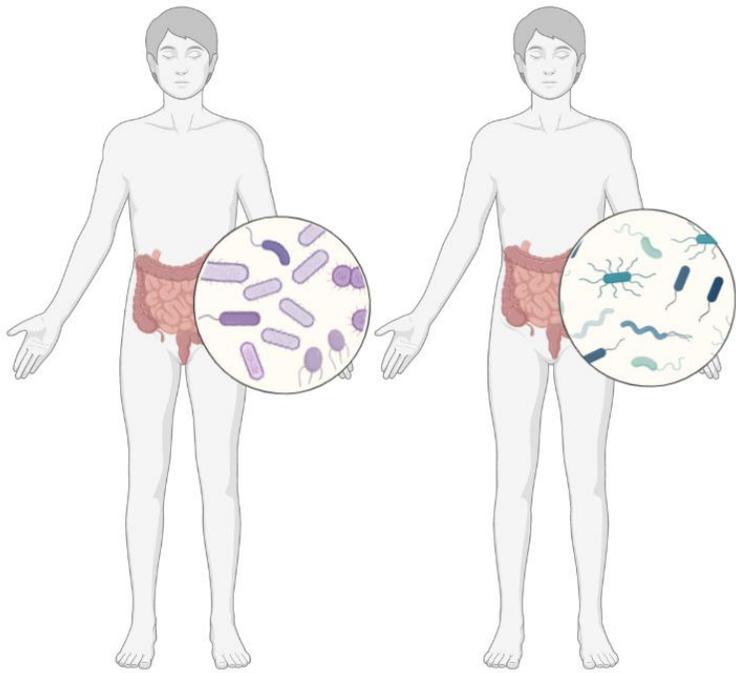
Single fibre structure with certain physicochemical properties

Fermentability

Physicochemical properties relevant to health

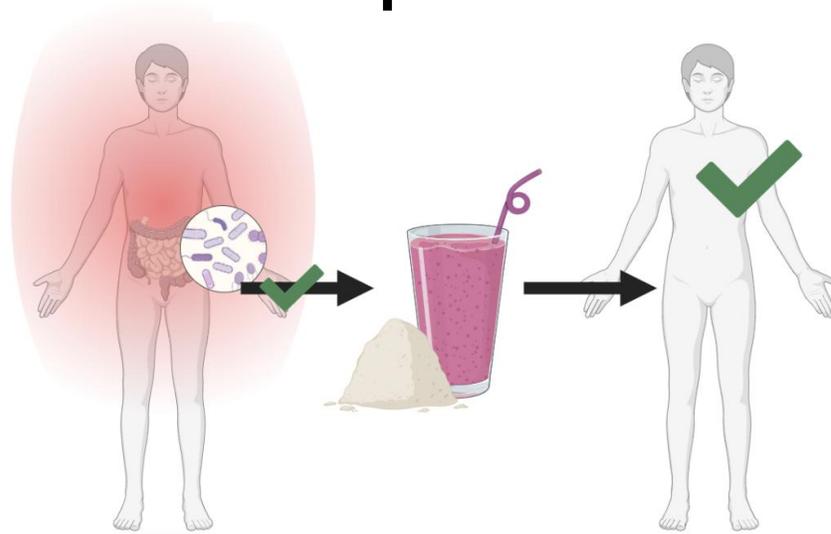
Viscosity

		Non-fermentable	Fermentable
Non-viscous	Fecal bulking/softer stools <i>e.g.</i> , cellulose	Nutrient bioavailability Fecal bulking(?) <i>e.g.</i> , inulin	
Viscous	Fecal bulking/softer stools Cholesterol-lowering Reduced glycemia <i>e.g.</i> , psyllium	Cholesterol-lowering Reduced glycemia <i>e.g.</i> , beta-glucan	

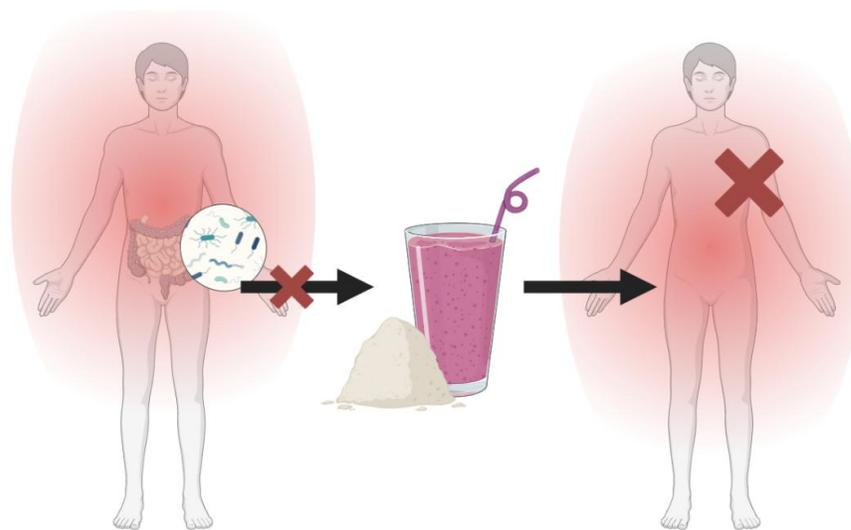


**Gut microbiome
inter-individual
variability**

Responder



Non-Responder



**Health benefits
may depend on
individual
microbiome
capacity
to ferment
dietary fibres**

Microbiome restoration using fibre-based nutritional strategies – *what is the ideal solution?*

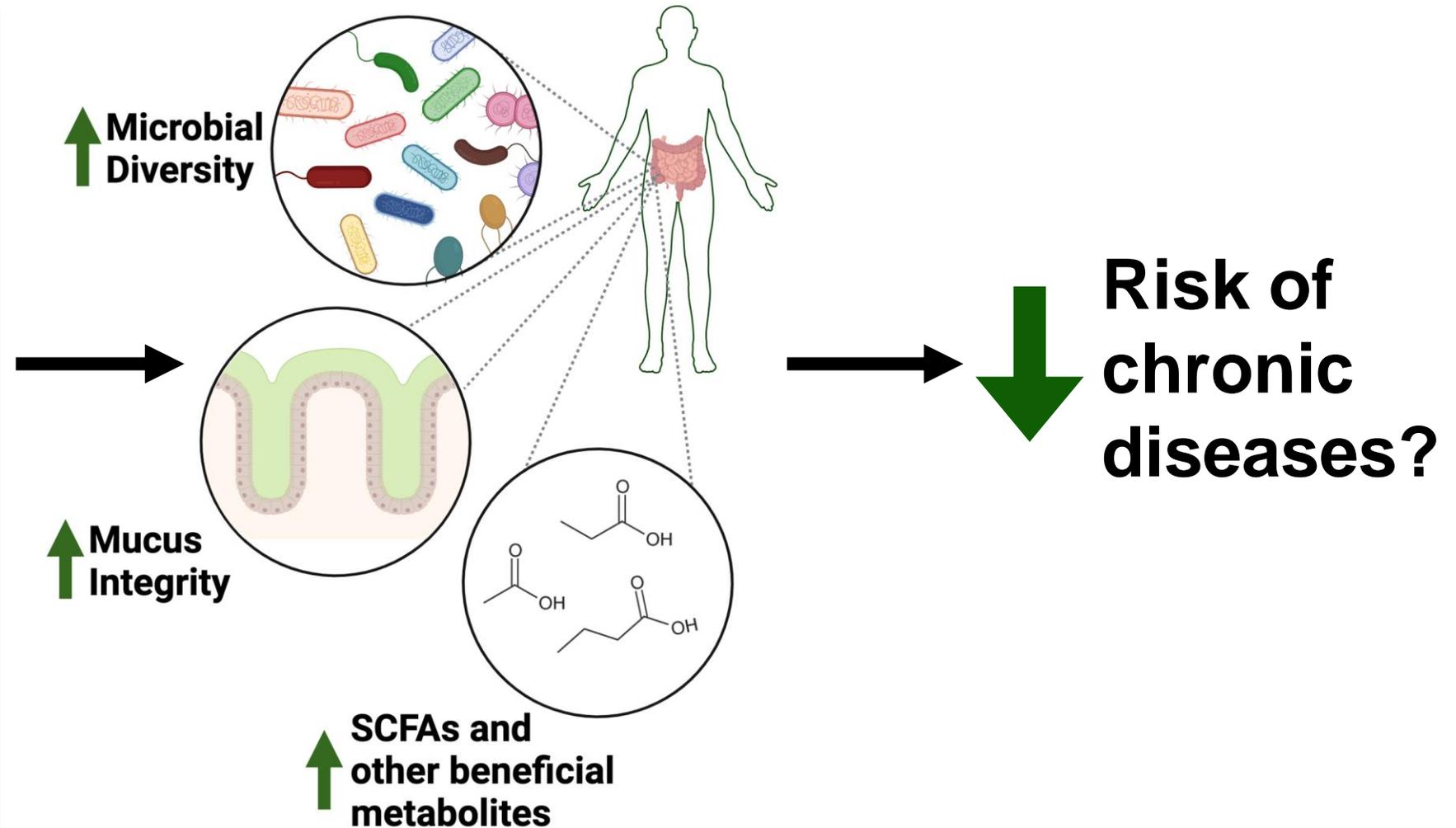
High fibre diet ?



