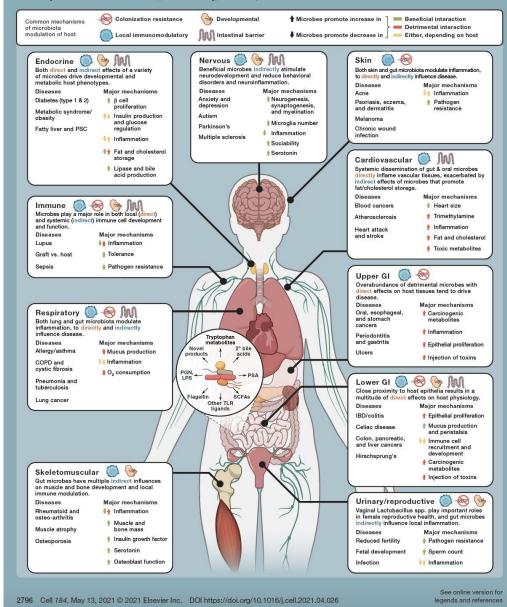
## Good gut health How different prebiotic fibres get your there

Dr Tim Crowe, AdvAPD

#### This is why gut health is the hottest of hot topics

#### SnapShot: Microbiota effects on host physiology

Jennifer H. Hill and June L. Round Department of Pathology, Division of Microbiology and Immunology, University of Utah School of Medicine, Salt Lake City, UT 84112, USA



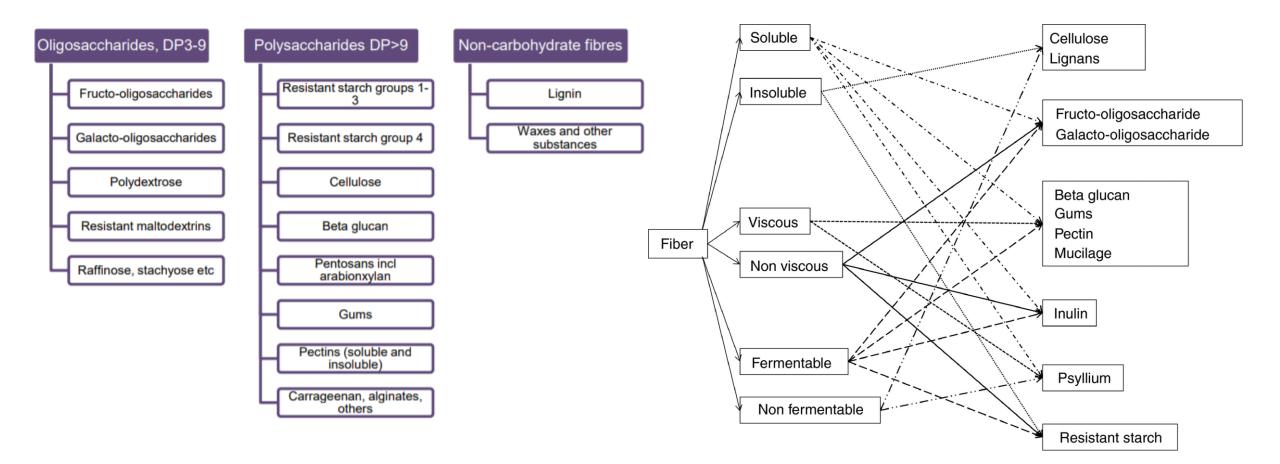
### What is fibre?

The fraction of the edible part of plants or their extracts (or synthetic analogues) that are resistant to digestion and absorption in the small intestine, usually with complete or partial fermentation in the large intestine

Promotes one or more of the following beneficial physiological effects:

