

LIVE WEBINAR

Personalised Prebiotic Prescription:

Optimising Gut Microbiome Health with Prebiotics

Tuesday 13 February 2024 | 7PM AEDT



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Meet your speakers



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All participants have been muted



There is an optional 15 minutes for questions at the end



Add your questions in the chat and we will come back to them at the end



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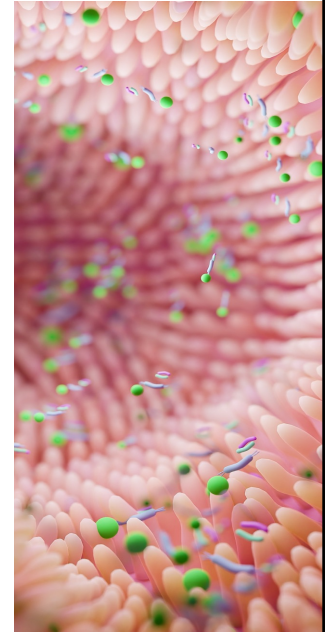
Disclaimers

- The information provided in this webinar is for the use of qualified healthcare professionals.
- The information contained in this webinar is in no way to be taken as prescriptive or to replace a healthcare professional's duty of care and personalised care practices.
- The clinical opinions and patient case studies shared by presenters are solely those of the individual presenters and do not necessarily represent the view of Co-Biome.

Learning objectives

1. Learn how the gut microbiome can be modulated using prebiotics to support patient outcomes in different clinical conditions
2. Become familiar with a variety of prebiotic foods and supplements that can be used in clinical practice
3. Understand how common clinical consideration such as a patient's dietary requirements, gut transit time, bowel habits and methane production can enable a personalised prebiotic prescription
4. Learn how gut microbiome testing can support personalised prebiotic prescription

Part 1: Introduction to prebiotics and the gut microbiome



What are prebiotics?

Substrates that are selectively utilised by host micro-organisms conferring a health benefit²⁹

Health promoting bacteria

Site of effect

Confirmed *in vivo*

Prebiotics: How are they different from fibre?¹



FIBRE

PREBIOTIC

Insoluble e.g. Cellulose	Soluble e.g. Psyllium	Fiber prebiotics Inulin, fructo-oligosaccharides (FOS), and galacto-oligosaccharides (GOS). Promising candidates are resistant starch, polydextrose, xylo-oligosaccharide (XOS) and isomalto-oligosaccharide (IMO).	Non-fiber prebiotics Lactulose, promising candidates Polyphenolics, and polyunsaturated fatty acids
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“selective”?

“health benefit”?



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Prebiotics: Patient translation

“Food for your good gut bugs, which results in them making compounds that benefit not only your gut health, but the health of your whole body”



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Mechanisms

Modulation of the gut microbiome

- Increase in butyrogenic bacteria
- Bifidogenic
- "Crowding out" pathobionts
- Altering colonic pH

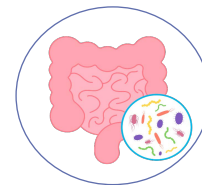
Immunomodulatory

- Anti-inflammatory
- ↓ reactive oxygen species (ROS)

Increase in SCFA production

Decrease in secondary bile acid formation²

Effect on gut epithelial barrier



Prebiotics: Impact on gut microbiome ^{3,4,5,6,7,8,9}

Prebiotic	Influence on microbial metabolites	Influence on microbial taxa
Inulin (medium/long-chain)	<ul style="list-style-type: none"> ↑ methane production* ↓ faecal beta-glucuronidase activity* 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.^{3,4,5} ↑ <i>Faecalibacterium</i> spp.³ ↑ <i>Akkermansia muciniphila</i>⁶ ↑ <i>Veillonella parvula/atypica</i>⁷ ↓ <i>Bilophila</i> spp.^{4,5}
FOS and short-chain inulin	<ul style="list-style-type: none"> ↓ hydrogen sulphide production* 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.^{8,9} ↑ <i>Faecalibacterium</i> spp.^{8,9} ↓ <i>Ruminococcus/Faecalicatena</i> spp.^{8,9}

* Co-Biome Insight

Prebiotics: Impact on gut microbiome

Prebiotic	Influence on metabolite production via microbial populations	Other microbiome impacts
GOS	<ul style="list-style-type: none"> ↓ hexa-LPS-producing microbes (↓ <i>E. coli</i>)* ↓ faecal beta-glucuronidase activity* ↑ faecal secretory IgA* 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.^{11,12,13,14} ↑ <i>Anaerostipes</i> spp.^{11,12} ↓ <i>Bacteroides</i> spp.^{13,14}
PHGG	<ul style="list-style-type: none"> ↑ butyrate-producing microbes¹⁰ 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.¹⁰ ↑ <i>Faecalibacterium</i> spp.¹⁵
Oat beta-glucan	<ul style="list-style-type: none"> ↑ butyrate-production* 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.^{16,17}
Resistant starch type 2 (RS2)	<ul style="list-style-type: none"> ↑ butyrate-producing microbes* ↑ acetate production* ↑ methane production* 	<ul style="list-style-type: none"> ↑ <i>Ruminococcus_E bromii</i>¹⁸

* Co-Biome Insight



Prebiotics: Impact on gut microbiome

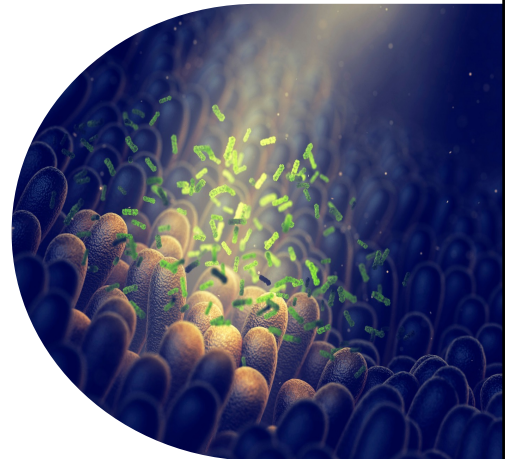
Prebiotic	Influence on metabolite production via microbial populations	Other microbiome impacts
Glucomannan	<ul style="list-style-type: none"> ↓ faecal beta-glucuronidase activity* 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.²⁴
Acacia gum	<ul style="list-style-type: none"> ↑ butyrate production¹⁹ 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.^{25,26}
Lactulose	<ul style="list-style-type: none"> ↑ propionate production* ↓ colonic production and absorption of ammonia^{20,21,22} ↓ faecal beta-glucuronidase²³ 	<ul style="list-style-type: none"> ↑ <i>Bifidobacterium</i> spp.²⁷ ↓ <i>Faecalibacterium</i>²⁸ ↓ <i>Enterococcus</i>²⁷ ↓ <i>Escherichia-Shigella</i>²⁹

* Co-Biome Insight



What impacts do prebiotics have via gut microbiome modulation?

