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Myth-busting gut pathogens

A microbiome-informed approach to management

Introductions

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A precision microbiome company delivering clinical-grade gut microbiome testing for healthcare professionals.

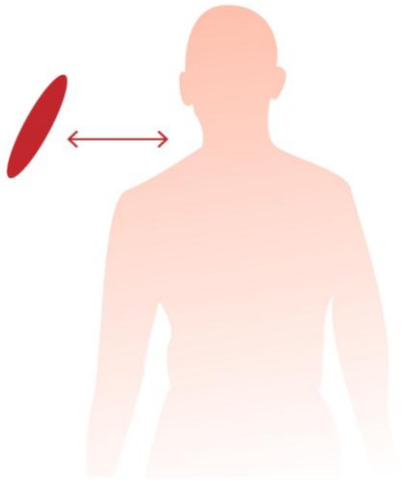
- Founded in 2017 as a spiin-out from the University of Queensland, Australia
- Co-founded by Professors Philip Hugenholtz and Gene Tyson, renowned microbiome experts
- Clinical-grade gut-health testing, using world-leading metagenomic sequencing technology
- NATA-accredited laboratory, meeting ISO 15189 medical laboratory standards

First, do no harm.

HIPPOCRATES

Evolution in clinical thinking

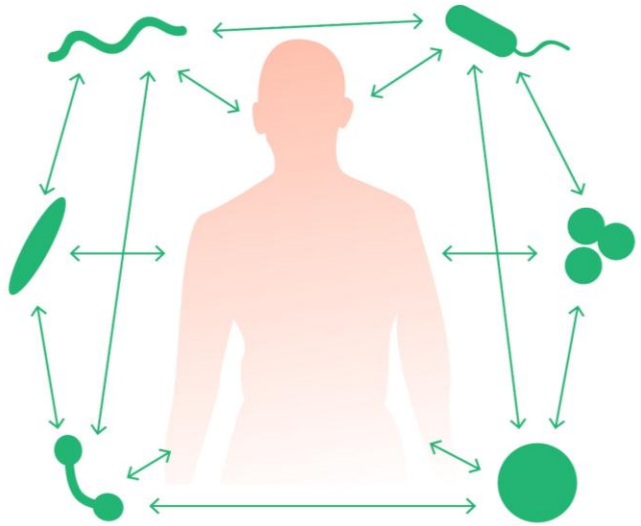
Then:



Pathogen

Identify and eradicate pathogens and pathobionts with antimicrobials or antibiotics

Now:



Microbiome

Assess the whole microbiome and clinical case to address the underlying cause

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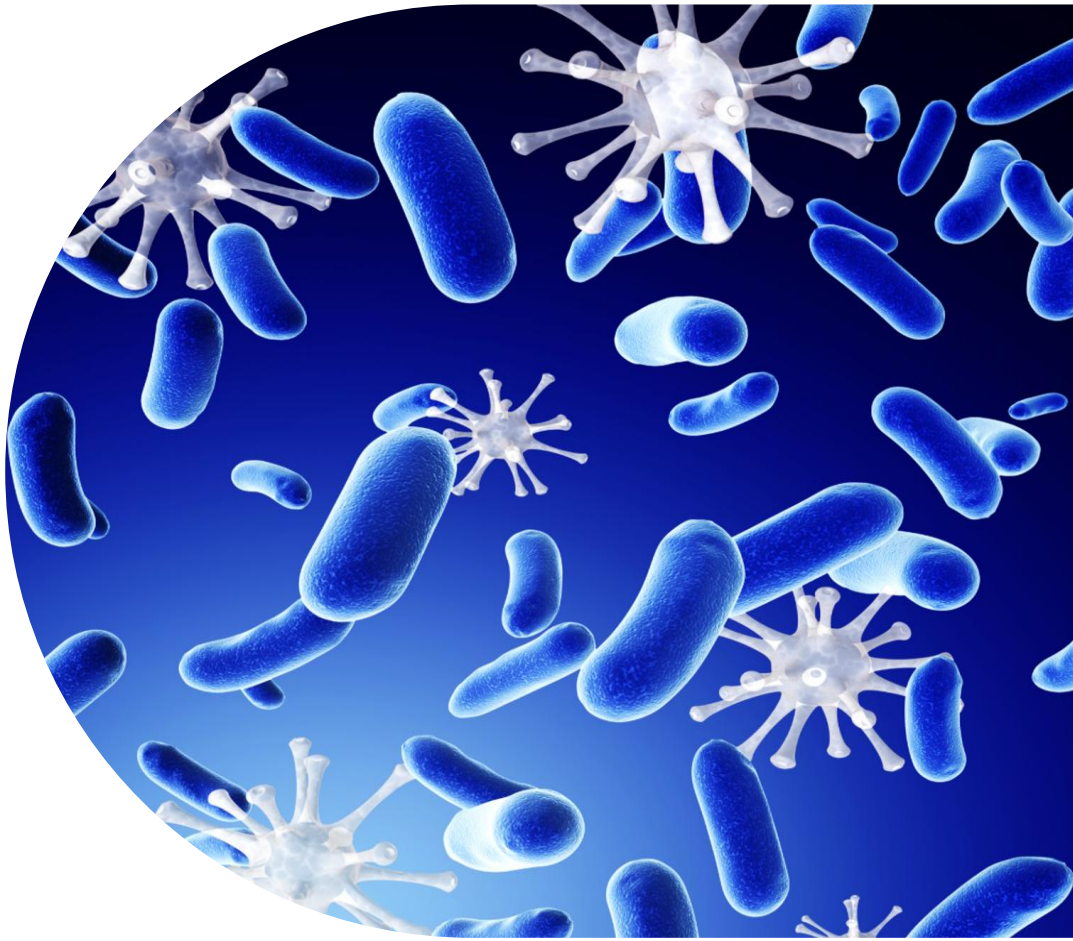
Myth: All dysbiotic microbes are pathogens

Pathogen	a microbe that can cause disease e.g. *Entamoeba histolytica*
Opportunistic pathogen	a microbial strain that can cause disease in susceptible hosts e.g. *Klebsiella oxytocca*
Pathobiont	a microbial species associated with negative health outcomes e.g. *Bilophila wadsworthia*
Commensal	a microbial species associated with positive health outcomes e.g. *Faecalibacterium prausnitzii*



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Myth: Because something natural, it is automatically gentler or more selective

- Action considered to be **selective** or **non-selective**.
- This refers to the specificity of the antimicrobial action.