- Laxation
- Reduction in blood cholesterol
- Modulation of blood glucose

Includes oligosaccharides, polysaccharides and lignins



Westenbrink S et al. Food Chem 2013;140:562-7

O'Grady J et al. *Aliment Pharmacol Ther* 2019;49:505-15

Fibre subtype	Structure	Source	Metabolic effect
Cellulose	Linear chains of glucose units with beta-1, 4 glucosidic linkage	Cereals, legumes, nuts	Increases stool bulk and stimulates peristalsis
Hemicellulose	As cellulose with xylose, galactose, mannose and arabinose sugar branches	Cereals, cell walls of fruits, vegetables	Varies with source; mix of insoluble, soluble and viscous properties
Lignan	Complex polymer of aromatic alcohols. Not a polysaccharide	Cereals, plant cell walls	Increases stool bulk and stimulates peristalsis
Gums	Mannose backbone with galactose side chains	Legumes, nuts	Cholesterol and glucose lowering effects, slow digestion and absorption, Fermentation by microbiota
Pectin	Polygalacturonic acid, D-galacturonic acid unit backbone, substituted with arabinans, galactin, arabinogalactin side chains	Fruit peel, legumes, beetroot	Cholesterol and glucose lowering effects, Slow digestion and absorption, Fermentation by microbiota
Beta glucan	Beta-D glucose linear backbone with 1-3 beta glycosidic linkage	Cereals and grains, yeasts, fungi and bacteria	Cholesterol and glucose lowering effects, Fermentation by microbiota
Inulin	Beta 1-2-fructan residue backbone, often glucosyl units as chain terminating moieties	Chicory root, onion, cereals	Lower triglyceride concentration, Fermentation by microbiota
Psyllium	Heteroxylan with 1:4, 1:3 linkage backbone, side chains of arabinose, xylose, galactose and rhamnose	Plantago Ovata	Cholesterol and glucose lowering, Stool forming effects
Oligosaccharides	Beta- fructo- oligosaccharides (FOS) Alpha and beta- galactooligosaccharides (GOS)	Polymers derived from polysaccharides by hydrolysis	Fermentation by microbiota
Resistant starch (RS1-5)	Alpha-1,4-D-glucan links	Cereals, legumes, fruits	Cholesterol and glucose lowering, Fermentation by microbiota

O'Grady J et al. Aliment Pharmacol Ther 2019;49:505-15

### The health benefits

Effect	Health Benefit
Metabolic	Improved insulin sensitivity (mainly insoluble fibres), reduced risk of developing T2D (mainly insoluble cereal fibres and whole grains) Improved glycaemic status and lipid profiles (mainly soluble fibres), reduced body weight and abdominal adiposity
Gut microflora	Gut microbial viability and diversity, metabolites from gut microflora (including SCFAs)
Cardiovascular	Chronic inflammation, cardiovascular risk, mortality
Depression	Chronic inflammation, gut microbiota
Gastrointestinal Localised	Colonic health and integrity, colonic motility, colorectal carcinoma

Prebiotic fibre is like fertiliser for your gut microbiota

And what defines prebiotic fibre continues to broaden as too the health links being made



The evolution of the changes in the scientific definitions of "prebiotic",1

Year	Definition	Reference
1995	A nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health.	Gibson and Roberfroid ( <u>1</u> )
2003	Nondigestible substances that provide a beneficial physiologic effect on the host by selectively stimulating the favorable growth or activity of a limited number of indigenous bacteria.	Reid et al. ( <u>2</u> ) Inaugural ISAPP Meeting
2004	A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well- being and health.	Gibson et al. ( <u>3</u> )
2007	A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora, that confer benefits upon host well- being and health.	Roberfroid ( <u>4</u> ) IDF/FAO Meeting
2008	A nonviable food component that confers a health benefit on the host associated with the modulation of the microbiota.	FAO Technical Meeting ( <u>5</u> ) (2007)
2010	A selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefits upon host health.	Gibson et al. ( <u>6</u> ) ISAPP 6th Annual Meeting
2015	A nondigestible compound that, through its metabolization by microorganisms in the gut, modulates the composition and/or activity of the gut microbiota, thus conferring a beneficial physiologic effect on the host.	Bindels et al. (7)

<sup>1</sup>IDF, International Dairy Federation; ISAPP, International Scientific Association for Prebiotics and Probiotics.