- Neurological
- Detoxification
- Immune
- Inflammation
- Cardiometabolic
- Gastrointestinal



Neurological impacts^{8,13,30,31}

Prebiotic	Condition	Impact	Associated gut microbiome effects
Inulin (MC)	Obesity	Moderate ↑ mood, cognition	↑ <i>Bifidobacterium</i> spp., ↑ response in those with ↑ baseline <i>Coprococcus</i>
Inulin (MC)	Alcohol use disorder	↑ serum BDNF (brain derived neurotrophic factor)	↑ <i>Bifidobacterium</i> spp., <i>Faecalibacterium</i> spp. ↓ <i>Dorea</i> , <i>F. torques</i> , <i>E. ruminantium</i>
GOS 6.9g/d	Anxious young females	No change in anxiety	↑ <i>Bifidobacterium</i> spp, <i>Bacteroides</i> spp ↓ <i>Clostridium</i> spp
	IBS	? ↓ depression	

Indirect research / areas to watch

MC = medium chain

- Brain ageing and cognitive decline
- Neurogenerative disease and metagenomics
- Neuroinflammation in Alzheimer's disease
- Gut microbiome and depression – teasing associations apart from medication use

Detoxification impacts^{7,23,24,32,33,34,35,36,37}

Prebiotic	↓ Faecal beta-glucuronidase	Alters bile acid metabolism	↓ Blood urea nitrogen	↓ Colonic production/absorption ammonia
Inulin (MC/LC)	✓	✓	✓	
Resistant starch type 2 (RS2)		✓	✓	
Glucomannan	✓			
Lactulose	✓			✓
GOS	✓	✓		
PHGG		✓		

MC = medium chain; LC = long chain



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Immune impacts^{38,39}

	GOS
URTI duration	↓
Gastroenteritis incidence/severity	↓

Production of T-regulatory cells stimulated by *Bifidobacterium* spp. as well as microbially-derived butyrate → → →

Can we promote *Bifidobacteria* and butyrate-producing taxa for immunoregulatory effects?



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Inflammation impacts^{7,14,40,41,42,43,44,45,46,47}

	Inulin (LC/MC)	FOS /Inulin (SC)	GOS	PHGG	RS2	Lactulose
CRP	↓	↓	↓	↓	=	↓
Inflammatory cytokines	↓		=		=	
Faecal calprotectin	↓	↓	↓			
Intestinal permeability			↓(colonic)			

SC = short chain; MC = medium chain; LC = long chain



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Cardiometabolic impacts^{41,43,48,49,50,51,52,53,54,55,56}

	Inulin (LC/MC)	FOS/Inulin (SC)	PHGG	Oat BG	RS2	Acacia gum	Lactulose
Fasting glucose	↓	↓			↓	↓	
Fasting insulin	↓	↓	↓		↓		
HbA1c	↓	↓			↓		
HOMA-IR	↓	↓			↓		
NASH/steatosis		↓					
TG	=		↓	↓	↓		↓
TC	=			↓	↓		
LDL-C	↓		↓	↓	↓		
HDL-C	=		↑	=			
ApoB				↓			
BMI/BW					↓	↓	
BP						↓	
Lactate threshold		↑					

SC = short chain; MC = medium chain; LC = long chain



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Gastrointestinal impacts^{30,34,57,58,59,60}

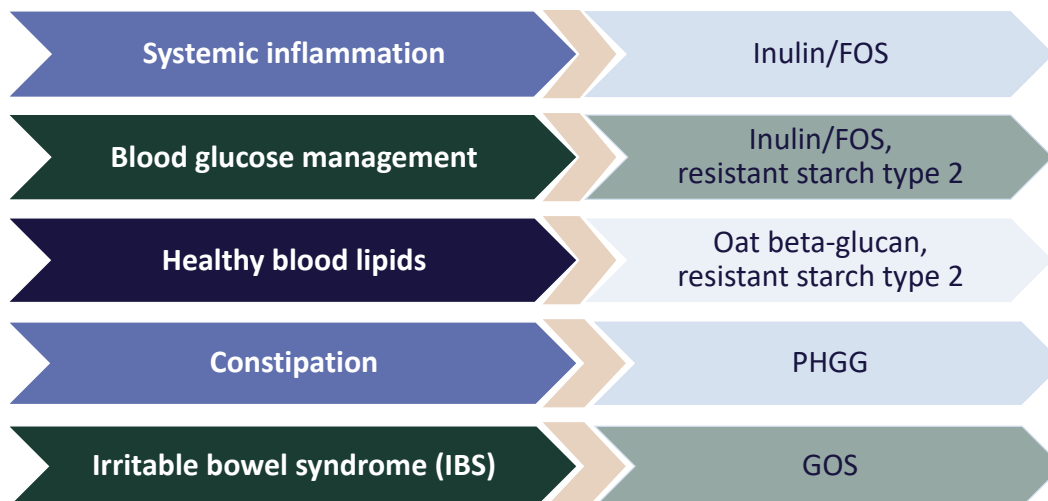
GI IMPACTS	Inulin (LC/MC)	FOS/Inulin (SC)	GOS	PHGG	RS2	Lactulose
Transit time				↓	↑	
Improved stool form	↑		=	↑	=/↑	
Incomplete emptying	=		=	=		
Straining			↓	=/↓		
Flatulence	↑	↑	↓	↓<6g	↑	↑
Bloating	↑		↓	↑/=/↓	=	
Abdominal pain	↑		↓	=/↓	=	
Diarrhoea				↓	↓	

SC = short chain; MC = medium chain; LC = long chain



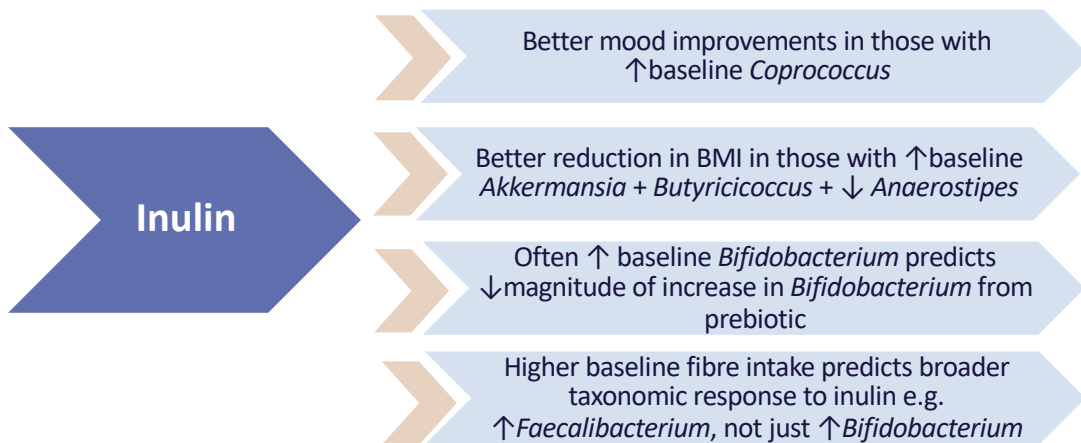
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Clinical takeaways