Selective	Non-selective
Specifically suppress the growth of pathogens (e.g. *E. coli*)	May have antimicrobial effect on a wide variety of microbes including favourable commensal bacteria
Herbs: unknown due to limited research	Herbs: vast majority

Spotlight on berberine

An alkaloid found in several herbs and is often used to support blood sugar management

Study One by Zhang et al., 2020[1]

- Multi-centre, double-blind, randomised, placebo-controlled study
- 409 newly diagnosed diabetic patients
- 7 days of antibiotics
- 600mg of berberine twice daily for 12 weeks
- Microbiome measured with metagenomics with FDR* corrections

Study Two by Ming et al., 2021[2]

- Multi-centre, double-blind, randomised, parallel-controlled study
- 300 newly diagnosed hyperglycaemia patients
- 2-week run-in period with diabetes education
- 500mg of berberine twice daily for 16 weeks
- Microbiome measured with metagenomics without FDR corrections

1. *Zhang et al. 2020, Nat Commun, doi:10.1038/s41467-020-18414-8*

2. *Ming et al. 2021, Genome Med, doi:10.1186/s13073-021-00942-7*

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Increase in disease associated species

Bacteria	Disease Association and Features
E. coli[1,2]	Hexa-LPS producer High levels associated with Crohn's Disease and advanced liver fibrosis
Klebsiella oxytocca[1]	Hexa-LPS producer High levels associated with opportunistic infections and gastroenteritis
Ruminococcus gnavus[1,2]	High levels associated with IBS, Crohn’s disease, atherosclerosis and obesity
Klebsiella pneumoniae[1,2]	Hexa-LPS producer High levels associated with hypertension, intestinal inflammation, NAFLD and Crohn's disease
Bilophila wadsworthia[1]	Hydrogen sulphide producer High levels associated with colon cancer and intestinal inflammation
Klebsiella variicola[1]	Hexa-LPS producer High levels associated with multiple myeloma and gestational diabetes
Bacteroides_B dorei[1]	High levels associated with colon cancer and type 1 diabetes
Erysipelatoclostridium ramosum[1]	High levels associated with obesity, type 2 diabetes, Crohn’s disease, asthma
Citrobacter koseri[1]	Hexa-LPS producer
Enterobacter cloacae[1]	Hexa-LPS producer
Enterobacter hormaechei[1]	Hexa-LPS producer

Decrease in health associated species

Bacteria	Disease Association and Features
Bifidobacterium longum[1]	Reduction in harmful bacteria, anti-allergy effect, anti-obesity
Bifidobacterium adolescentis[1]	Anti-obesity effect, immune support Low level are seen in Crohn's disease, obesity, coeliac disease
Bifidobacterium catenulatum[1]	Low levels associated with colon cancer
Bacteroides_F pectinophilus[1]	Low levels associated with insulin resistance and metabolic syndrome
Roseburia hominis[1]	Primary producer of butyrate, supports immune system and reduces inflammation Low levels associated with IBD, hypertension
Roseburia inulinivorans[1,2]	Primary producer of butyrate Low levels associated with type 2 diabetes
Roseburia intestinalis[1,2]	Primary producer of butyrate Low levels associated with type 2 diabetes and Crohn's disease
Ruminococcus_E bromii[1]	Stimulates the growth of butyrate producing bacterial species
Faecalibacterium prausnitzii[1]	Butyrate producer
Coprococcus eutactus[1]	Butyrate producer
Bifidobacterium longum[1]	Reduction in harmful bacteria, anti-allergy effect, anti-obesity

Myth: You can tell if someone has a pathogen by symptoms alone

Acute pathogenic infection

- Watery diarrhoea, often sudden onset
- Urgency
- Blood or mucus in stools
- Abdominal pain and cramping
- Nausea and vomiting
- Fever
- Bloating
- Loss of appetite
- Fatigue / malaise

Chronic / unresolving infection

- Persistent or intermittent loose stools
- Steatorrhoea (greasy, floating stools)
- Unintentional weight loss
- Malabsorption & nutrient deficiencies (B12, iron)
- Persistent bloating and flatulence
- Chronic fatigue
- Post-infectious IBS-like symptoms
- Recurrent or relapsing episodes
- Reduced appetite

Test, don't guess

These symptoms overlap with many non-infectious conditions: IBS · IBD (Crohn's & ulcerative colitis) · coeliac disease · microscopic colitis · SIBO · bile-acid malabsorption · food intolerances · pancreatic insufficiency · medication effects · colorectal cancer