Fibre-enriched foods



Fibre supplements



NiMe Diet™

**Non-industrialized
Microbiome Restore Diet**

STUDY TEAM

Dr. Jens
Walter (PI)



Nutrition and Metabolism

- Janis Cole
- Tianna Rusnak
- Adele Gagnon
- Susan Goruk
- Edward Deehan
- Dr. Catherine Field
- Dr. Carla Prado

Clinicians

- Dr. Andrea Haqq
- Dr. Laurie Mereu



Bioinformatics and Statistics

- Katri Korpela
- Francesco Asnicar
- Dr. Nicola Segata



HELSINGIN YLIOPISTO
HELSINGFORS UNIVERSITET
UNIVERSITY OF HELSINKI



UNIVERSITY
OF TRENTO

Machine Learning

- Dr. Russ Greiner
- Dr. Dan Knights



UNIVERSITY
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UNIVERSITY
OF MINNESOTA

Metabolomics

- Dr. Liang Li Lab
- Novozymes



UNIVERSITY
OF ALBERTA

novozymes 

Laboratory Assistance



- Junhong Liu
- Rodrigo Quevedo
- Zhihong Zhang



Weston Family
Foundation

ALBERTA
INNOVATES 

 PrecisionBiotics™



Lauréats
KILLAM
Laureates 

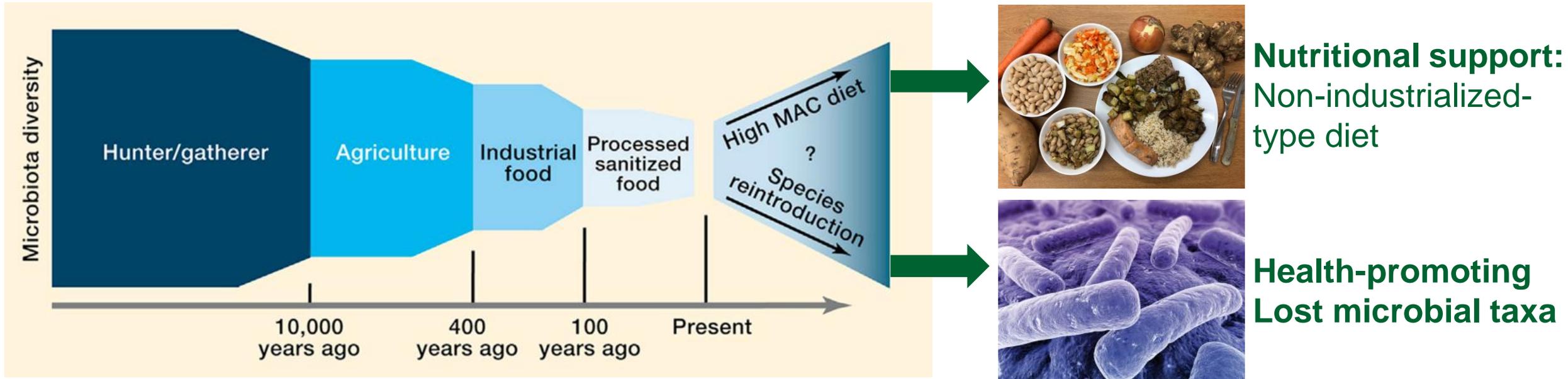


Canadian Institutes of
Health Research
Instituts de recherche
en santé du Canada



PAPUA NEW GUINEA
INSTITUTE OF
MEDICAL RESEARCH

Is microbiome restoration possible?

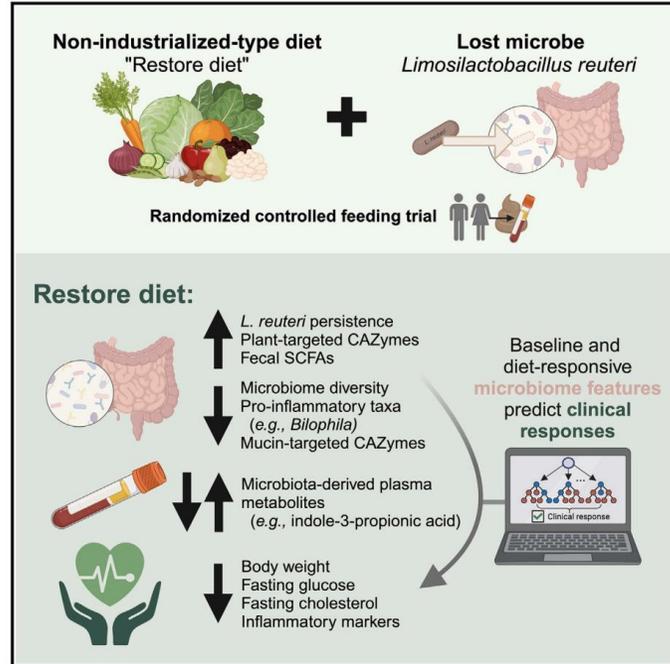


Sonnenburg & Sonnenburg, *Cell Metabol* 2014;20:779–786.

Can microbial diversity, specific taxa, and/or microbial functions be restored? Would this improve human health in industrialized societies?

Cardiometabolic benefits of a non-industrialized-type diet are linked to gut microbiome modulation

Graphical abstract



Highlights

- The restore diet reduced microbiome diversity but enhanced *L. reuteri* persistence
- The diet redressed several microbiome features altered by industrialization
- The diet induced beneficial changes to microbiota-derived plasma metabolites
- Cardiometabolic benefits of the diet were predicted by microbiome features

Authors

Fuyong Li, Anissa M. Armet, Katri Korpela, ..., Liang Li, Carla M. Prado, Jens Walter

Correspondence

jenswalter@ucc.ie

In brief

Is it possible to restore the human gut microbiome in industrialized settings and reintroduce microbial species that have been lost? In healthy adults, Li et al. found that consuming a diet mimicking non-industrialized dietary patterns (restore diet) together with a bacterium rarely found in industrialized human gut microbiomes (*Limosilactobacillus reuteri*) enhanced persistence of the latter. The diet also redressed several microbiome features altered by industrialization, which was linked to considerable cardiometabolic benefits.



Open-Access!

Microbiome Restoration Strategy in Humans

Lost microbe:

Limosilactobacillus reuteri



Nutritional support:
Non-industrialized-type diet
(*NiMe*TM Diet,
AKA restore diet)

Nutritional Support: Non-Industrialized-Type Diet

- Based on dietary pattern of rural Papua New Guineans
 - Chose foods that were:
 - Readily available in Canada
 - Rich in raffinose and stachyose, growth substrates of *L. reuteri*

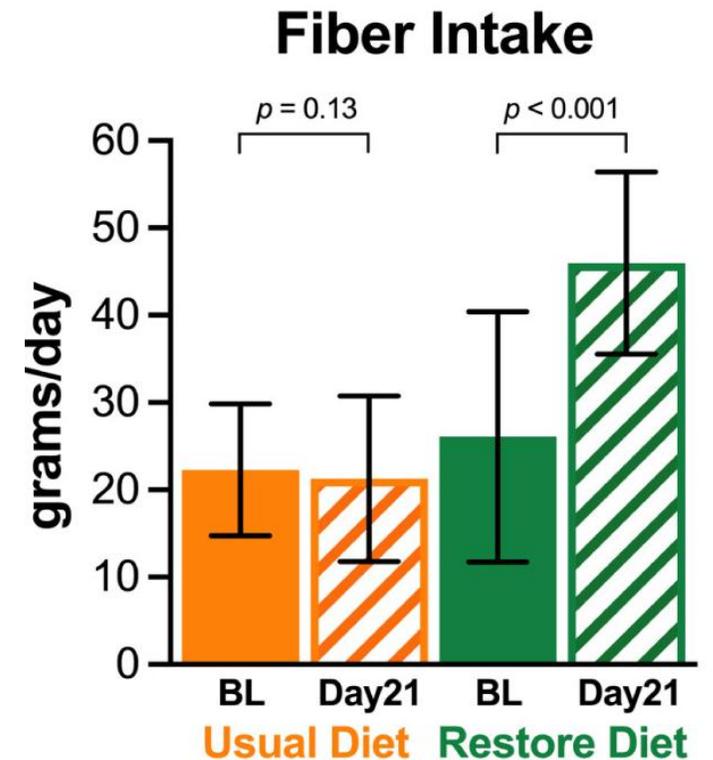


Supplementary Table S1_ Related to Figure 1. Diet of Asaro and Sausi people based on a dietary survey conducted through interviews with study participants*.

	Asaro	Sausi
Sources of carbohydrate	1. Sweet potato (kaukau) 2. Plantain 3. Cassava (tapiok) 4. Rice 5. Sago	1. Sweet potato 2. Taro 3. Banana 4. Cassava 5. Yam Others: sago, rice, plantain, pumpkin
Sources of protein**	1. Tinned fish 2. Pork 3. Tinned meat 4. Chicken (karkaruk) 5. Lamb flaps	1. Pork 2. Fresh fish 3. Chicken 4. Tinned fish 5. Tinned meat Others: cassowary (muruk), bandicoot
Fruits, vegetables and legumes	1. Bush kumu (leafy green) 2. Aibica (type of kumu) 3. Beans 4. Ripe bananas 5. Peanuts Others: pumpkin leaves, guava, pawpaw, tamarillo, corn, cucumber, avocado, karuka nuts	1. Aibica 2. Bush kumu 3. Tulip (leafy green) 4. Beans 5. Pawpaw Others: pineapple, coconut, peanuts, aupa, mango, guava, mon, cucumber, melon, sago leaves, pumpkin leaves, pitpit, cabbage, sugar cane

Non-Industrialized-Type Diet ('restore diet')