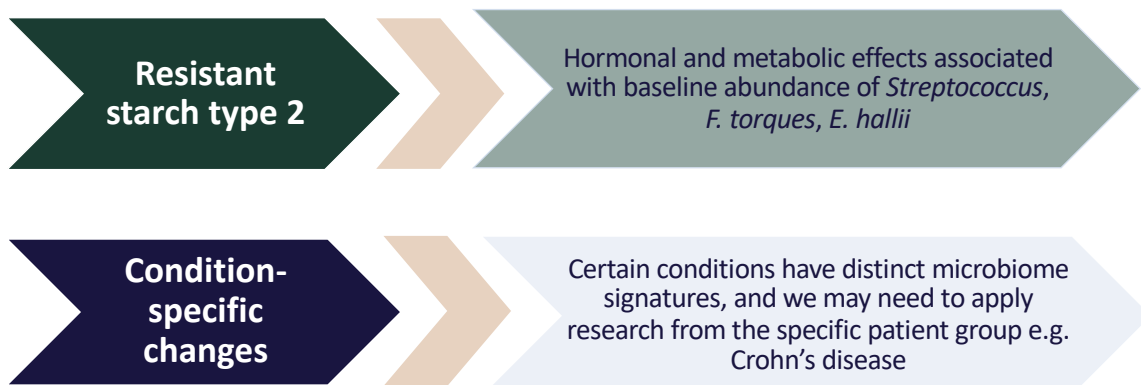


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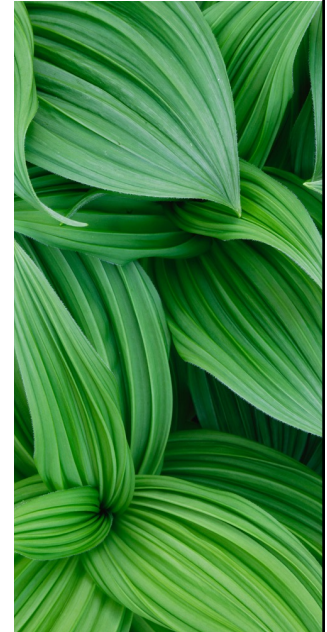
Individualised response ^{61,62, 63}



Individualised response ^{63,64}



Part 2: Prebiotics in the diet vs supplements



Prebiotics in the diet

Prebiotic	Food sources	
Fructooligosaccharides (FOS)	Jerusalem artichoke Broccoli stalks	Red onion Watermelon
Galactooligosaccharides (GOS)	Borlotti beans Chickpeas	Green lentils Soy flour
Inulin	Jerusalem artichoke Asparagus	Globe artichoke Leek
Pectin	Mandarins Kale	Blackberries Avocado
Arabinoxylan	Pumpernickel bread Wholegrain rye	Wheat bran Popcorn
Resistant starch (RS)	Green banana Green banana flour	Barley Lentils
Beta-glucan	Oats Wholegrain barley	Wheat bran Sorghum

Why not just a high-fibre diet, rather than using prebiotics?

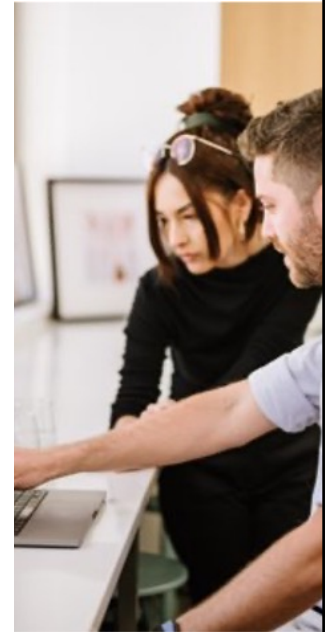
Effect on gut metabolites	Evidence for high-fibre diet/foods	Evidence for supplemental prebiotics
↑ butyrate microbes	Rye bran-enriched bread (6-10 pieces/d)	RS2 with high RS foods (combination) PHGG (6g/d)
↓ BCAAs	Rye bread (8 pieces/d)	
↑ IPA production	Very high fibre diet; wholegrain wheat, rye	
↓ TMAO	Brussel sprouts (300g/day)	
↓ beta-glucuronidase enzyme	Grain/legume fibres	Glucomannan with low-fat diet (4.5 g/d) Inulin (5-20g/d) Lactulose (3g/d)
↓ hydrogen sulphide microbes		FOS (12g/d)
↓ hexa-LPS microbes		GOS (5.5g/d)
↑ secretory IgA		GOS (5.5g/d)

Summary of dietary fibre vs dietary prebiotics vs supplemental prebiotics

- Considerable overlap
- Some metabolites have fibre studies but not prebiotic studies to support
- Overall, effective dietary studies use (often unrealistically) high quantities of high-prebiotic food (e.g. 6, 8, 10 pieces of bread/day)
- Non-athletes and those on restricted diets may find it difficult to meet these dietary targets



Part 3: Clinical considerations for personalised prebiotic intervention



Questions I ask before prescribing prebiotics

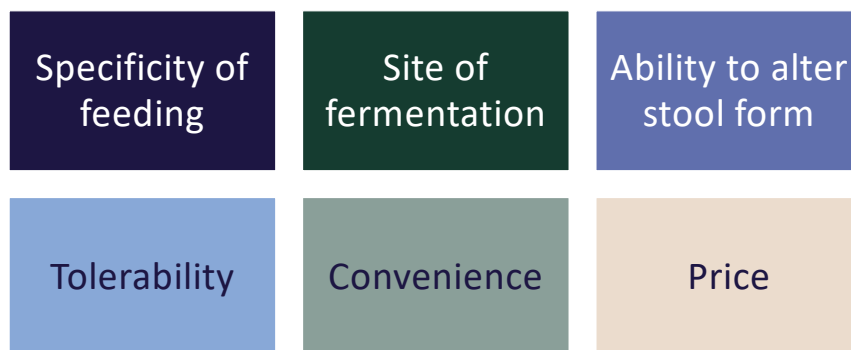
Part 1: IF a prebiotic is indicated

- How is a prebiotic likely to influence the clinical picture?
- Is now a good time to start a prebiotic?