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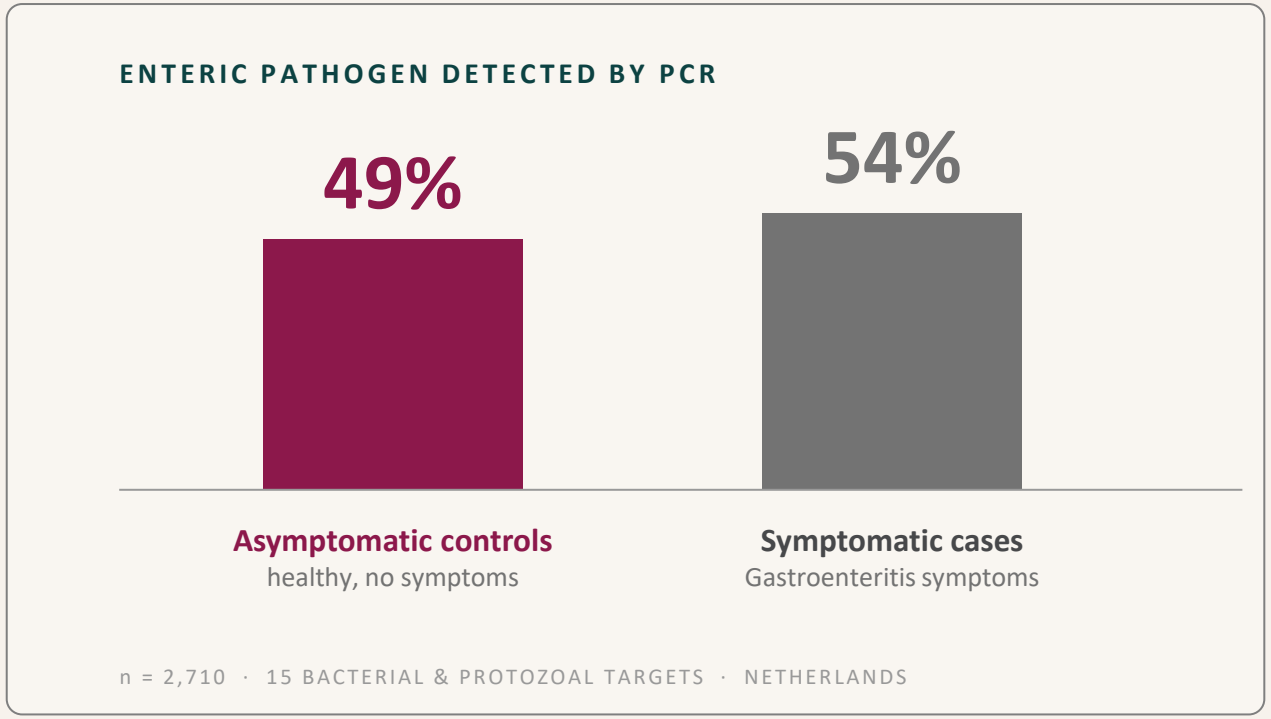
Myth: detection equals causation

The reality

- Many pathogens can be carried asymptomatically, without causing disease
- Some sensitive detection methods can detect clinically insignificant levels of microbes
- The same finding can be clinically significant in one patient and irrelevant in another.
- Detection must be interpreted alongside symptoms and clinical context



Carriage rates vary widely with the pathogen, the detection method and the population sampled.

Finding a pathogen confirms it is present – not that it is causing the patient's symptoms

Bruijnesteijn van Coppenraet et al. 2015, Clin Microbiol Infect, doi:10.1016/j.cmi.2015.02.007

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Myth: Every pathogen detected requires treatment

PATHOGEN MANAGEMENT GUIDELINES

Treat if detected	*Entamoeba histolytica*
Treat if symptomatic	*Clostridium difficile pathogenic strains (toxin B; hypervirulent C. difficile); Giardia lamblia*
Refer if symptomatic	*Escherichia coli pathogenic strains (ETEC, EAEC, EPEC, O157 , Shiga toxin, Shigella spp / EIEC)*
Clinical judgement required — not necessarily pathogenic	*Aeromonas, Campylobacter, Cryptosporidium, Salmonella, Vibrio spp.; Cyclospora cayetanensis; Yersinia enterocolitica; metagenomic potential pathogens (e.g. Campylobacter_D upsaliensis, Clostridium_P perfringens)*
Pathogenic role unclear — exclude other causes of symptoms first	*Dientamoeba fragilis; Blastocystis sub-types*

Management depends on the specific microbe and the clinical presentation.

Source: Microba Pathogen and Pathobiont Management Guide

Indications for medical assessment

	Bacterial diarrhoea	IBD	Colo-rectal cancer
↑ Calprotectin	🚩	🚩	
↑ Lactoferrin	🚩	🚩	
Occult blood	🚩	🚩	🚩

Vulnerable patient

Immunocompromised

Elderly / Frail

Child

These indicate possible **severe or systemic infection**:

- Bloody diarrhoea
- High fever (>38.5°C)
- Severe abdominal pain or tenderness
- Persistent vomiting (unable to keep fluids down)
- Signs of dehydration
- Bruising easily or jaundice (suggests hepatic or haematologic involvement)
- Unexplained weight loss

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Informed practice via whole ecosystem analysis

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You need a complete picture of the microbiome and gut environment

DIVERSITY

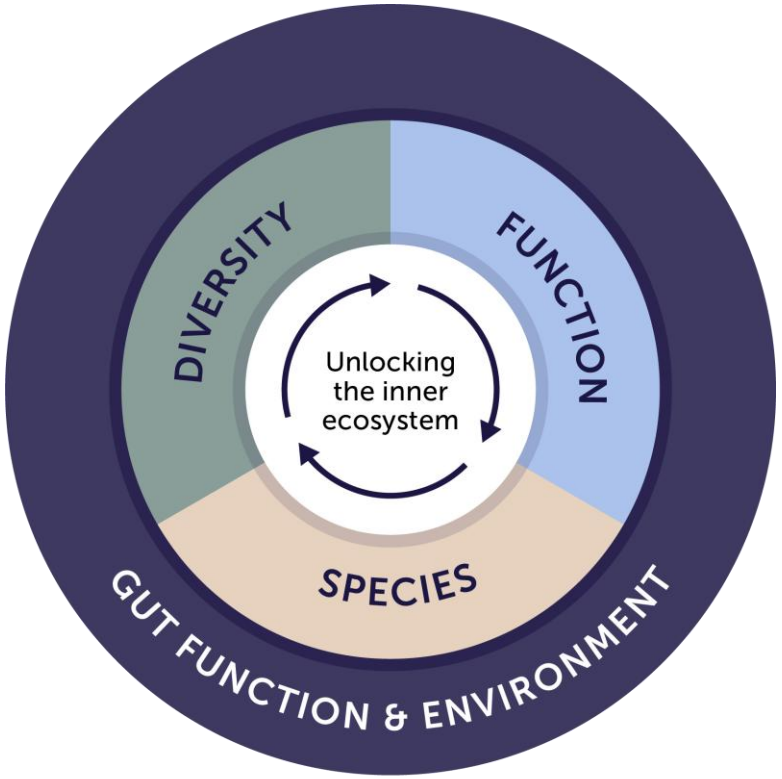
What is the microbial diversity and richness?