#### The evolving definition of a prebiotic

#### Today's definition of a prebiotic

#### Open Access | Published: 14 June 2017

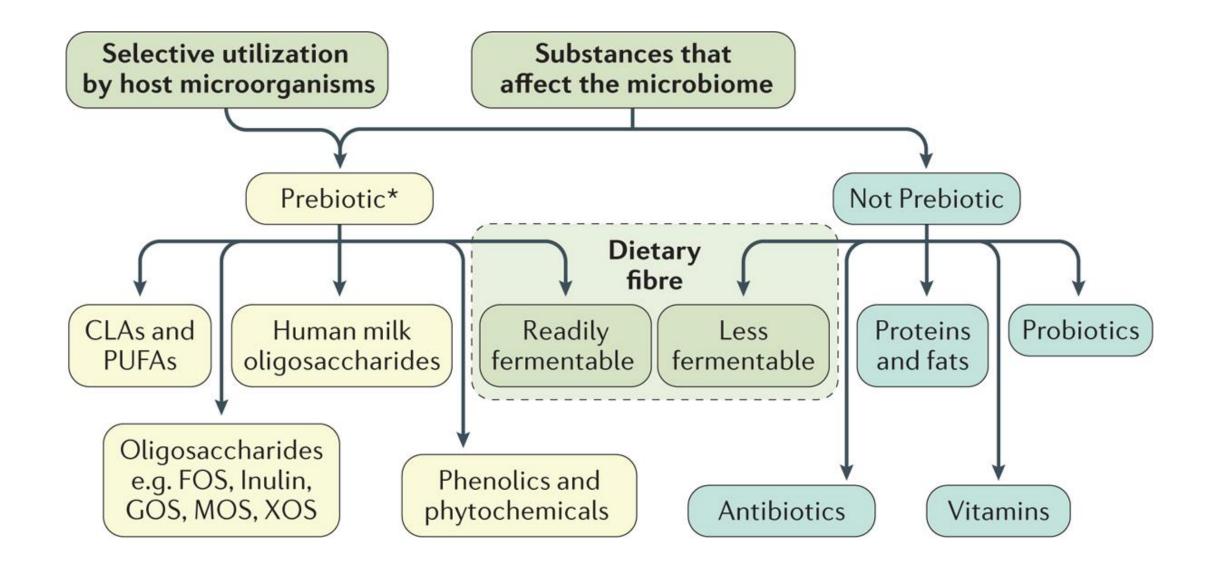
Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics

Glenn R. Gibson <sup>™</sup>, Robert Hutkins, Mary Ellen Sanders, Susan L. Prescott, Raylene A. Reimer, Seppo J. Salminen, Karen Scott, Catherine Stanton, Kelly S. Swanson, Patrice D. Cani, Kristin Verbeke & Gregor Reid

*Nature Reviews Gastroenterology & Hepatology* **14**, 491–502(2017) Cite this article

"A substrate that is selectively utilized by host microorganisms conferring a health benefit."

The definition expands the concept of prebiotics to possibly include non-carbohydrate substances, applications to body sites other than the GI tract, and diverse categories other than food



# Health effects of prebiotics

#### Include benefits to:

GI tract (inhibition of pathogens, immune stimulation, gut barrier permeability)

Cardiometabolism (↑ insulin sensitivity, blood lipids)

Mental health (metabolites that influence brain function and cognition) Bone (↑ mineral bioavailability)



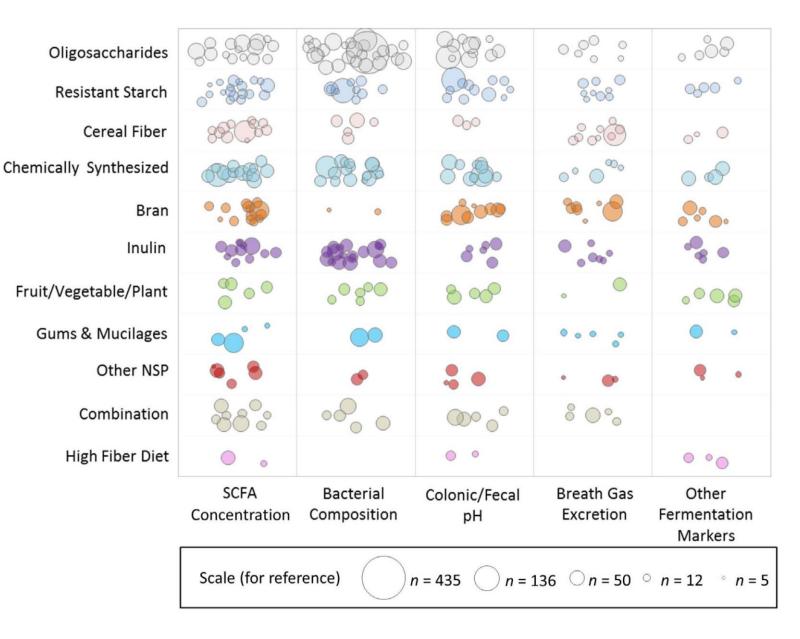
Health end point	Prebiotic used	Refs
Metabolic health: overweight and obesity; type 2 diabetes mellitus; metabolic syndrome and dyslipidaemia; inflammation	Inulin, GOS, FOS	22,74,75,83–90
Satiety	FOS	75,76,90–92
Stimulation of neurochemical-producing bacteria in the gut	GOS	93,94
Improved absorption of calcium and other minerals, bone health	Inulin, FOS	95–99
Skin health, improved water retention and reduced erythema	GOS	100,101
Allergy	FOS, GOS	102–105
IBD	Inulin, lactulose	106
Urogenital health	GOS	107
Bowel habit and general gut health in infants	GOS, FOS,	108,109
Infections and vaccine response	FOS, GOS, polydextrose	110–114
Necrotizing enterocolitis in preterm infants	GOS, FOS	115
IBS	GOS	116
Traveller's diarrhoea	GOS	117
Constipation	Inulin	118,119
Immune function in elderly individuals	GOS	56,120
FOS, fructooligosaccharides; GOS, galactooligosaccharides.		