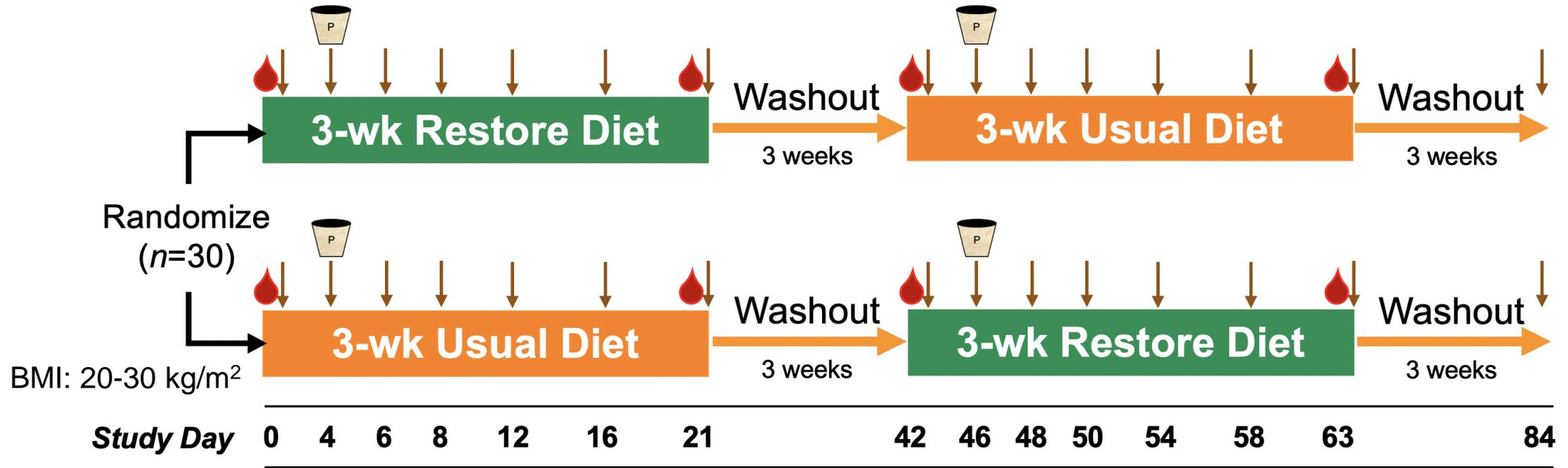
- Minimally-processed, mainly plant-based
 - Rich in vegetables, legumes, whole grains
 - Very high in fibre
 - 1 serving animal protein/day
 - No dairy or wheat
- **Macronutrient distribution:**
 - 60% carbohydrate
 - 15% protein
 - 25% fat



Controlled Feeding Trial

- All meals and snacks prepared in metabolic kitchen.
- **Highly precise and standardized**
- Diet provided to participants for three weeks, based on their calculated caloric (energy) requirements.

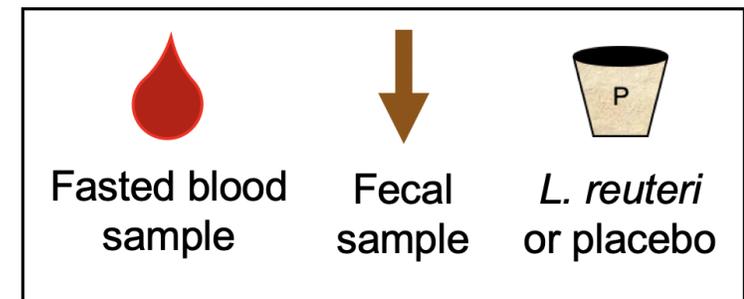
Study Design



Crossover design: non-industrialized-type diet (Restore Diet); $n=30$

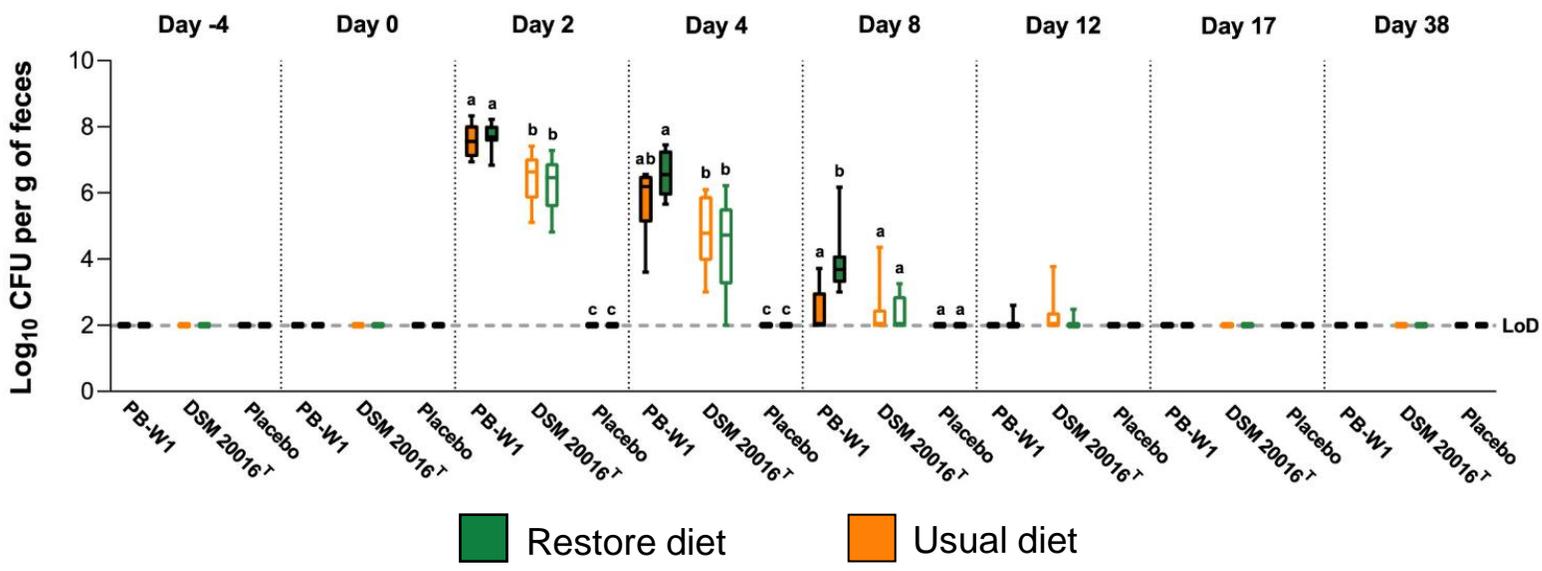
Parallel design: lost microbe (*L. reuteri*)

- **PB-W1** $n=9$;
- **DSM20016^T** $n=11$;
- **Placebo**; $n=10$



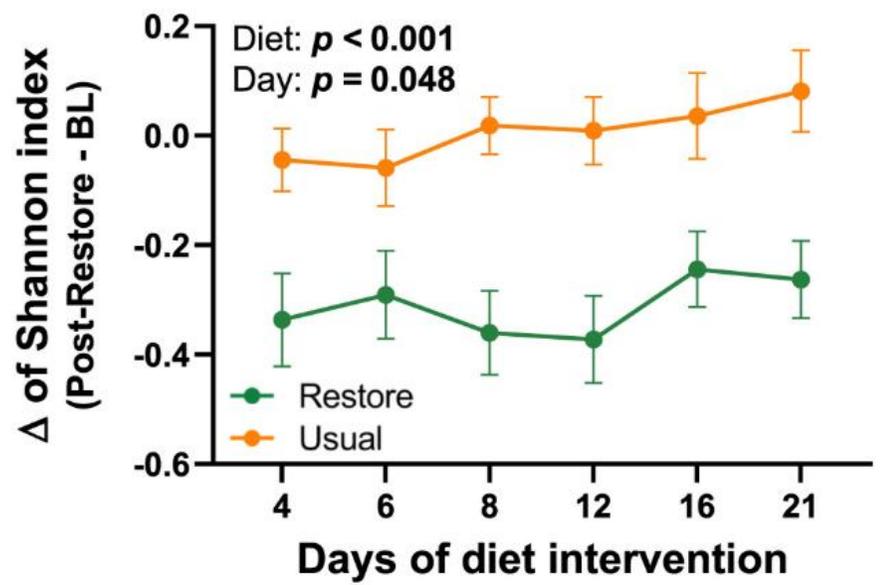
L. reuteri persistence enhanced by the **restore diet** but gut microbiome diversity reduced

Abundance of *L. reuteri* (quantitative culture)