SPECIES

Who makes up the whole ecosystem – bacteria, archaea, fungi, protists?

Which species are present and what is their abundance?

Which species are under or overabundant?



MICROBIAL FUNCTION

What is the whole microbiome's capacity to produce or consume metabolites associated with health?

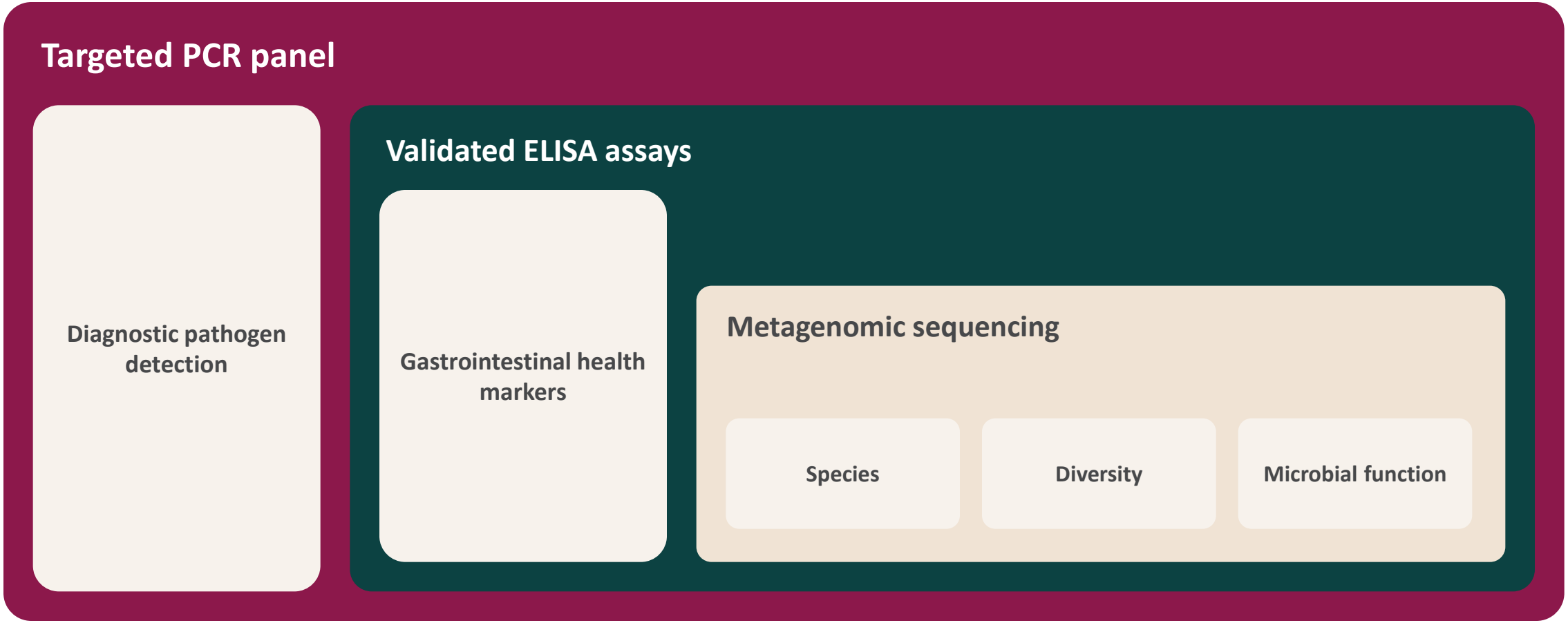
GUT FUNCTION & ENVIRONMENT

Are there alterations in transit time, gut barrier integrity, digestive secretions or intestinal inflammation?

PATHOGENS

Are pathogenic bacteria or protist parasites present?

Microba combines multiple technologies for the most comprehensive assessment



Two complementary viewpoints

PCR

Targeted detection

Highly sensitive diagnostic detection of specific target pathogens

“Is this specific pathogen present?”

+

Metagenomics

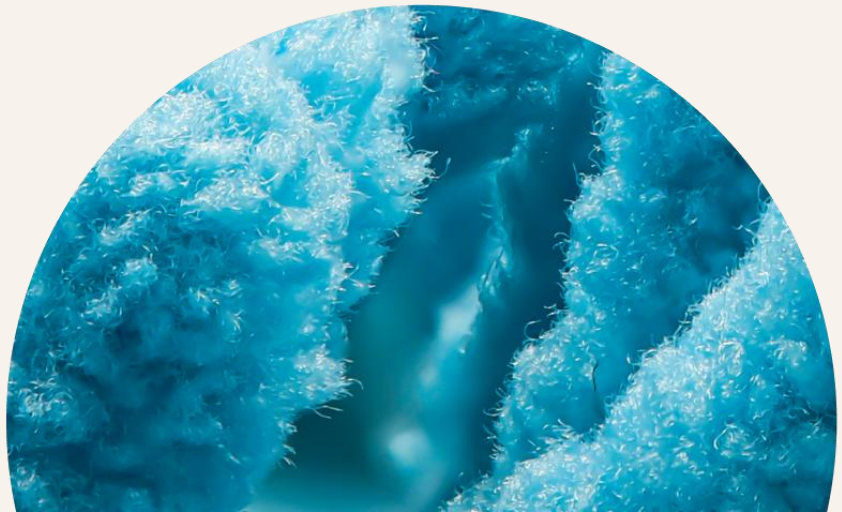
Whole-ecosystem view

Analyses the whole microbial community — including pathogens you’re not specifically looking for, and their relative abundance

“What broader microbiome factors may be driving symptoms?”

Used together in the Microba test — a precise answer and the full picture.