#### Table 1 | Health end points targeted in human trials of orally administered prebiotics

Gibson GR et al. *Nature Reviews* 2017;14:491-502

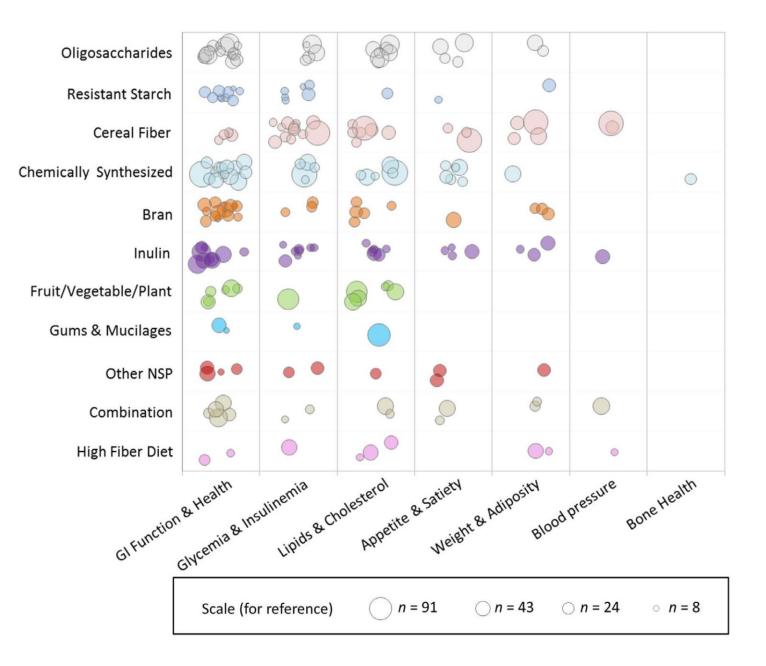
# Health effect of prebiotics

Sawicki CM et al. *Nutrients* 2017;9:125

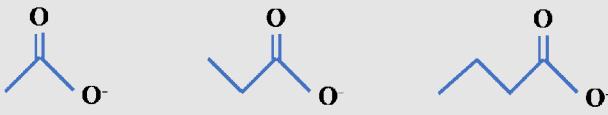


# Health effect of prebiotics

Sawicki CM et al. *Nutrients* 2017;9:125



### SCFAs (Short-chain fatty acids)



Acetate

Propionate

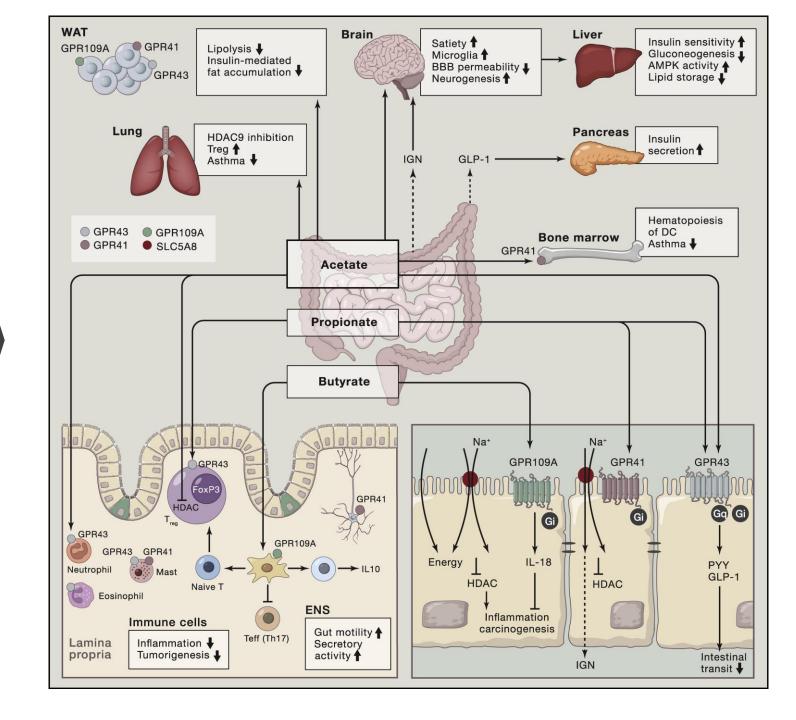
Butyrate

Metabolites of bacterial fermentation of prebiotic fibre and resistant starch

Used as an energy source by enterocytes and for microbial growth (butyrate) or transported into the bloodstream (acetate and propionate)

Modulate aspects of metabolic activity including colonocyte function (nutrient absorption, pH and motility), pathogen proliferation, intestinal barrier integrity, inflammation, blood lipids and appetite

#### SCFAs – it's complex



Koh A et al. Cell 2016;165:1332-45

#### Fructans

Polymers of fructose found in onions, garlic, barley, wheat, agave, artichokes, asparagus and leeks

Includes:

- Inulin (11-60 chain length)
- Oligofructose (3-10 chain length) derived from inulin
- Fructo-oligosaccharides (3-5 chain length) derived from sucrose

Rapidly fermented by *Bifidobacterium* and *Lactobacillus* which are preferentially stimulated to grow, causing significant changes in the composition of the gut microbiota