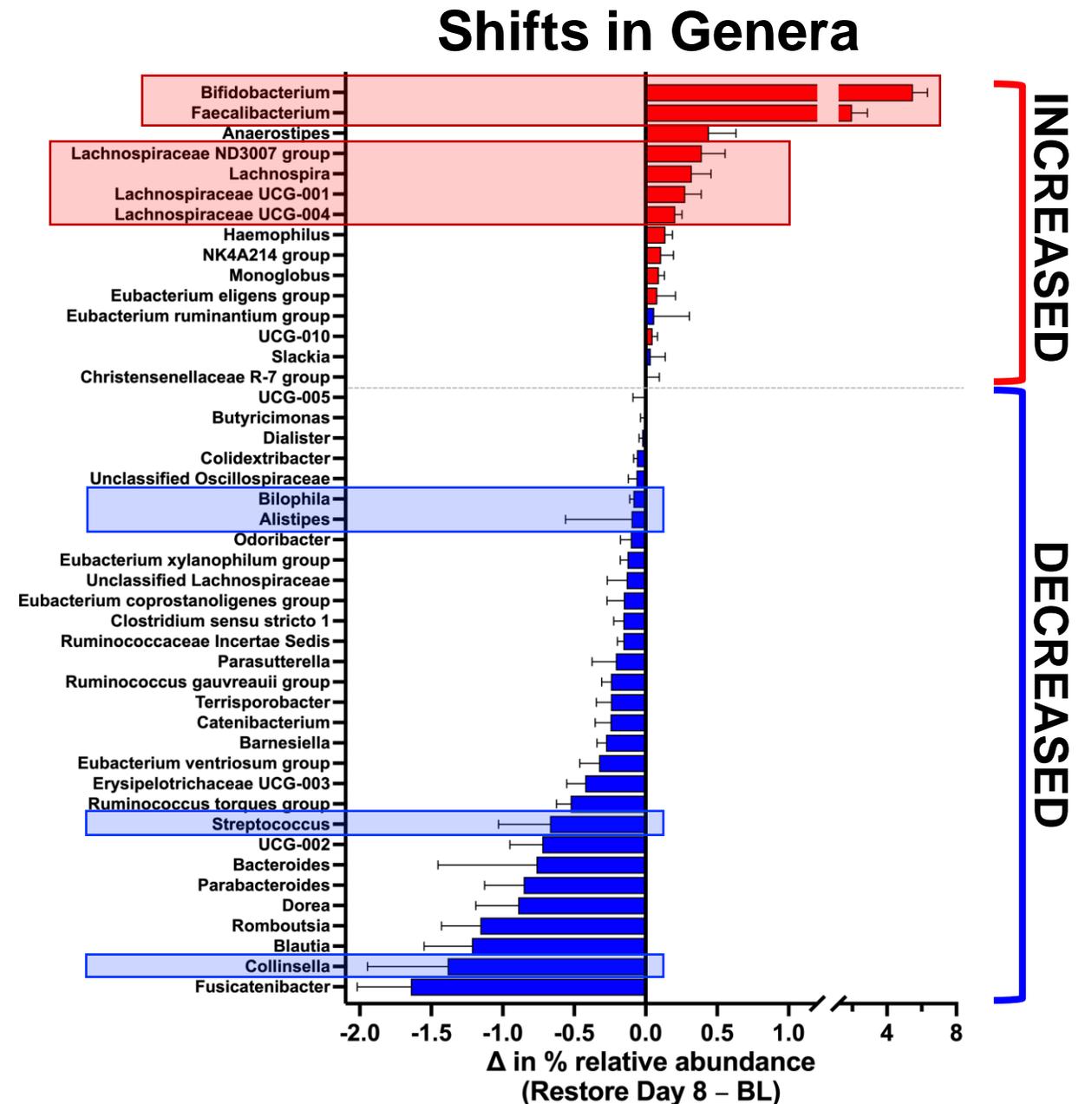
L. reuteri had **no** effect on microbiome or host

Shannon index (ASVs)



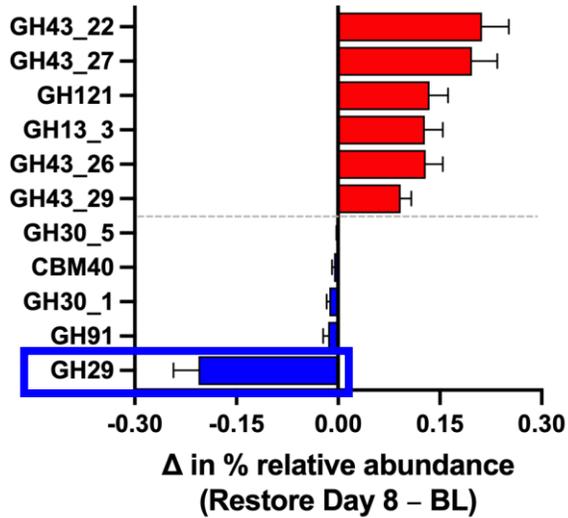
The **restore diet** shifted gut microbiome composition

- **Increased** abundance of potentially health-promoting taxa (e.g. *Bifidobacterium*, *Faecalibacterium*, *Lachnospira*)
- **Decreased** abundance of potentially pro-inflammatory taxa (e.g., *Bilophila*, *Alistipes*, *Streptococcus*, *Collinsella*)

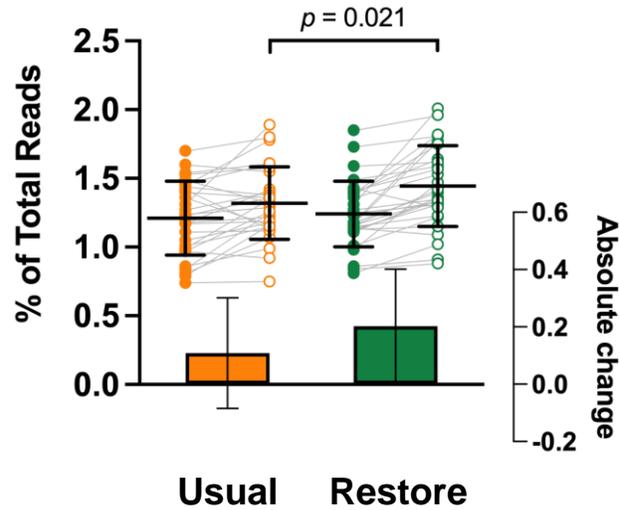


The restore diet enhanced fibre fermentation

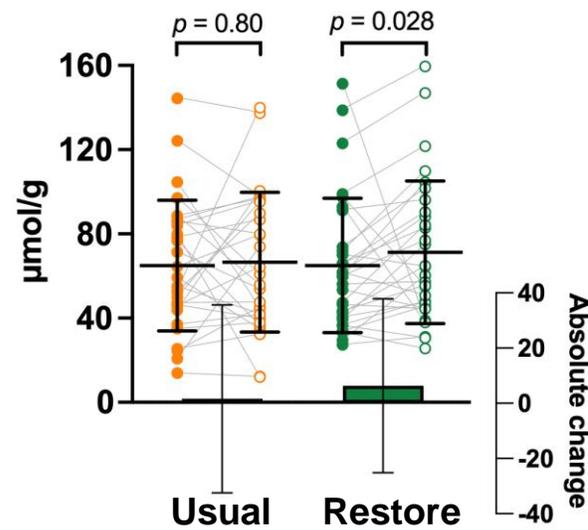
Shifts in CAZymes



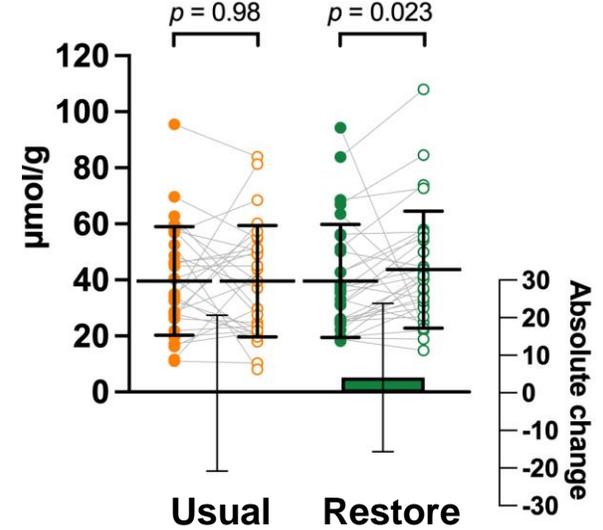
Plant-Targeted CAZymes



Total SCFAs



Acetate



↓ GH29: Mucin-targeted CAZyme

↑ Plant-targeted carbohydrate-active enzymes (CAZymes)