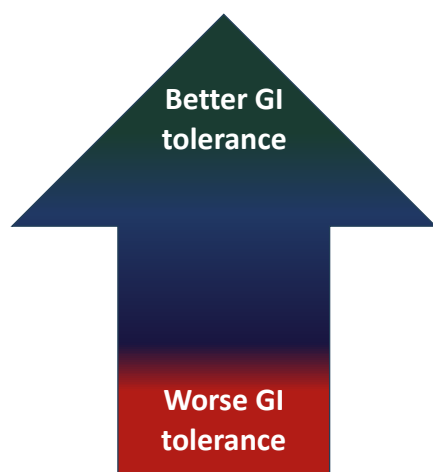
Part 2: WHICH prebiotic options we have

- Which of the six Personalised Prebiotic Prescription (PPP) factors are important here?
- In what order are they important?

Personalised Prebiotic Prescription (PPP) Factors – which are important?



Tolerability and acceptability^{30,47,48,49,50}



Acacia gum
Oat beta glucan
PHGG

Resistant starch
Glucomannan
GOS
MC and LC inulin

FOS and SC inulin
Lactulose



Prescribing practicalities: Flavour, texture, convenience

Prebiotic	Flavour	Texture	Convenience
Lactulose	✓ Sweet	Liquid	X Must be poured
FOS/Inulin	✓ Sweet	Soluble	✓ Mixes in food, drink
GOS	✓ Sweet	Soluble	✓ Mixes in food, drink
PHGG	✓ Neutral	Soluble	✓ Mixes in food, drink
Oat beta-glucan	Slight oat	Viscous	X Thickens, creates lumps
Resistant starch banana flour	Slight banana	Viscous	X Thickens, separates

Prescribing practicalities: Dosing guidelines

Prebiotic	Research - supported daily dosage range	Approx. equivalent	Common clinically effective dose	Approx. equivalent	References
Inulin	10g – 15g	8 tsp – 12 tsp	10g	8 tsp	7,8,31,32,33,40,42,47,49,51,56,58,59
FOS	7.5g – 30g	3.75 tsp – 15 tsp	10g	5 tsp	7,8,31,32,33,40,42,47,49,51,56,58,59
GOS	3g – 11g	½ tsp – 2 tsp	5.5g	1 tsp	13,14,30,33,39,43,44,58,59
PHGG	5g – 20g	2.5 tsp – 10 tsp	8g	4 tsp	34,58
Oat beta-glucan	3g – 6.6g	1 ½ tsp – 3 ¼ tsp	3.5g (lipids) 10g (stool form)	1 ¼ tsp 5 tsp	50,55
RS2	10g – 40g	3 ¼ tsp	15g	5 tsp	35,37,41,45,46,53,54,57,60
Glucomannan	4.5g	7 x 600mg capsules	4.5g	7x 600mg capsules	24
Lactulose	3g – 25g	5-40 mL	10g	15mL	23,48,52

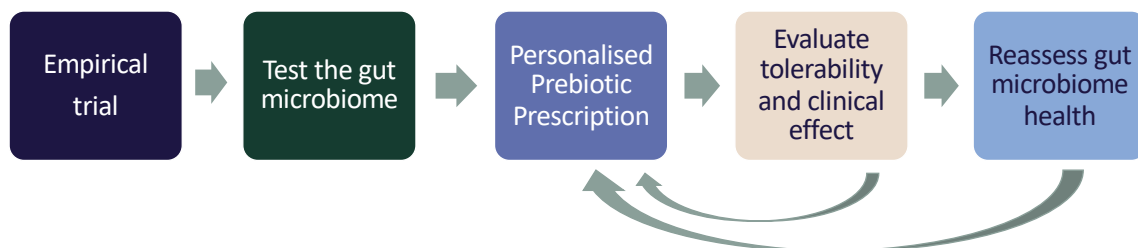
Prescribing practicalities: Cost (Australia, 2024)

Prebiotic	Approx. cost/serve (low end dosage)	Approx. cost for common clinical serve	Approx. cost/serve (high end dosage)
Inulin (long-chain)	\$1.20 for 10g	\$1.20 for 10g	\$1.80 for 15g
FOS/Inulin	\$0.70 for 5g	\$1.40 for 10g	\$2.80 for 20g
GOS	\$0.70 for 3g	\$1.20 for 5.5g	\$2.60 for 11g
PHGG	\$0.50 for 5g	\$0.80 for 8g	\$2.00 for 20g
Oat beta-glucan	\$0.80 for 3.5g	\$0.80 for 3.5g	\$2.30 for 10g
Resistant starch banana flour	\$1.00 for 10g	\$1.50 for 15g	\$4.00 for 40g
Lactulose	\$0.10 for 3g	\$0.33 for 10g	\$0.80 for 25g (\$1.60 if bd)
Glucomannan	\$2.20 for 4.5g in capsules	\$2.20 for 4.5g in capsules	\$2.20 for 4.5g in capsules



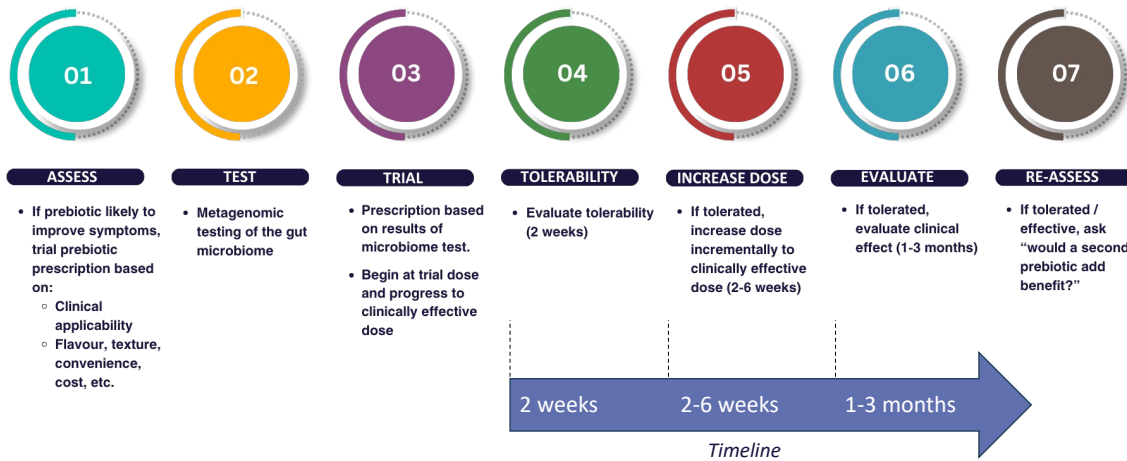
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How does gut microbiome testing allow me to make personalised prebiotic recommendations for my patient?