### GOS

Galacto-oligosaccharides (GOS) are made from lactose by the trans-glycosylating activity of  $\beta$ -galactosidase

Human studies show a change in colon flora composition and activity following consumption of GOS

Favourable physiologic benefits linked to relieving constipation, improving calcium absorption, and retarding the development of colon cancer in rat model systems

# Top prebiotic foods

Aromatic vegetables including onions, leeks, celery, asparagus, garlic and Jerusalem artichokes are high in fructans (inulin and FOS)

Legumes (esp. lentils) high in GOS

Barley and oats (beta-glucan)

Foods high in resistant starch such as cooked and then cooled potatoes, legumes and green bananas



Dietary fibre interventions (particularly involving fructans and GOS)  $\uparrow$  faecal abundance of *Bifidobacterium* and *Lactobacillus* as well as faecal butyrate concentration but did not affect  $\alpha$ -diversity (number of distinct organisms)

#### Dietary fiber intervention on gut microbiota composition in healthy adults: a systematic review and meta-analysis

Daniel So, Kevin Whelan, Megan Rossi, Mark Morrison, Gerald Holtmann, Jaimon T Kelly, Erin R Shanahan, Heidi M Staudacher, Katrina L Campbell ∞

The American Journal of Clinical Nutrition, nqy041, https://doi.org/10.1093/ajcn/nqy041 **Published:** 11 May 2018 Article history ▼