Case Example - **Pathogen**



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PCR Panel

Bacterial

Detected *Aeromonas* spp. Bacterial	Detected *Campylobacter* spp. Bacterial	Not Detected Shiga Toxin Bacterial	Not Detected Enterotoxigenic *E. coli*... Bacterial	Not Detected Enteropathogenic *E. coli*... Bacterial
Not Detected *Salmonella* spp. Bacterial	Not Detected Enteroaggregative *E. coli*... Bacterial	Not Detected *Yersinia enterocolitica* Bacterial	Not Detected *E. coli* O157 Bacterial	Not Detected *Vibrio* spp. Bacterial
Not Detected Hypervirulent *Clostridium*... Bacterial	Not Detected *Clostridium difficile* toxin B Bacterial	Not Detected *Shigella* spp./EIEC Bacterial		

Parasitic

Not Detected *Entamoeba histolytica* Parasitic	Not Detected *Cryptosporidium* spp. Parasitic	Not Detected *Dientamoeba fragilis* Parasitic	Not Detected *Giardia lamblia* Parasitic	Not Detected *Cyclospora cayetanensis* Parasitic

Metagenomic Analysis

	Phylum	Species	Abundance	Prevalence	Distance from Average
	Campylobacterota	*Campylobacter_D coli*	0.40%	Rare	

Clinical context

Aeromonas spp.

- Food- and water-borne.
- Presents as asymptomatic carriage or traveller's diarrhoea.
- Usually self-limiting
- Treat only if immunocompromised or symptoms are severe or persistent — guided by clinical presentation.

Campylobacter (C. jejuni & C. coli)

- Food-borne;
- Causes gastroenteritis.
- Usually self-limiting
- Treat only if immunocompromised or symptoms are severe or persistent — guided by clinical presentation.
- Faecal occult blood or suspected haemorrhagic colitis, arrange urgent investigation and specialist referral.

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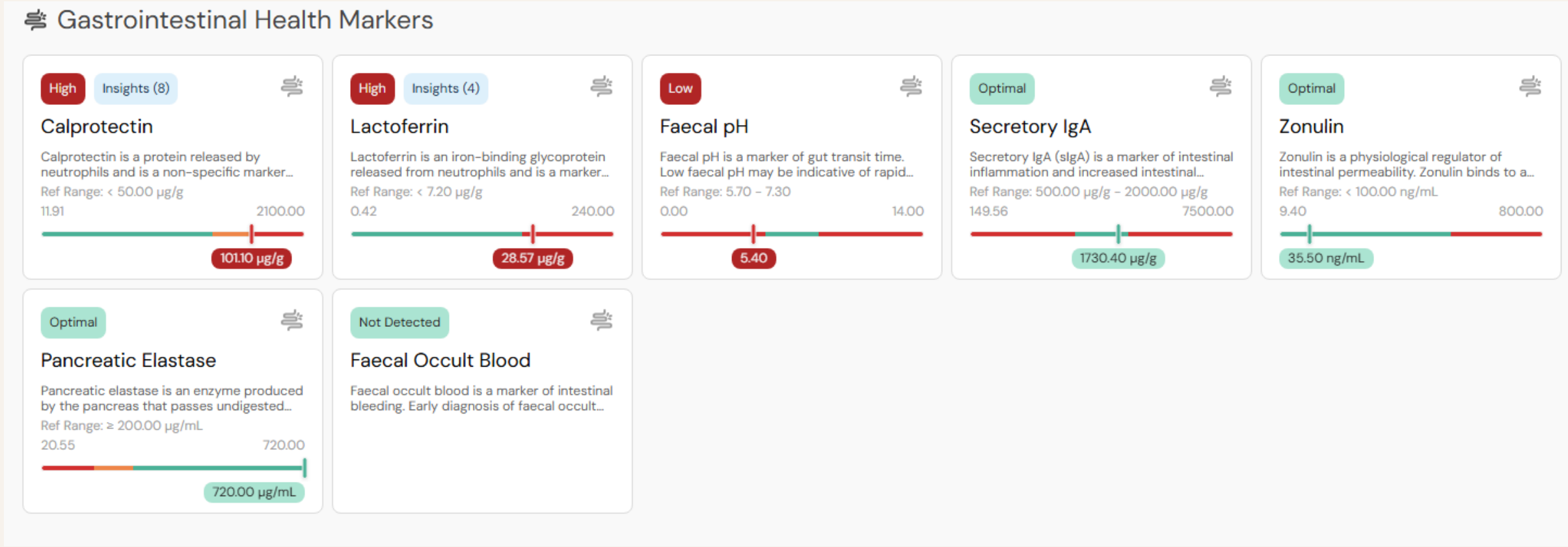
Gut Function & Environment