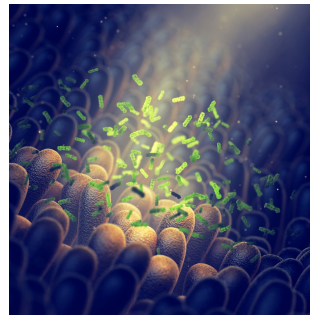
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Framework for Personalised Prebiotic Prescription: which prebiotics are in the shortlist for my patient?



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Part 4: Prebiotic prescription for gut microbiome modulation



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Age - 61 years

Gender - Female

Case history – Lifelong constipation, history of “methane-dominant SIBO” with use of herbal antimicrobials e.g. berberine. Keen to re-start berberine

Medication - prucalopride prokinetic 1-2x/week; continuous antibiotics for chronic UTI, plus:

- 1 year of trimethoprim + sulfamethoxazole for skin condition in 1992
- 7 courses of antibiotics in 2007 and 7 courses in 2017
- 2017-2022 prophylactic nitrofurantoin post-intercourse

Diet - Paleo diet (no grains) and time-restricted eating

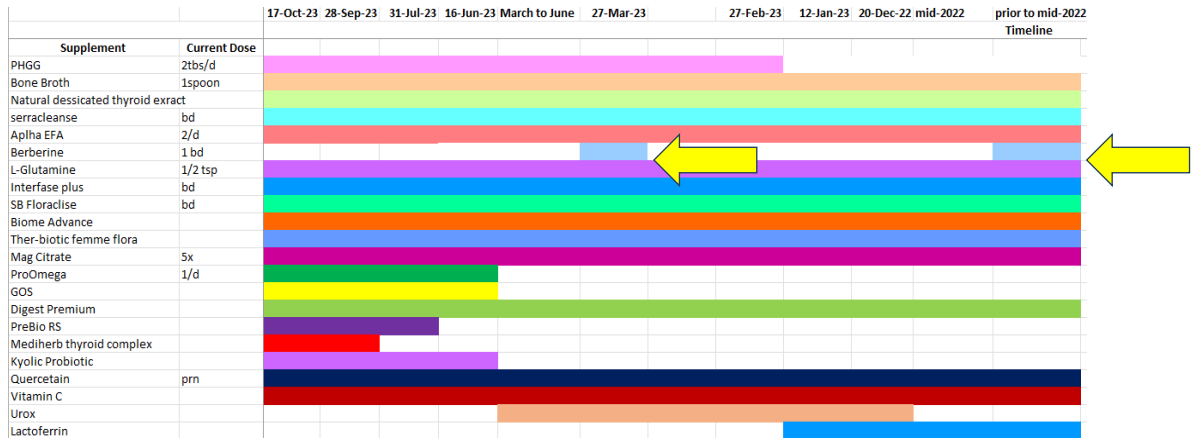
Case 1: Buffering the impact of continuous antibiotics



Her recent antibiotic history

Medication	Current Dose	17-Oct-23	28-Sep-23	31-Jul-23	16-Jun-23	March to June	27-Mar-23	27-Feb-23	12-Jan-23	20-Dec-22	mid-2022	prior to mid-202	
LDN	1/d	[Green bar]											
Cephalexin	qid	[Blue bar with 'restart' text]											
Trimethoprim 300mg	1/d prn	[Orange bar]											
Nitrofurantoin 50mg		[Orange bar]											
Hiprex	1/d	[Orange bar with 'restart' text]											
Cipramil		[Yellow bar]											
Amoxicillin+clavulanic acid	125g/d	[Yellow bar with 'stopped around this time' text]											
Citalopram	20mg/d	[Dark orange bar]											
Ovestin pessary/ cream	2x week	[Blue bar]											
Prucalopride	1/d	[Pink bar]											
Symbicort	6mcg as req	[Orange bar]											

Her supplementation regime



Part 1: Personalised Prebiotic Prescription - is a prebiotic indicated?

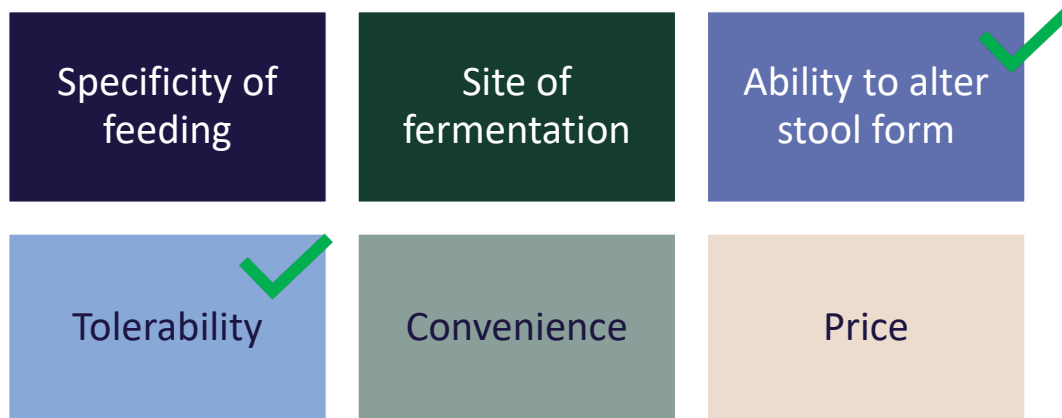
How is a prebiotic likely to influence the clinical picture?