	S	Std. Mean Difference						
Study or Subgroup	Weight	IV, Random, 95% CI	IV, Random, 95% CI					
1.1.1 Subgroup: Accepted prebiotic fibers								
Alles 1999 (52)	1.9%	-0.53 [-1.30, 0.24]						
Bouhnik 1996 (54)	1.7%	0.60 [-0.30, 1.50]	+					
Bouhnik 1999 (58)	1.6%	0.48 [-0.52, 1.48]						
Bouhnik 2004 (57)	1.8%	-0.22 [-1.02, 0.58]	-+-					
Bouhnik 2006 (56)	1.6%	0.45 [-0.54, 1.45]						
Bouhnik 2007 (55)	2.0%	0.41 [-0.23, 1.04]	+					
Clarke 2016 (86)	2.2%	0.91 [0.38, 1.44]						
Costabile 2010 (90)	2.2%	0.12 [-0.38, 0.62]						
Depeint 2008 (92)	2.1%	1.79 [1.18, 2.39]						
Dewulf 2013 (61)	1.9%	0.78 [0.03, 1.52]						
Gopal 2003 (65)	1.5%	1.65 [0.57, 2.72]						
Holscher 2015 (97)	2.2%	0.71 [0.17, 1.24]						
Kleessen 2007 (67)	2.1%	0.47 [-0.16, 1.10]	+					
Lomax 2012 (70)	2.1%	0.84 [0.21, 1.46]						
Maneerat 2013 (100)	2.2%	-0.39 [-0.86, 0.08]						
Petry 2012 (102)	2.2%	1.06 [0.54, 1.59]						
Ramnani 2010 (74)	2.1%	1.88 [1.27, 2.49]						
Ramnani 2015 (103)	2.2%	0.49 [0.04, 0.95]	——					
Slavin 2011 (105)	1.8%	0.02 [-0.86, 0.89]						
Ten 2006 (107)	2.1%	1.48 [0.90, 2.07]						
Vulevic 2008 (109)	2.2%	2.05 [1.51, 2.59]						
Vulevic 2015 (110)	2.3%	0.06 [-0.38, 0.50]						
Walton 2012 (111)	2.2%	0.50 [0.04, 0.97]						
Subtotal (95% CI)	46.1%	0.68 [0.38, 0.98]	( )					
Heterogeneity: Tau <sup>2</sup> = 0.41; Chi <sup>2</sup> = 117.80, df = 22 ( $P < 0.00001$ ); $I2 = 81\%$ Test for overall effect: Z = 4.49 ( $P < 0.00001$ )								

An acute change in diet (going from strictly animal-based to plantbased diet) alters microbial composition within just 24 h, with reversion to baseline within 48 h of diet discontinuation

#### Published: 11 December 2013

#### Diet rapidly and reproducibly alters the human gut microbiome

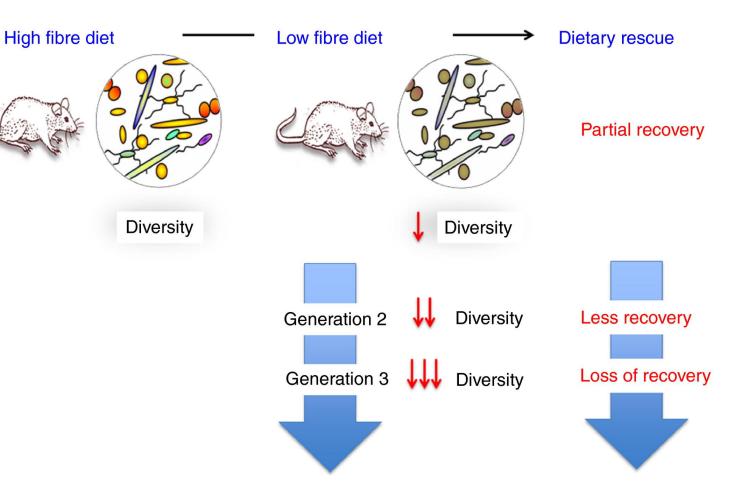
Lawrence A. David, Corinne F. Maurice, Rachel N. Carmody, David B. Gootenberg, Julie E. Button, Benjamin E. Wolfe, Alisha V. Ling, A. Sloan Devlin, Yug Varma, Michael A. Fischbach, Sudha B. Biddinger, Rachel J. Dutton & Peter J. Turnbaugh

Nature 505, 559–563(2014) Cite this article



## A long-term game

Response to  $\uparrow$  dietary fibre is not uniform and varies depending on the composition of an individual's pre-existing microbiota which is influenced by previous dietary habits

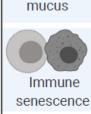


### The ageing gut microbiota

The ageing microbiota, just like the ageing person, suffers from reduced resilience

Exposure to antibiotics, changes in diet, medication, and lifestyle have a large effect on the composition of the gut microbiota in older adults

Aging Gut Physiology



Inflammation

Thinning



Specific microbial metabolites Prevotellaceae Baceroidaceae Lachnospiraceae Venillonellacease Rikenllaceae Ruminococcaceae Methanobacteriaceae Eubacteriaceae Enerobacteriaceae

Clostridiaceae,

Clostridiaceae

Bifidobacteriaceae

Lachnospiraceae

Overall diversity

Lachnospiraceae

Overall diversity

Rikenellaceae

(e.g. SCFA)

Coriobacteriaceae

Possible mechanisms Observed changes in: Bacteroidaceae - altered redox. Erysipelotrichaceae - altered geographic niches, - nutrient availability - reduced mucin as a nutrient. Akkermansiaceae. - disrupted niche Bifidobacteriaceae Bacteroidaceae

> - loss of barrier function. - loss of immune tolerance.