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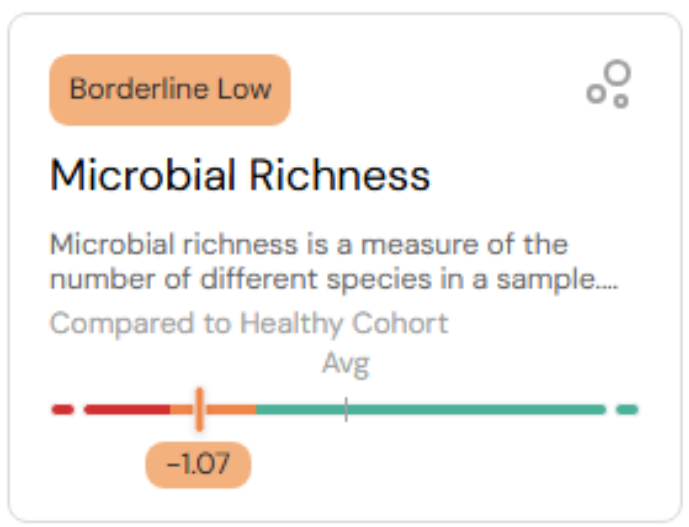
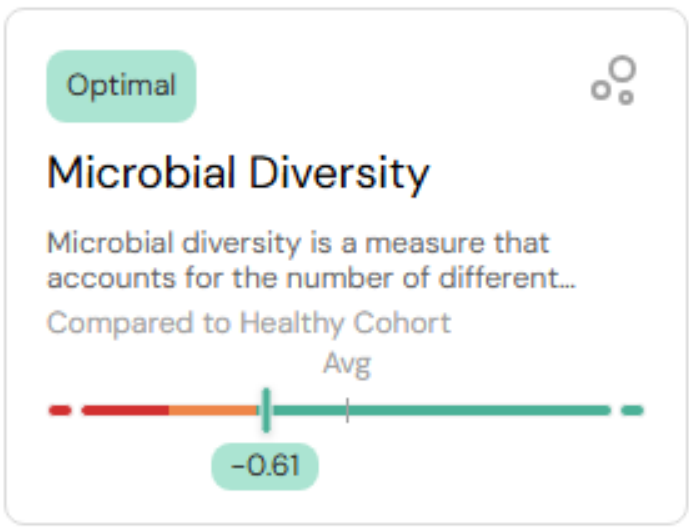
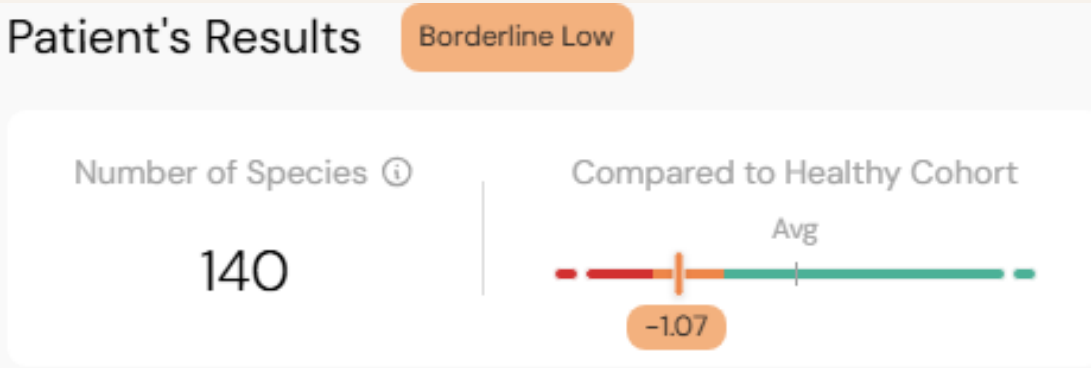
Diversity & Richness







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Microbial Function

Microbiome Markers

High | Insights (6)

BCAA producing microbes

Branched-chain amino acids (BCAAs), which include valine, leucine and isoleucin...

Compared to Healthy Cohort

Low | Insights (7)

Microbial Diversity

Microbial diversity is a measure that accounts for the number of different...

Compared to Healthy Cohort

Low

Microbial Richness

Microbial richness is a measure of the number of different species in a sample....

Compared to Healthy Cohort

Borderline High | Insights (2)

Hydrogen sulphide...

The gas hydrogen sulphide is produced by gut microbes when they break down...

Compared to Healthy Cohort

Borderline High | Insights (5)

Beta-glucuronidase...

Inulin supplementation may reduce faecal beta-glucuronidase activity.

Compared to Healthy Cohort

Optimal

Acetate producing microbes

Acetate is the most abundant short-chain fatty acid produced by our gut microbiom...

Compared to Healthy Cohort

Optimal

Oxalate consuming microbes

Oxalate is a key component of calcium oxalate kidney stones. Low microbial...

Compared to Healthy Cohort

Optimal

IPA producing microbes

3-indolepropionic acid (IPA) is a beneficial substance produced by some gut bacteri...

Compared to Healthy Cohort

Optimal

Butyrate producing...

Butyrate is a beneficial short-chain fatty acid that is important for gut health. Low...

Compared to Healthy Cohort

Optimal

Propionate producing...

Propionate is a short-chain fatty acid produced by the gut microbiome. Optimal...

Compared to Healthy Cohort

Optimal

Hexa-LPS producing...

Hexa-acylated lipopolysaccharides (hexa-LPS) are bacterial cell wall components of...

Compared to Healthy Cohort

Optimal

Mucin Degradation

Mucin is a component of the mucus layer that lines and protects the epithelial gut...

Compared to Healthy Cohort

Optimal

Trimethylamine producing...

Trimethylamine is produced by gut microbes from the breakdown of choline...

Compared to Healthy Cohort

Not Detected

B. fragilis toxin producing...

Bacteroides fragilis is a normal inhabitant of the human gut. A small proportion of B....

Not Detected

Methane producing archaea

Methane is an odourless gas produced by Archaeal species which can also be called...

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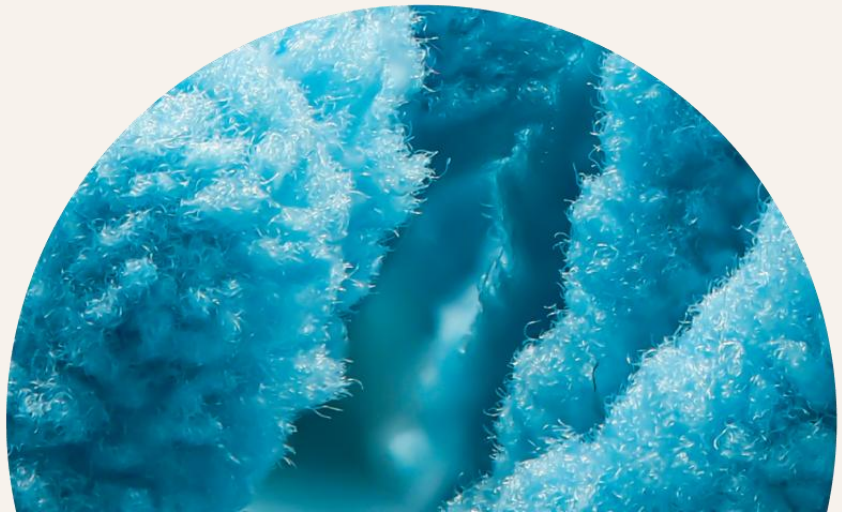
Case Example - **Pathobiont**