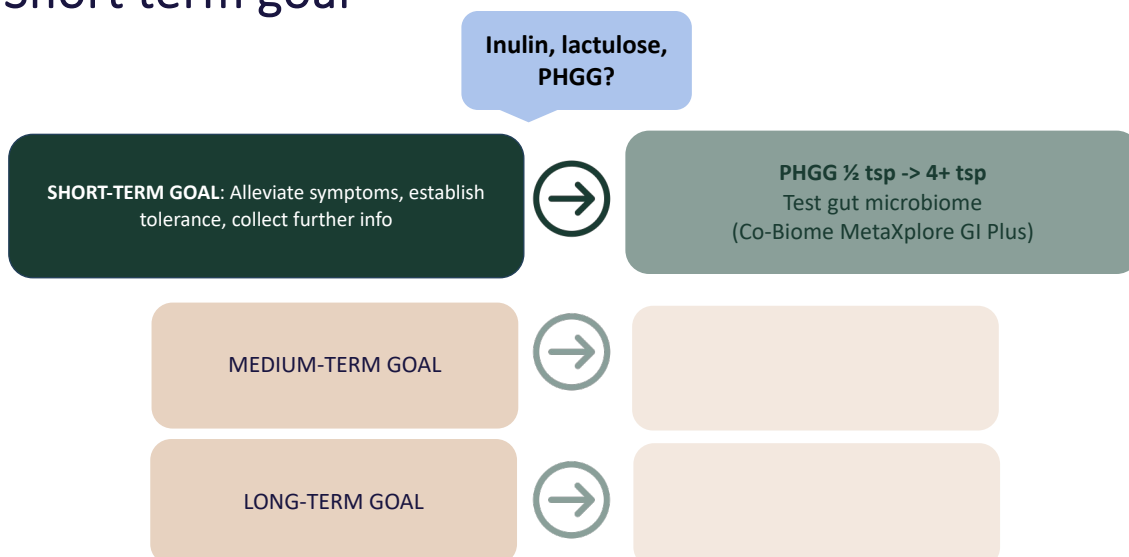
Is now a good time to start a prebiotic?



Part 2: Personalised Prebiotic Prescription (PPP) Factors – which are important?



Short term goal



Test Results



Initial management

- Stay off berberine
- Stop time-restricted eating
- Increase fibre – quinoa, daily cruciferous vegetables
- Increase healthy oils (olive, macadamia)
- Replace coconut cream/milk with coconut flour
- Increase seafood and reduce red meat
- Add omega 3 supplement
- Add *Lactobacillus gasseri* KS-13, *Bifidobacterium bifidum* G9-1 and *Bifidobacterium longum* MM2 to reduce *E. coli*
- Add GOS to reduce hexa-LPS via ↓ *E. coli*
- Add resistant starch to reduce faecal pH



Medium term goal

SHORT-TERM GOAL: Alleviate symptoms, establish tolerance, collect further info



PHGG

MEDIUM-TERM GOAL: Attenuate antibiotic impacts on microbiome



Resistant starch
GOS

LONG-TERM GOAL



Initial outcome: Clinical



↑ frequency of bowel movement, upon awakening

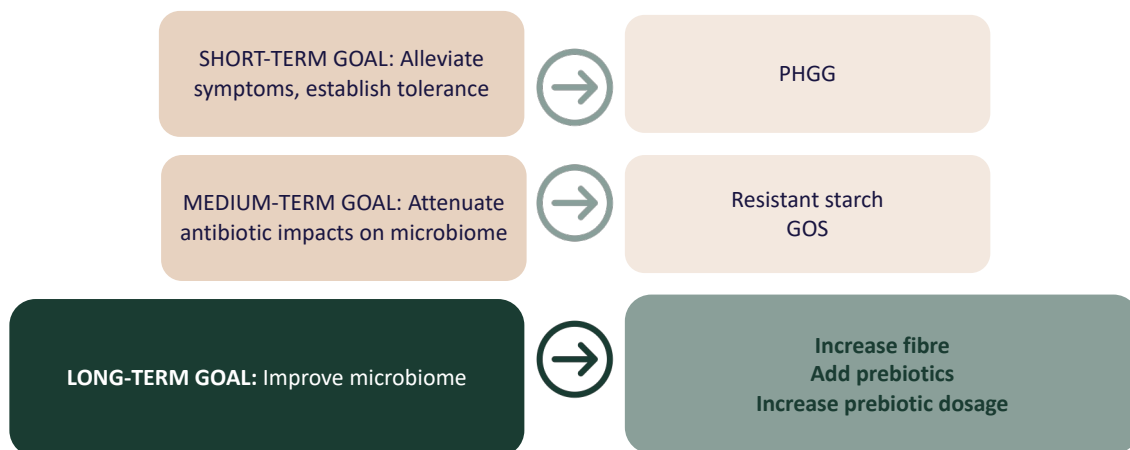
↓ prucalopride usage



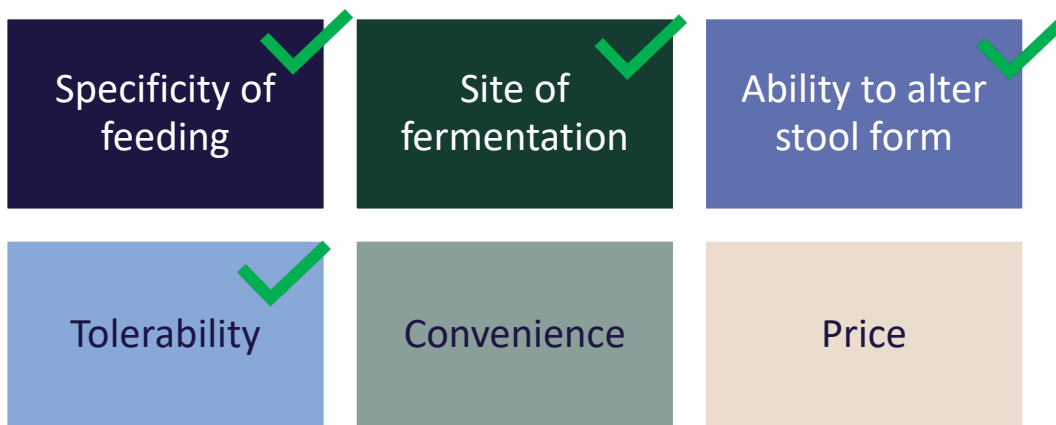
Results of treatment: Testing



Long term goal



How will I decide whether to add different prebiotics, or increase prebiotic dose?



Clinical outcome and plan

Current issue	Possible action	Potential problem	Alternative
pH remains high	Add lactulose	Tolerability Site of fermentation (too proximal)	Increase RS2 dose
Hexa-LPS microbes remain high	Add inulin or lactulose	Tolerability	Increase GOS dose
↓ Acetate and butyrate microbes	Add inulin	Tolerability	Increase RS2/GOS Counsel re trial off antibiotics
Persistent “thought viruses” around SIBO and fibre	Gradual increase in fibre		

Prebiotic	Current dose	Dose to trial
GOS	1 tsp (5g)	2 tsp (10g)
Resistant starch banana flour	2 scoops (30g)	2.5 scoops (37.5g)

Age - 65 years

Gender - Female

Case history – faecal urgency, occasional incontinence, nocturnal nausea, bloating affecting sleep, high LDL and total cholesterol, anxiety re impending trip to South America

Medication - Relying on loperamide

Case 2: If you're not testing, you're guessing (the underlying cause of symptoms)



Part 1: Personalised Prebiotic Prescription - is a prebiotic indicated?