● Baseline – Usual Diet

● Baseline – Restore Diet

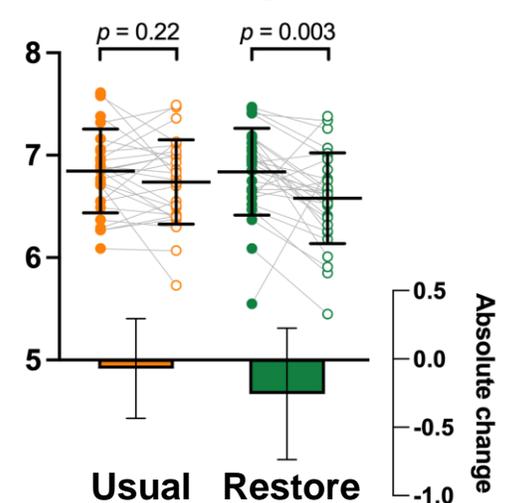
○ Day 21 – Usual Diet

○ Day 21 – Restore Diet

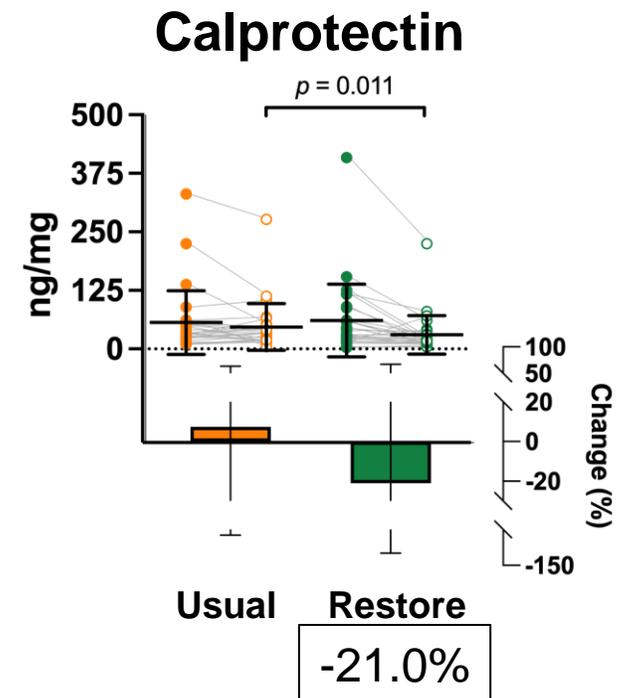
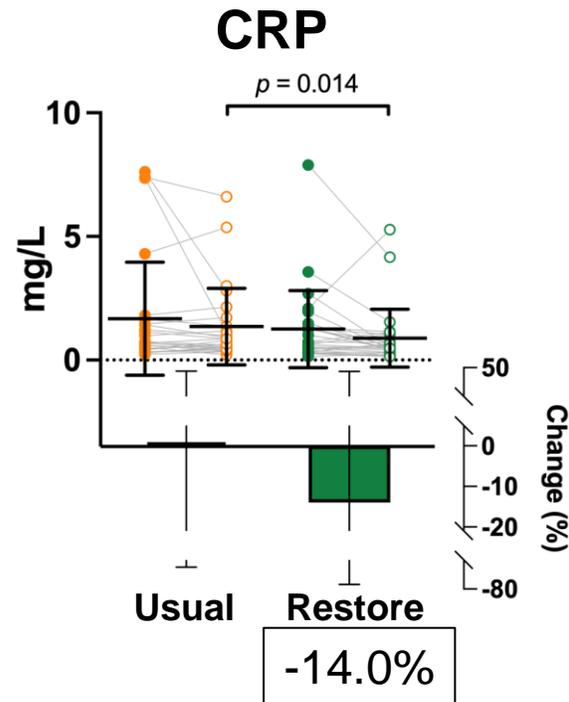
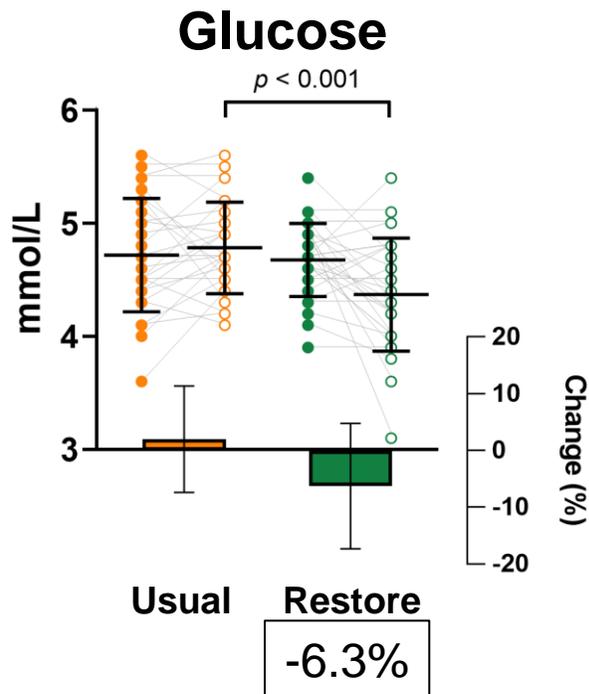
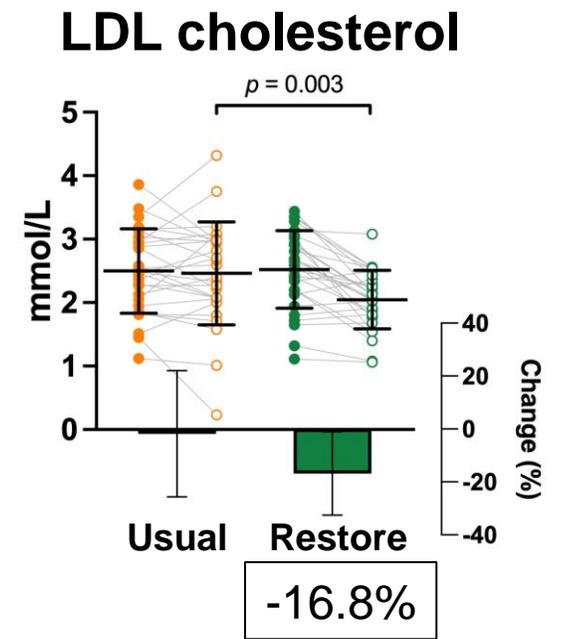
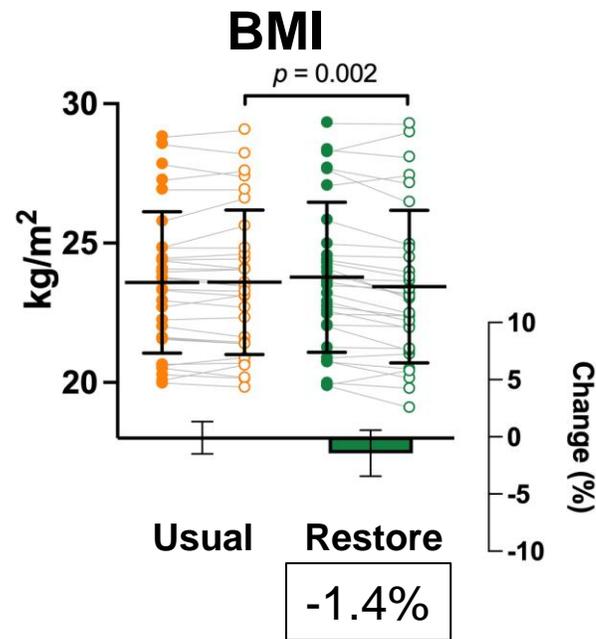
↑ Fecal SCFAs

↓ Fecal pH

Fecal pH

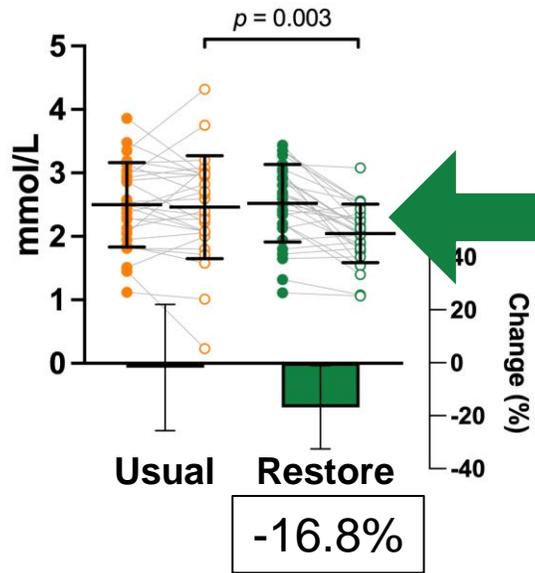


The **restore diet** improved several risk markers of chronic diseases

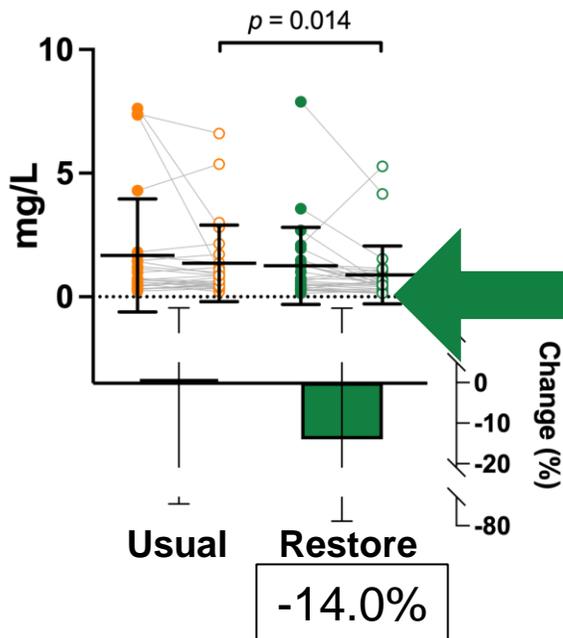


- Baseline – Usual Diet
- Day 21 – Usual Diet
- Baseline – Restore Diet
- Day 21 – Restore Diet

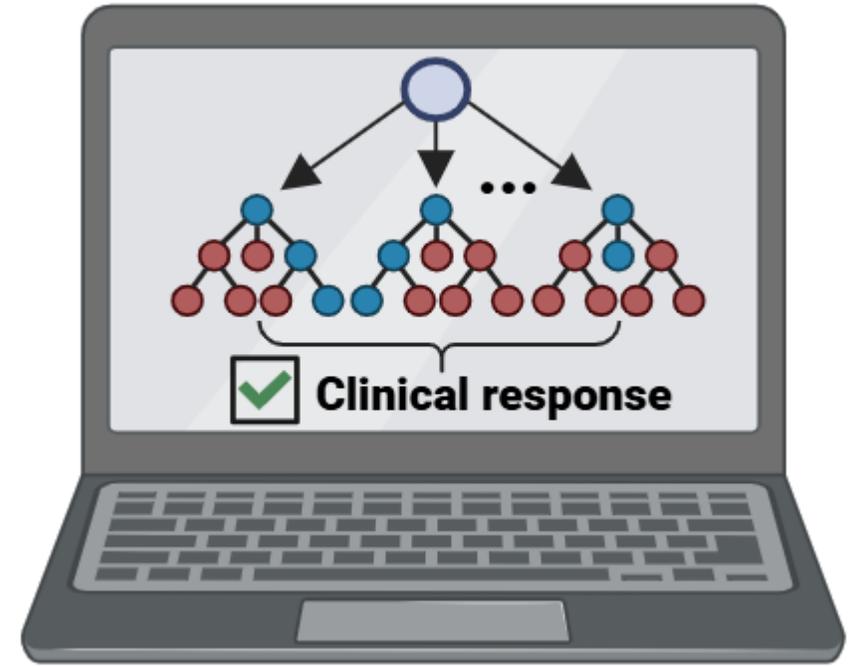
LDL cholesterol



CRP



**Similar
responses
across
individuals**



**Baseline and diet-
responsive microbiome
features predict certain
clinical responses**

NiMe Diet™

**Non-industrialized
Microbiome
restore diet**

- NiMe™ diet redressed several microbiome features altered by industrialization, despite reducing microbiome diversity.
 - Reduced pro-inflammatory microbes
 - Reduced mucus degradation potential
 - Increased fibre fermentation
- Risk markers of chronic diseases were significantly improved.
- Diet-induced changes to microbiome are linked to cardiometabolic benefits.