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Parasitic

Not Detected *Giardia lamblia* Parasitic	Not Detected *Entamoeba histolytica* Parasitic	Not Detected *Cyclospora cayetanensis* Parasitic	Not Detected *Dientamoeba fragilis* Parasitic	Not Detected *Cryptosporidium* spp. Parasitic

Metagenomic Analysis

pathogen

All Associations

We've tested but no were detected

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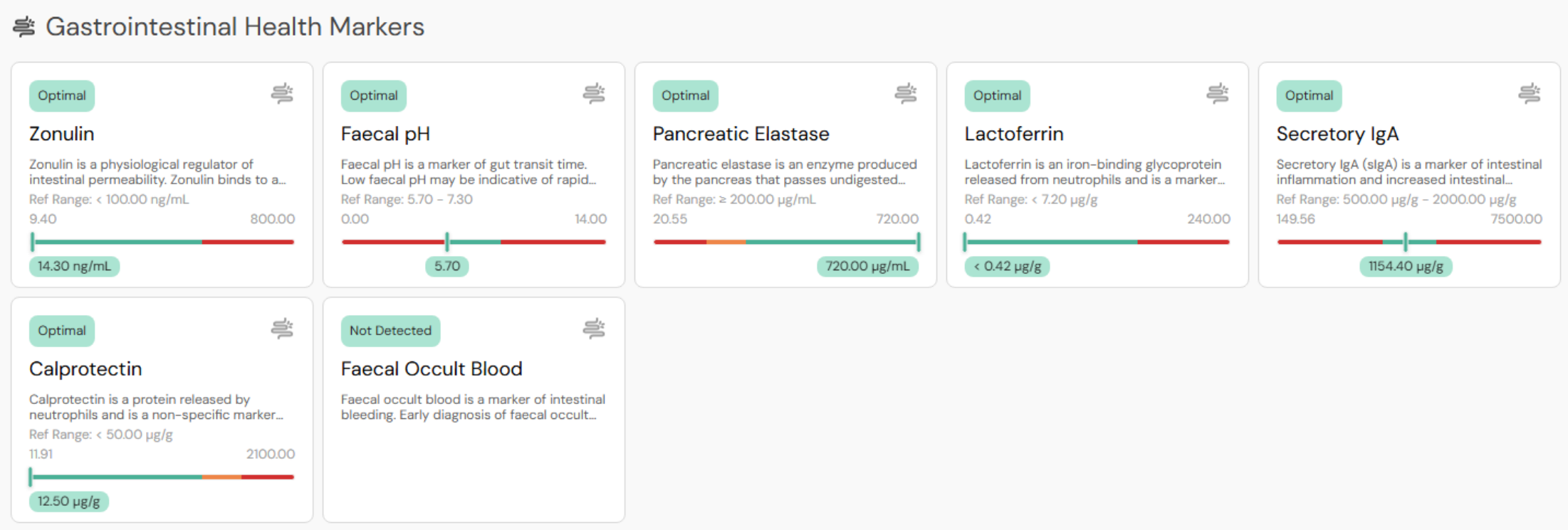
Gut Function & Environment



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Microbial Function

Microbiome Markers

High | Insights (5)

Beta-glucuronidase...

Inulin supplementation may reduce faecal beta-glucuronidase activity.

Compared to Healthy Cohort

Avg

+1.99

High | Insights (6)

BCAA producing microbes

Branched-chain amino acids (BCAAs), which include valine, leucine and isoleucin...

Compared to Healthy Cohort

Avg

+1.65

Low | Insights (7)

Microbial Diversity

Microbial diversity is a measure that accounts for the number of different...

Compared to Healthy Cohort

Avg

-1.63

Low

Microbial Richness

Microbial richness is a measure of the number of different species in a sample....

Compared to Healthy Cohort

Avg

-2.73

Borderline High | Insights (1)

Mucin Degradation

Mucin is a component of the mucus layer that lines and protects the epithelial gut...

Compared to Healthy Cohort

Avg

+0.78

Borderline Low | Insights (3)

IPA producing microbes

3-indolepropionic acid (IPA) is a beneficial substance produced by some gut bacteri...

Compared to Healthy Cohort

Avg

-1.17

Optimal

Trimethylamine producing...

Trimethylamine is produced by gut microbes from the breakdown of choline...

Compared to Healthy Cohort

Avg

+0.22

Optimal

Hydrogen sulphide...

The gas hydrogen sulphide is produced by gut microbes when they break down...

Compared to Healthy Cohort

Avg

-0.49

Optimal

Acetate producing microbes

Acetate is the most abundant short-chain fatty acid produced by our gut microbiom...

Compared to Healthy Cohort

Avg

+1.46

Optimal

Propionate producing...

Propionate is a short-chain fatty acid produced by the gut microbiome. Optimal...

Compared to Healthy Cohort

Avg

+0.18

Optimal

Oxalate consuming microbes

Oxalate is a key component of calcium oxalate kidney stones. Low microbial...

Compared to Healthy Cohort

Avg

+0.80

Optimal

Butyrate producing...

Butyrate is a beneficial short-chain fatty acid that is important for gut health. Low...

Compared to Healthy Cohort

Avg

-0.64

Not Detected

B. fragilis toxin producing...

Bacteroides fragilis is a normal inhabitant of the human gut. A small proportion of B....

Not Detected

Methane producing archaea

Methane is an odourless gas produced by Archaeal species which can also be called...

Not Detected

Hexa-LPS producing...

Hexa-acylated lipopolysaccharides (hexa-LPS) are bacterial cell wall components of...