- promotes local inflammation

- changes in dietary diversity Specific microbial metabolites and fibre content

- opportunity/ability to exercise

- co-morbidities/medication

- physiologic changes due to specific health conditions

- medications

- frequency of antibiotic use

- physiologic and immune adaptations to frailty

- ability/opportunity to exercise

- socio-emotional stressors (e.g. isolation, financial concerns)

- ability to access and prepare a healthy diet

DeJong EN et al. Cell Host Microbe 2020;28:180-9



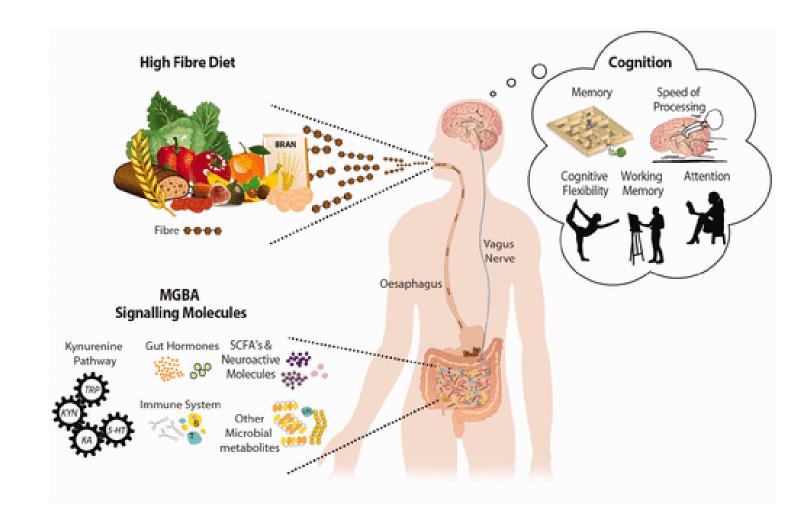
Health

Living



# Prebiotic fibre and cognition

Berding K et al. Exp Biol Med 2021;246:796-811

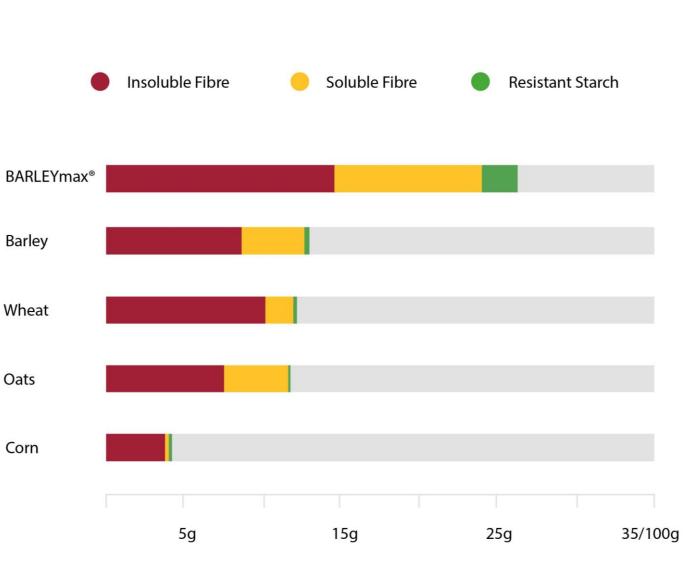


## High-fructan barley

BARLEYmax<sup>™</sup> is a naturally bred barley cultivar developed by CSIRO

Much higher fibre than regular barley and other grains and rich in resistant starch and fructans

Fructans mainly in the length of 3 to 12 which includes both FOS and inulin



# Fructans and bowel health

Meta-analysis of RCTs comparing low and high fructan diets on stool frequency

Favourable effect of fructans on increasing the mean number of stools per week by an additional 1.6 bowel movements