Isolated fibre supplements

Alberta FYBER Study

STUDY TEAM

Dr. Jens
Walter (PI)



Nutrition and Metabolism

- Dr. Edward Deehan
- Janis Cole
- Junhong Liu
- Khoi Nguyen Nguyen
- Dr. Mingliang Jin
- Dr. Yuan-Yuan Zhao
- Dr. Arya Sharma
- Dr. Jonathan Curtis
- Dr. Spencer Proctor
- Dr. Wendy Wismer
- Dr. Jeffrey Bakal
- Dr. Catherine Field
- Dr. Carla Prado



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Bioinformatics and Statistics

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- Dr. Omar Delannoy-Bruno
- Dr. Léa Siegwald
- Dr. Bernard Berger
- Dr. Kaori Minehira Castelli
- Dr. Dmitry Rodionov
- Dr. Aleksandr Arzamasov
- Dr. Andrei Osterman



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Machine Learning

- Dr. Russ Greiner



- Dr. Dan Knights



Barrier Function

- Dr. Benjamin Seethaler
- Dr. Stephan Bischoff



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JPI
a healthy diet
for a healthy life



Fibre Supplements



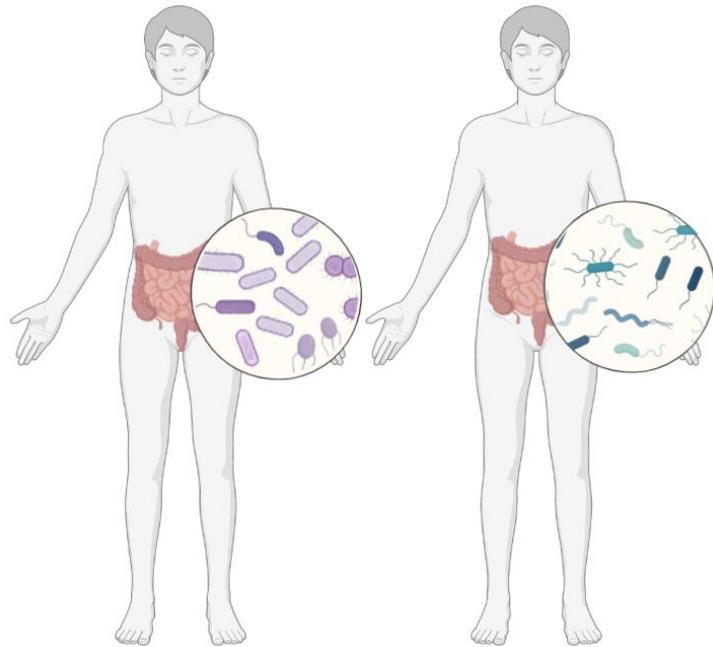
Acacia gum



Resistant starch type 4



Microcrystalline cellulose



**Gut microbiome
inter-individual
variability**

**How do distinct fibre
structures affect the
gut microbiome and
human health?**

**Are health effects
linked with individual
microbiome
signatures?**

The Alberta FYBER Study



Acacia Gum (AG)

Low-viscosity, soluble, fermentable
Agrigum International, UK



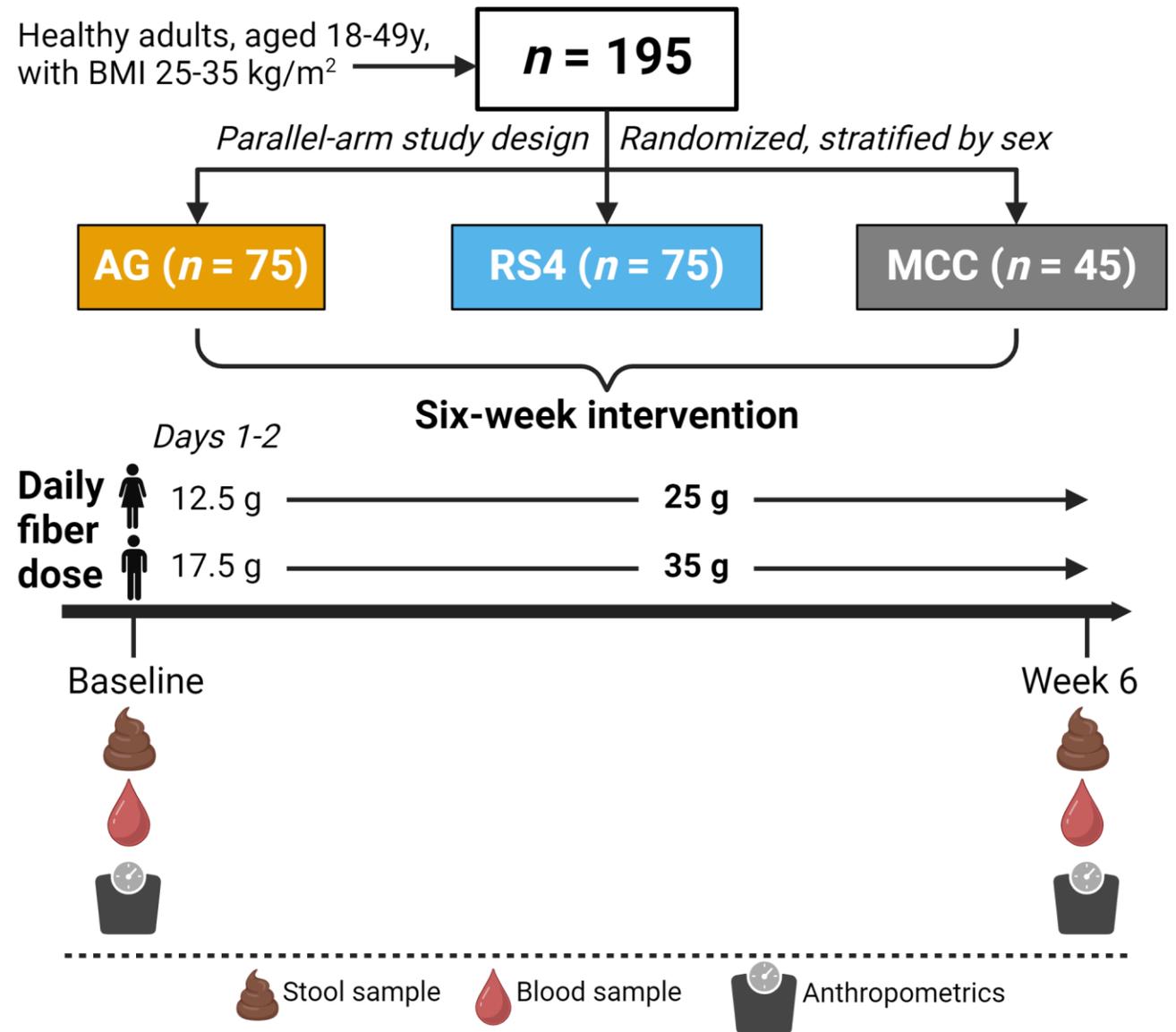
Resistant Starch Type IV (RS4)

Low-viscosity, insoluble, fermentable
MGP Ingredients, USA



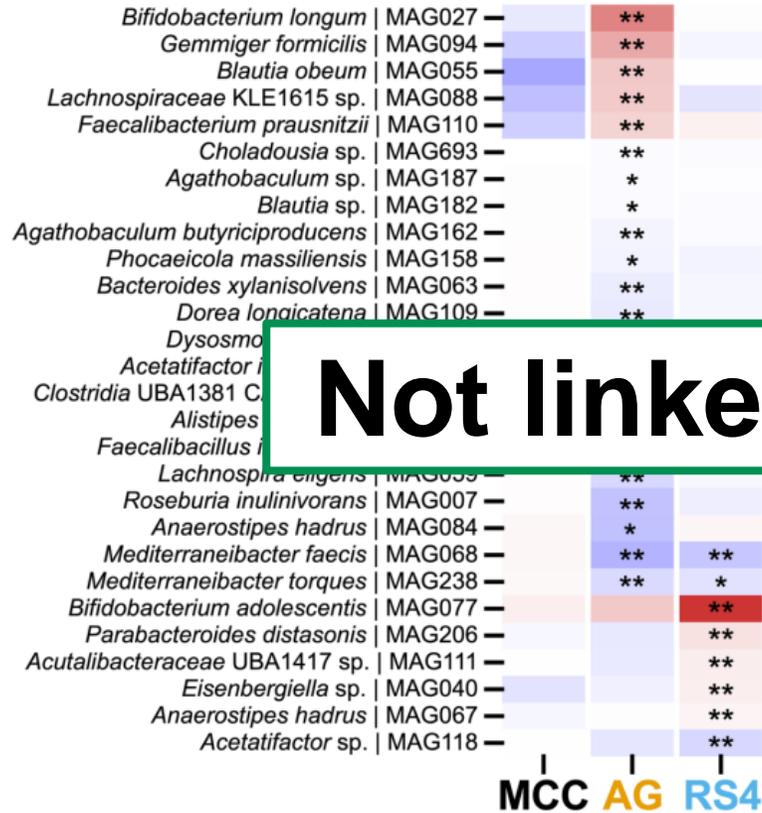
Microcrystalline Cellulose (MCC)

Non-viscous, insoluble, non-fermentable
Blanver Farmquimica LTDA, Brazil



Distinct fermentables fibres induce selective microbiome shifts

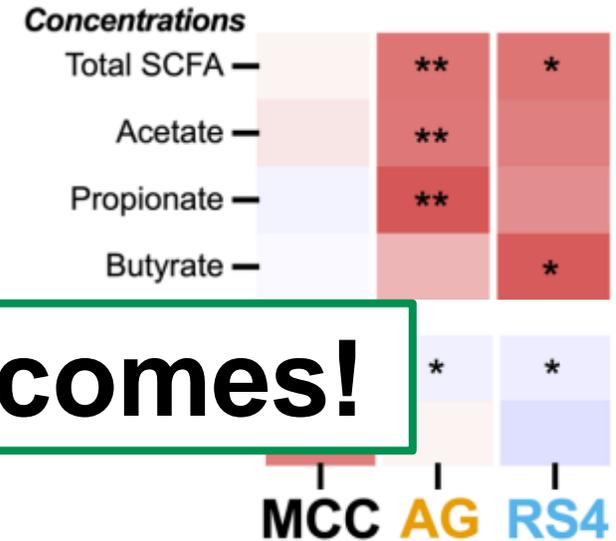
Shifts in Microbiome Composition (Abundance of MAGs)



Shifts in Fermentation Capacity (Abundance of CAZymes)



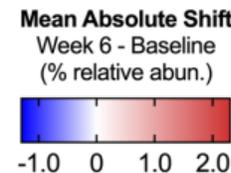
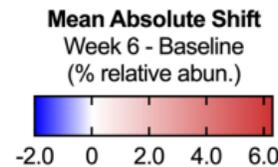
Shifts in Short-Chain Fatty Acids



Not linked with health outcomes!