How is a prebiotic likely to influence the clinical picture?



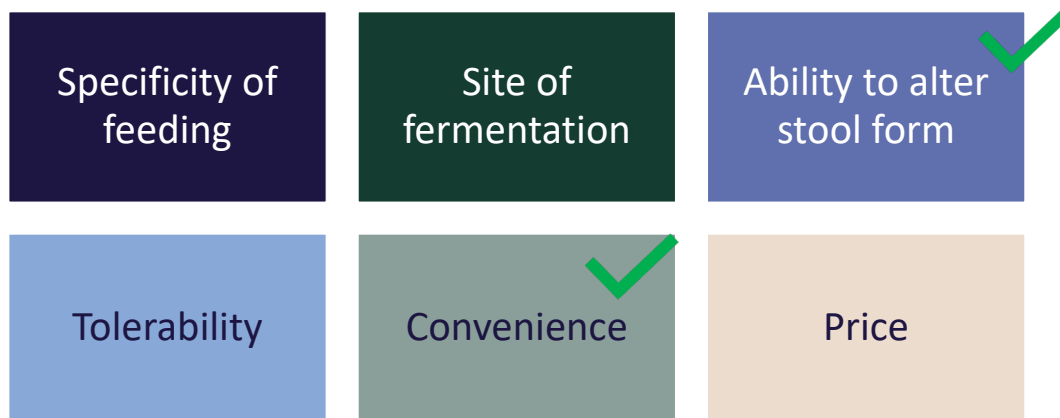
Symptoms

Is now a good time to start a prebiotic?

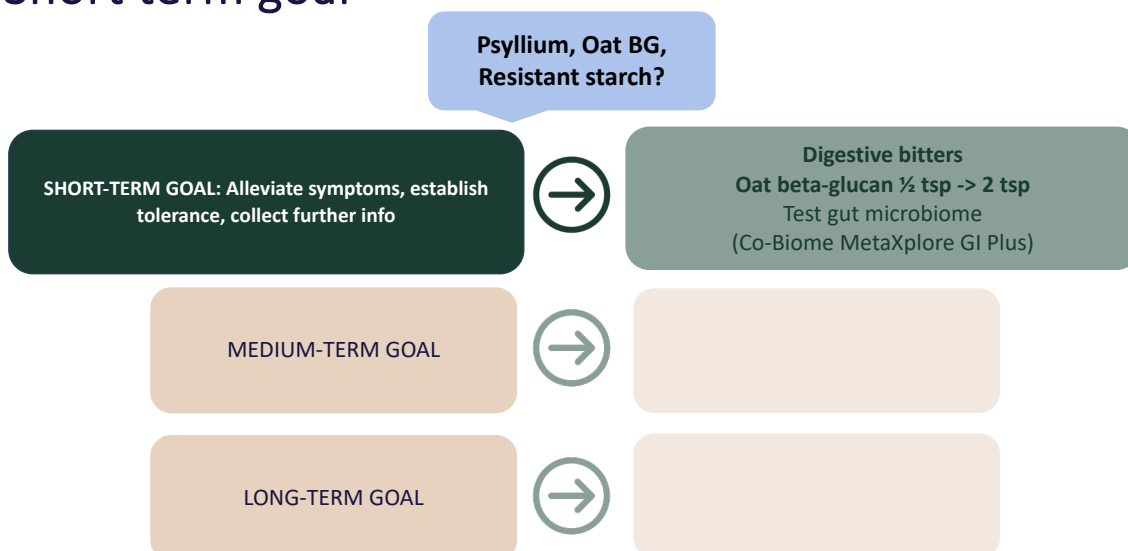


YES!

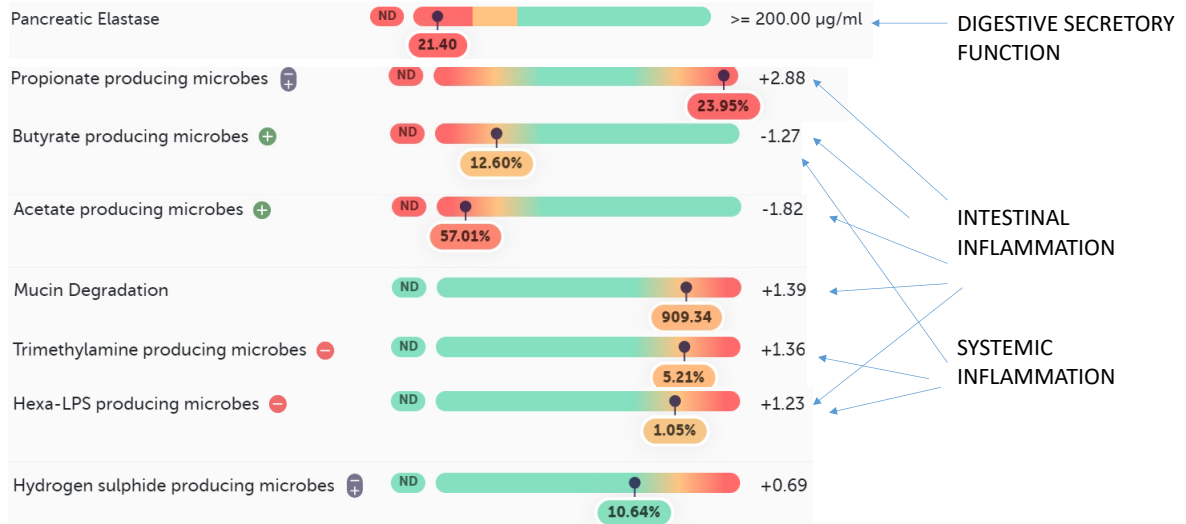
Part 2: Personalised Prebiotic Prescription (PPP) Factors – which are important?



Short term goal



Key functional marker and microbiome results



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Species results

Oral Species

<i>Streptococcus salivarius</i>	0.11%	Common
<i>Streptococcus anginosus</i>	0.06%	Less common
<i>Streptococcus parasanguinis</i>	0.04%	Rare
<i>Fusobacterium vincentii</i>	0.02%	Rare
<i>Peptostreptococcus anaerobius</i>	0.02%	Less common



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Outcome of screening and initial treatment

Oat beta glucan and bitters

- ↓ bloating
- ↓ nocturnal nausea
- No diarrhoea or faecal urgency
- ↓ faecal incontinence
- Complete emptying

Low pancreatic elastase suggests severe pancreatic exocrine insufficiency

→ Refer to specialist

Medium term goal

SHORT-TERM GOAL: Alleviate symptoms, establish tolerance, collect further info



Oat beta-glucan ½ tsp

MEDIUM-TERM GOAL: Establish tolerance, screen for causes



Medical review
Address pelvic floor dysfunction
Increase oat BG up to 4 tsp

LONG-TERM GOAL



CT ABDOMEN AND PELVIS WITH CONTRAST

HISTORY:

Pancreatic exocrine insufficiency? Previous gallbladder polyp and liver cyst.