Similar benefit for both FOS and inulin

		rventi			ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
Chen 2000	1.96	1.56	5	0.56	0.62	5	6.2%	1.40 [-0.07, 2.87]	
Closa-Monasterolo 2016	4.63	2.34	9	3.33	1.74	8	5.6%	1.30 [-0.65, 3.25]	
Cummings 2001	10.85	4	117	9.95	3.5	127	6.7%	0.90 [-0.05, 1.85]	<u>⊢</u>
Dahl 2005	3.23	1.13	15	3.33	1.3	15	6.8%	-0.10 [-0.97, 0.77]	-+-
de Souza 2015	6.08	1.69	24	2	0.59	24	6.9%	4.08 [3.36, 4.80]	
Den Hond 2000	6.5	2.45	6	4	0.98	6	5.4%	2.50 [0.39, 4.61]	
Francois 2014	8.4	2.8	20	8.4	2.1	20	6.1%	0.00 [-1.53, 1.53]	
Genta 2009	6.93	0.35	20	2.1	0.7	15	7.1%	4.83 [4.44, 5.22]	
Geyer 2008	9.1	3.15	16	7.7	2.94	16	5.4%	1.40 [-0.71, 3.51]	
Holscher 2014	9.1	3.76	29	8.4	3.76	29	5.7%	0.70 [-1.24, 2.64]	
Micka 2017	4	1.11	44	3	1.48	44	7.0%	1.00 [0.45, 1.55]	
Ramnani 2015	9.8	3.5	38	9.1	2.8	38	6.3%	0.70 [-0.73, 2.13]	
Scholtens 2006	10.5	1.45	12	8.4	1.45	12	6.5%	2.10 [0.94, 3.26]	
Slavin 2011	9.8	1.7	12	7.8	2.59	12	5.9%	2.00 [0.25, 3.75]	
Wang 2013	5.24	2.11	47	2.86	0.35	45	7.0%	2.38 [1.77, 2.99]	
Yen 2011	4.2	2.4	9	4.5	2.4	9	5.3%	-0.30 [-2.52, 1.92]	
Total (95% CI)			423			425	100.0%	1.61 [0.60, 2.62]	
Heterogeneity: Tau <sup>2</sup> = 3.71	: Chi <b>²</b> = 2	261.62	. df = 15	5(P<0	.00001	); <b>Iz</b> = 9	4%		
Test for overall effect: Z = 3									
	- •	,							Favours Control Favours Intervention

# Why is it so?

Fermentation of fructans leads to  $\uparrow$  bacterial biomass and production of SCFAs

SCFAs  $\uparrow$  absorption of salts and water into the bowel which  $\uparrow$  moisture content of the faecal bolus and also have neuronal effects on bowel smooth muscle resulting in  $\uparrow$ intestinal motility

Effect of fructans on biomass and faecal bulk can translate into  $\uparrow$  stool frequency and softer stools



# Resistant starch

Component of dietary fibre

CSIRO estimates put RS consumption of Australian adults at 3 to 9 g/d

Goal of 15-20 g/d recommended for optimal bowel health

Designation	Description	Examples
RSI	Physically inaccessible starch	Coarsely ground or whole-kernel grains
RS2	Granular starch	High-amylose maize starch, raw potato, raw banana starch
RS3	Retrograded starch	Cooked and cooled starchy foods
RS4	Chemically modified starches	Cross-linked starch
RS5	Amylose-lipid complex	Stearic acid-complexed high-amylose starch

## Resistant starch – health benefits

Functions like fermentable soluble fibre

Changes microbial composition

Fermentation by bacteria to SCFAs

BSL regulation and improvement in insulin sensitivity

Appetite regulation via SCFAs effect on appetite hormones (leptin, GLP-1 and peptide YY)



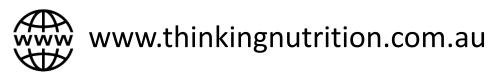
#### Summary

A wide variety of foods and substances are now considered prebiotics Health effects of prebiotics are diverse and growing as the evidence base grows

Fructans (inulin and FOS) and GOS are the best-studied prebiotics

Favourable changes in the gut microbiota from prebiotics commonly reported by changes in abundance of Bifidobacterium and Lactobacillus

All roads point to a dietary pattern rich in a diversity of plant-based foods of different fibre types as being the key way to gain the health benefits from prebiotics





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