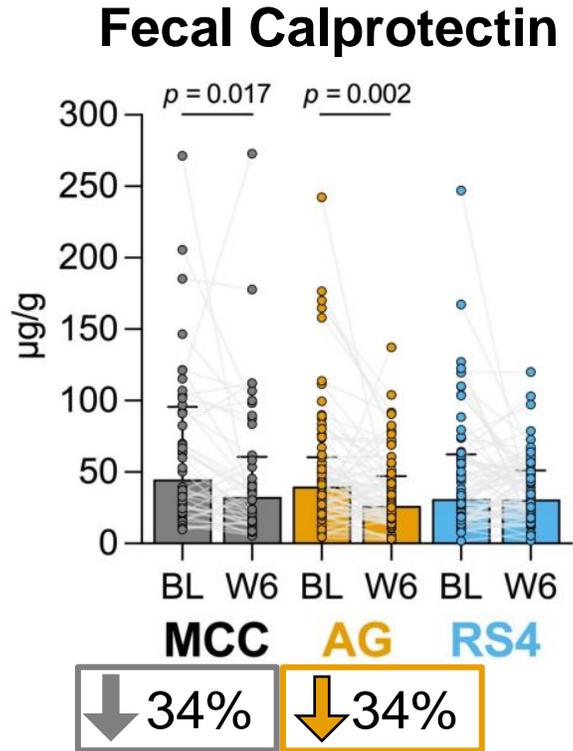
Non-fermentable MCC had no significant effects on microbiome features

Within Group Change
Wilcoxon test, FDR-corrected
* $p < 0.01$
** $p < 0.001$

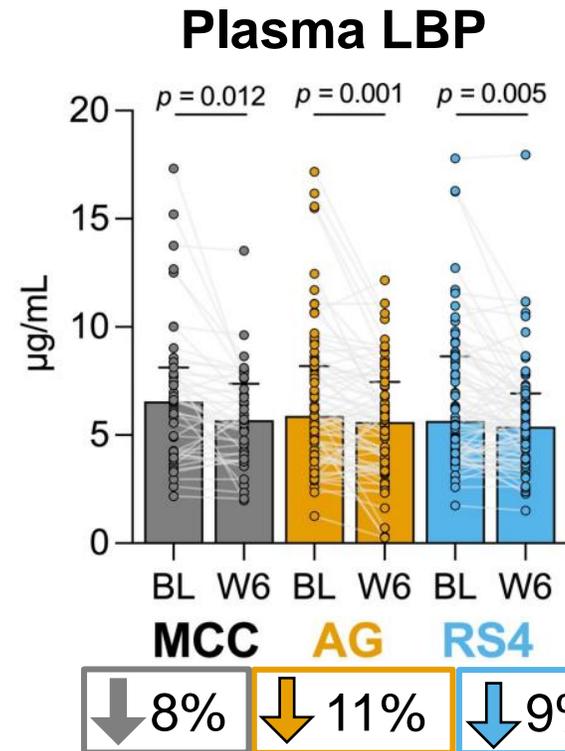


AG = Acacia gum
RS4 = Resistant starch type 4
MCC = Microcrystalline cellulose

Distinct dietary fibre structures improve markers of inflammation and gut barrier function

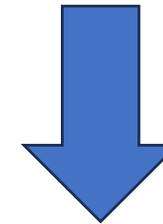


AG and **MCC** decreased marker of gut inflammation



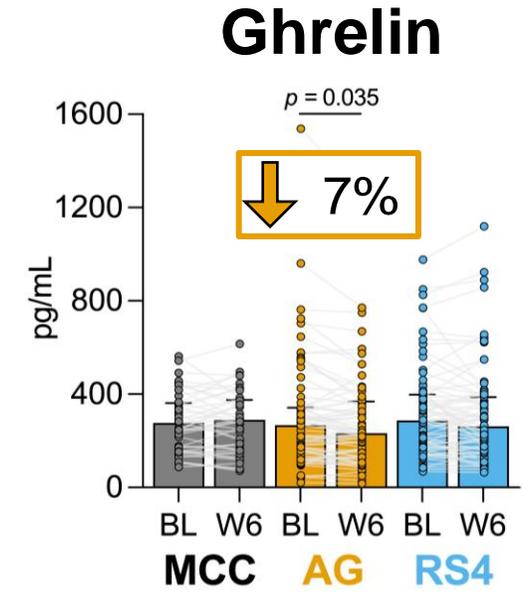
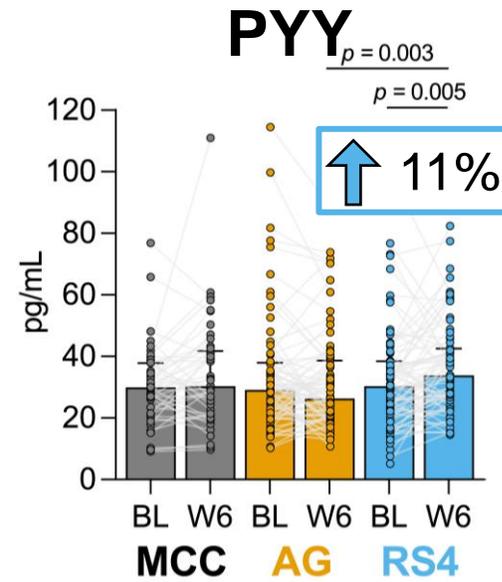
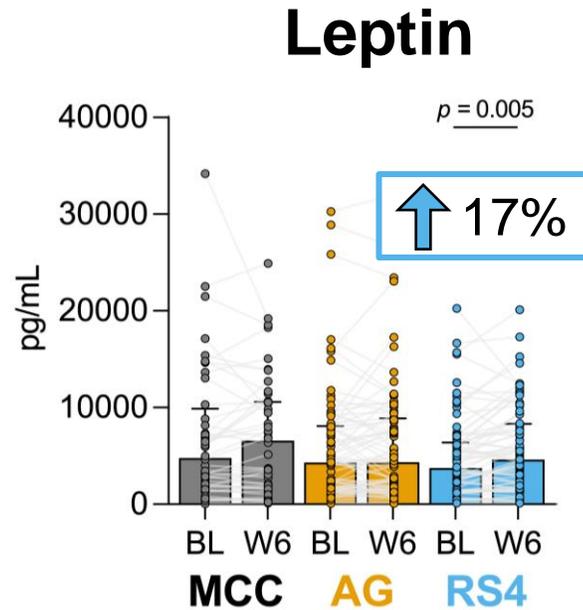
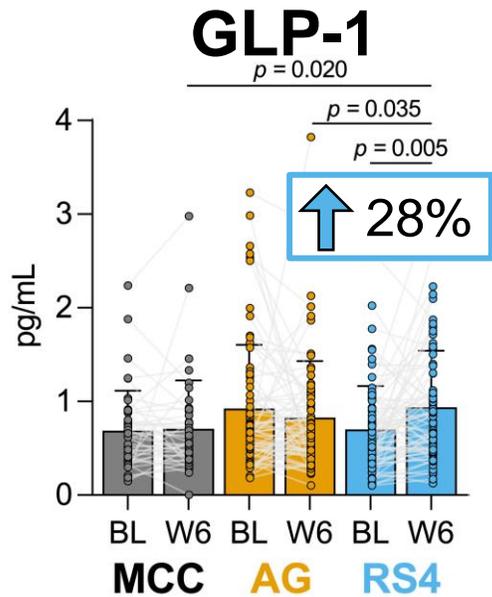
All three fibres decreased marker of gut barrier dysfunction

Non-fermentable MCC had similar effects as fermentable fibres

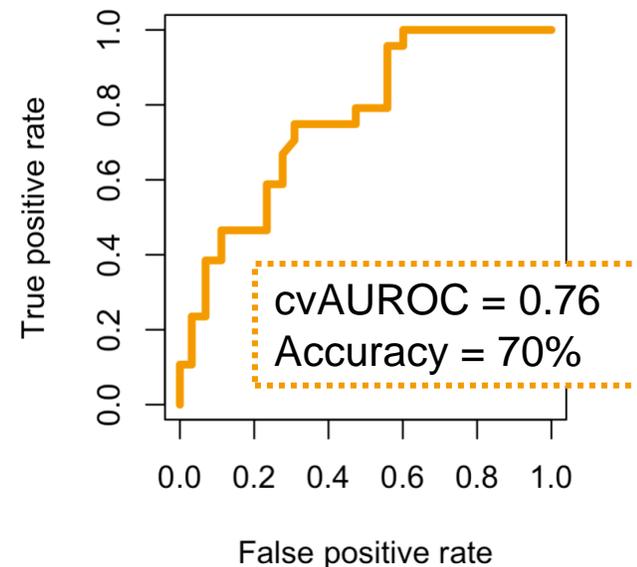


Effects independent of fibre fermentation?