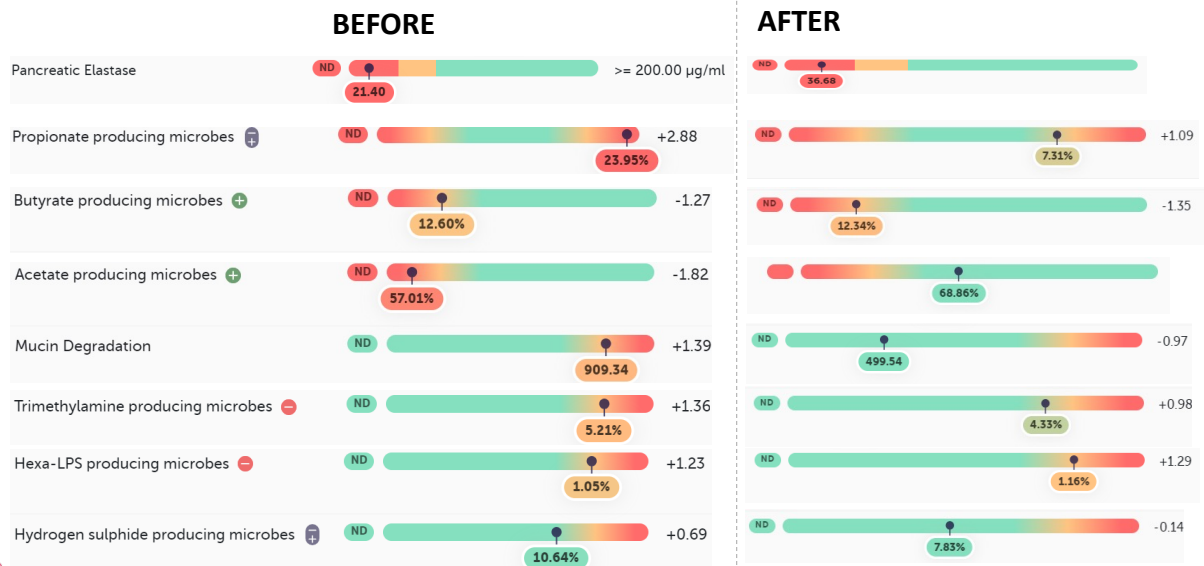
Moderate colonic faecal loading. No bowel obstruction. The bone mineral density appears reduced. Small sclerotic focus in the L2 vertebral body, likely a small bone island. No pleural or pericardial effusion.

CONCLUSION:

1. Significant pancreatic atrophy, particularly in the head, uncinate process, neck and proximal body, with a few small islands of normal tissue in the distal body and tail. No focal pancreatic lesion or main duct dilatation.

Prescription of enteric-coated pancreatic enzymes

Results of treatment: Testing



Long term goal

SHORT-TERM GOAL: Alleviate symptoms, establish tolerance, collect further info



Oat beta-glucan ½ tsp

MEDIUM-TERM GOAL: Establish tolerance, screen for causes



Medical review
Oat beta-glucan 3.5g
Address pelvic floor dysfunction

LONG-TERM GOAL: Increase butyrate microbes, optimise gut symptoms



Optimise Creon and oat beta-glucan compliance
Dietary modification

Meal	Day 1	Fibre (g)	Day 2	Fibre (g)
Breakfast	1 x low-FO bread Cheese 2 tsp protein powder	1	1x low-FO bread Goat's cheese 2 tsp protein powder	1
Morning tea	1 tb muesli 3 tb low-fat Greek yoghurt Strawberries	1 1	-	
Lunch	2 x low-FO bread Goat's cheese 5 cherry tomatoes	2 1	Quinoa Leek Celery Tomato Chicken	2.5 1 1 1
Afternoon tea	Ice cream with oat beta-glucan	4	Ice cream with oat beta-glucan	4
Dinner	Quinoa Chicken Leek, celery, tomato Watermelon	2.5 1 0.3	Broccolini 2g ½ cup brown rice 1.8g Chicken Celery 1g Mandarin 1.8g	2 1.8 1 1.8
TOTAL FIBRE		~13.8g		~17.1g

Outcome and plan

Outcome	Plan
Nocturnal nausea if has richer food like pizza for dinner	Discuss Creon dosage with specialist
Moderate compliance with oat beta-glucan ("if I put it in juice or yoghurt it gets gluggy")	Try mixing with protein powder smoothie If all else fails -> almond milk with a little soy ice cream mixed in -> Trial GOS
BMs occasionally too firm	Kiwifruit 2/day 2 nd daily legumes Track fibre intake on My Fitness Pal
Total cholesterol reduced from 6.3 -> 5.6 mmol/L LDL-C reduced from 4.5 -> 4.0 mmol/L (no change in HDL-C)	

Key takeaways

- Personalise your prebiotic to the patient, taking into account the clinical picture, goals and preferences, while being guided by the gut microbiome results.
- Dosage varies considerably according to condition – be aware of the research.
- Tolerance and acceptability can be a stumbling block – when in doubt, start conservatively and proceed with caution.
- Dosing via the instructions on the bottle is a minefield – be specific about dosing.
- Even if the clinical outcome improves, re-test the gut microbiome.



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Technology: metagenomics

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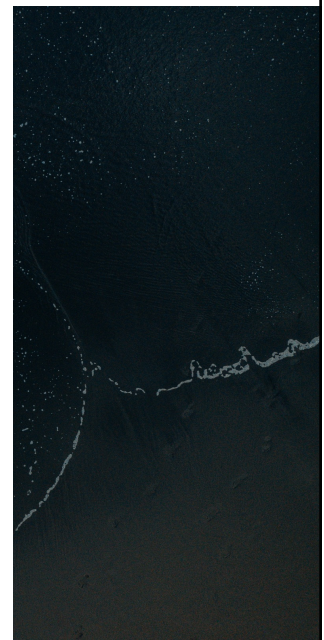
66

15 minutes

Q&A from the chat

Hayley Parcell

Alyssa Tait



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- Prebiotic Guide
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- Dietary Impacts on the Gut Microbiome Guide
- Interpretation Guide
- Pathogen and Pathobiont Management Guide



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