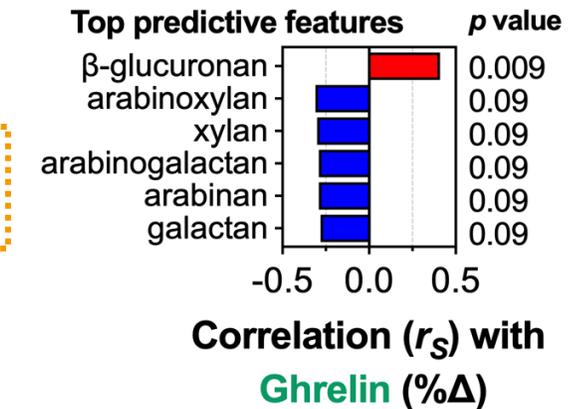
Effects on metabolic hormones are fibre-specific → some are linked to microbiome shifts



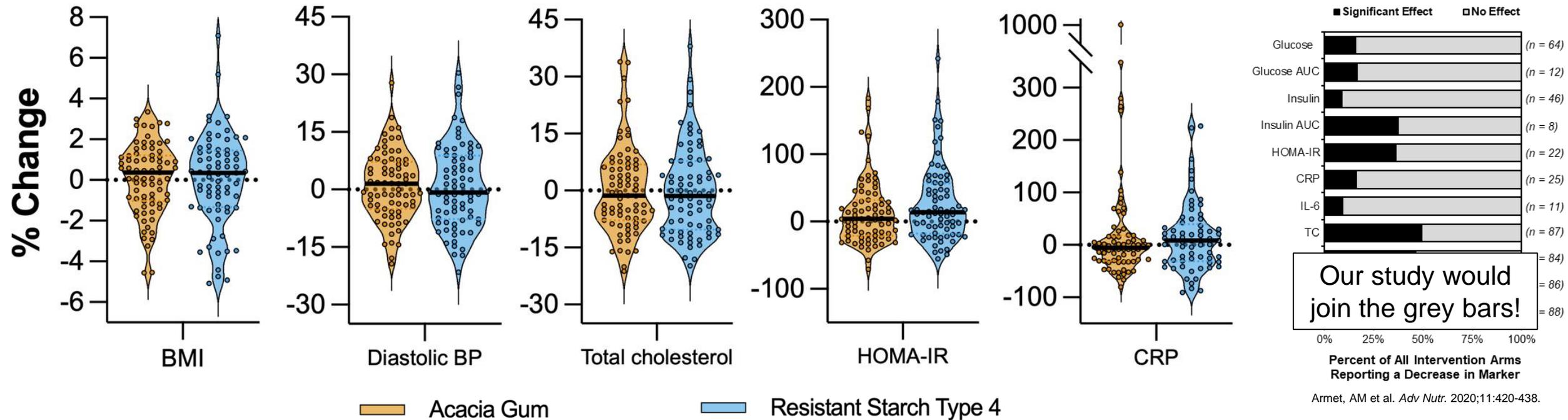
- **Resistant starch** increased GLP-1, leptin, and PYY – appetite-suppressing hormones.
- **Acacia gum** decreased ghrelin – orexigenic (hunger) hormone.



Ghrelin (AG) – Aggregated CAZymes



Fibres do not significantly improve risk markers of disease, but there is high variability in responses

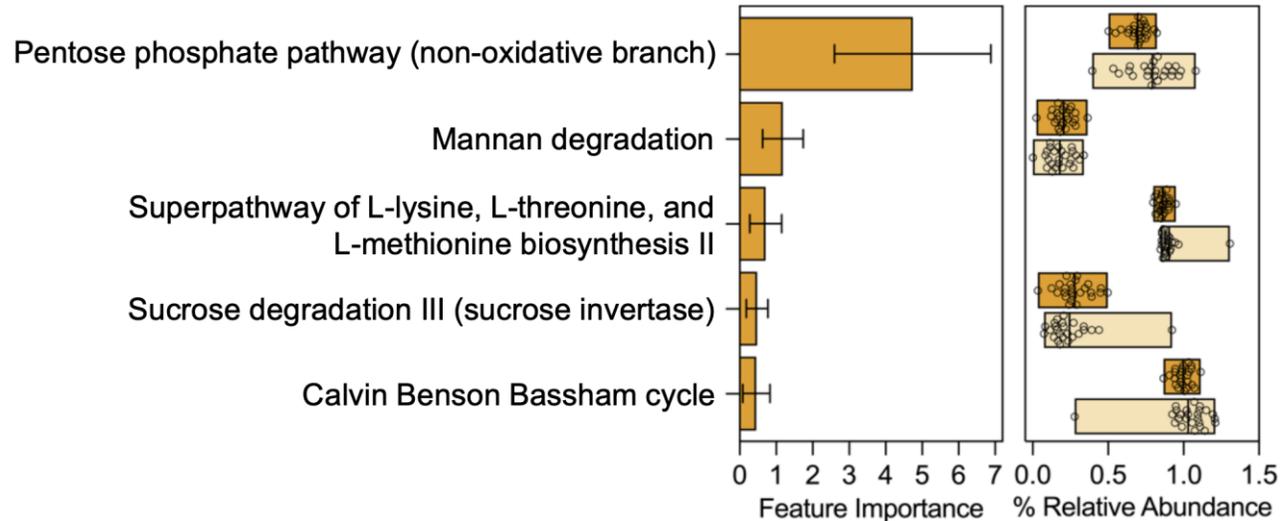


Percent changes from baseline in select risk markers in **AG** and **RS4** groups.

Can responder phenotypes be predicted based on baseline gut microbiome features?

Predictive capability of baseline gut microbiome features for blood pressure responses

Diastolic BP (AG) Top Predictors – Pathways



➤ **Responders** had **higher** relative abundances of microbial pathways involved in carbohydrate metabolism at baseline.

Boxplot Legend (AG): Responders Non-responders

cvAUROC = 0.77
Accuracy = 72%

➔ ***Increased capacity to ferment *acacia gum*?***

Isolated fibre supplements

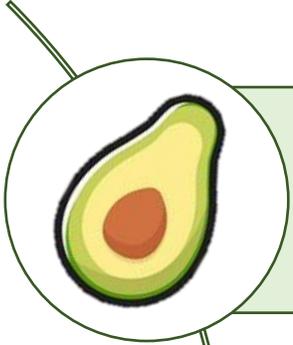
- Isolated fermentable fibres do not improve risk markers of chronic diseases, despite inducing putatively beneficial changes to microbiome.
- Benefits to gut inflammation and barrier function may be independent of fibre fermentation.
- Baseline microbiome signatures have predictive capacity for certain clinical responses to fermentable fibres.
- ***Targeted and personalized application of isolated fibre supplements may improve their clinical efficacy!***

SUMMARY

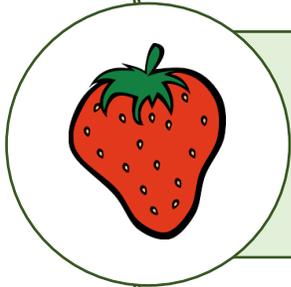
**Not all
 fibres
 are
 equal!**

Fiber-based strategies	Whole and minimally processed plant foods	Processed food with added whole-plant ingredients	Fiber-fortified foods	Fiber supplements					
	Examples	Whole-grain bread and pasta	Psyllium cookie RS bread	Nonviscous Nonfermentable	Viscous Nonfermentable	Nonviscous Fermentable	Viscous Fermentable	Short-chain oligosaccharides	
Microbiome features	Examples	Mediterranean NiMe™ Vegan	Whole-grain bread and pasta	Psyllium cookie RS bread	Cellulose	Psyllium	RS Inulin	AX β-glucan	FOS GOS
α-diversity		↕	↕	↕	—	—	↓ ↓	↓	↓
Bifidogenic effect		↑	↑	↕	—	—	↑ ↑	↑	↑
SCFAs or their pathways		↑	↑	↕	—	—	↑ ↑	↑	↑
Physiological outcomes									
Body weight		↓	↓	—	—	—	— —	↓	—
Laxation		↑	↑	↑	↑	↑	— ↑	—	↑
Risk markers									
Insulin, glucose		↓	↓	↓	—	↓	↓ —	↓	—
LDL cholesterol		↓	↓	↓	—	↓	— —	↓	—
Blood pressure		↓	—	—	—	—	— —	—	—
Mechanistic markers									
Proinflammatory cytokines and proteins		↓	↓	ND	↓*	—	— ↑	—	—
Satiety hormones		↑	↑	↕	—	↕	↑ ↕	↑	↕

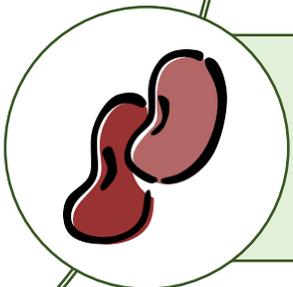
Key Takeaways



Fibre-rich, whole-plant foods generally provide greater health benefits than isolated/synthetic fibres.



A non-industrialized-type diet restores key microbiome functions negatively impacted by industrialization, which is linked to significant cardiometabolic benefits.



Fibre supplements *can* provide health benefits → applications should be targeted (based on fibre structure/properties); future may involve personalization based on gut microbiome.



Thank you!

Questions?

NiMe
DIET



FREE Online
Book!

 Dr. Anissa Armet, PhD, RD