Most abundant species

All Species

Species	Phylum	Prevalence	Relative Abundance %	Distance from Average
Bacteroides_B dorei	Bacteroidota	Common	20.00 %	+2.62
Blautia_A wexlerae	Firmicutes_A	Very common	8.00 %	+1.57
Bacteroides uniformis	Bacteroidota	Very common	6.00 %	+1.81
Agathobacter rectale	Firmicutes_A	Common	6.00 %	+1.05
Lachnospira MIC8634	Firmicutes_A	Rare	6.00 %	
Faecalibacterium prausnitzii_K	Firmicutes_A	Common	3.00 %	+1.10
Ruminococcus_E bromii_B	Firmicutes_A	Common	3.00 %	+0.27
Blautia_A MIC9206	Firmicutes_A	Less common	2.00 %	+1.84
Lachnospira rogosae	Firmicutes_A	Common	2.00 %	+1.72
Faecalibacterium prausnitzii_G	Firmicutes_A	Very common	2.00 %	+0.94
Anaerostipes hadrus	Firmicutes_A	Very common	2.00 %	+0.73
Roseburia inulinivorans	Firmicutes_A	Common	1.00 %	+1.82
Bacteroides ovatus	Bacteroidota	Common	1.00 %	+1.71
Fusicatenibacter saccharivorans	Firmicutes_A	Very common	1.00 %	-0.97
Eubacterium_E hallii	Firmicutes_A	Common	1.00 %	+0.58
Faecalibacterium prausnitzii_C	Firmicutes_A	Common	1.00 %	+0.27
Blautia_A obeum	Firmicutes_A	Common	1.00 %	+0.89

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Bacteroides_B dorei

This is a common inhabitant of the gut and is closely related to *Bacteroides vulgatus*.

Fuel Sources Used:
This species is a good degrader of fibre, a good degrader of mucin, and a moderate degrader of protein.

Metabolites produced:
Our genomic analysis indicates that most members of this species can produce the following metabolites: acetate, beta-glucuronidase, biotin (B7), branched chain amino acids, folate (B9), GABA, lactate, riboflavin (B2), vitamin K.

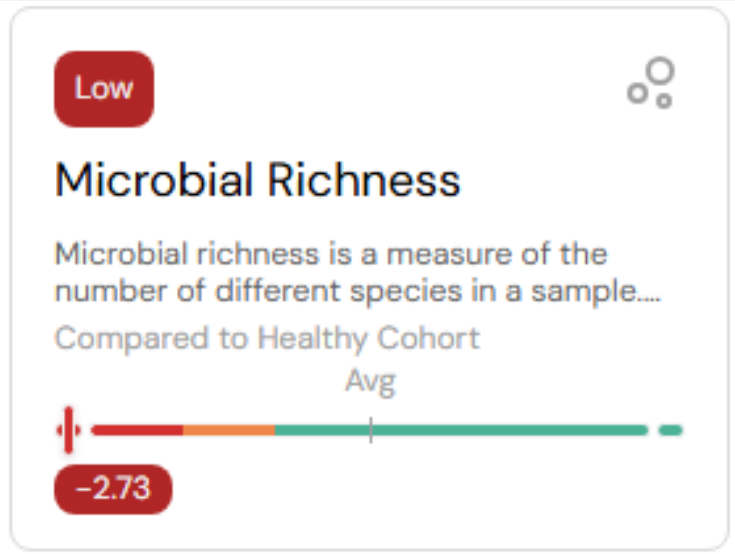
Metabolites consumed:
In addition, the genomic analysis shows that most members of this species can consume: GABA.

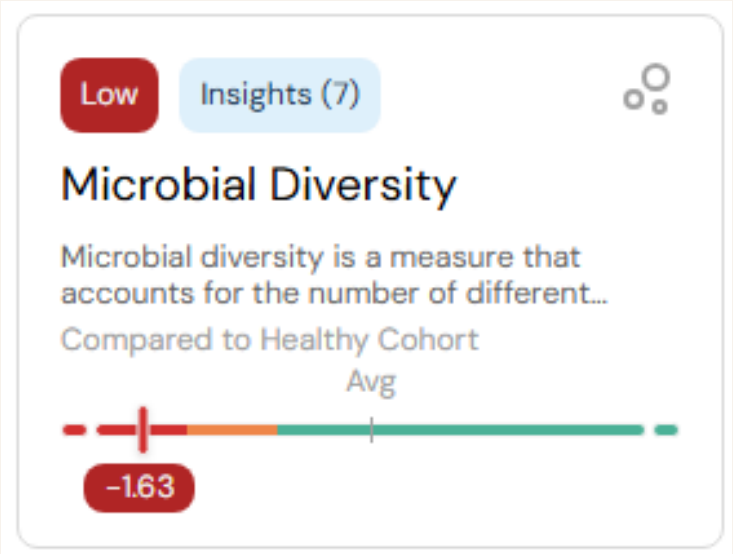
Emerging Research:
Higher levels of this species have been observed in patients with colon cancer and during the development of type 1 diabetes in children. This species has also been associated with diets high in red meat.

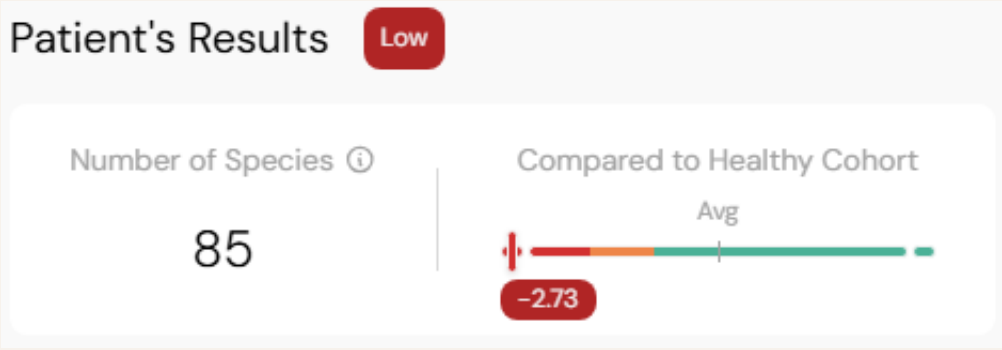
References

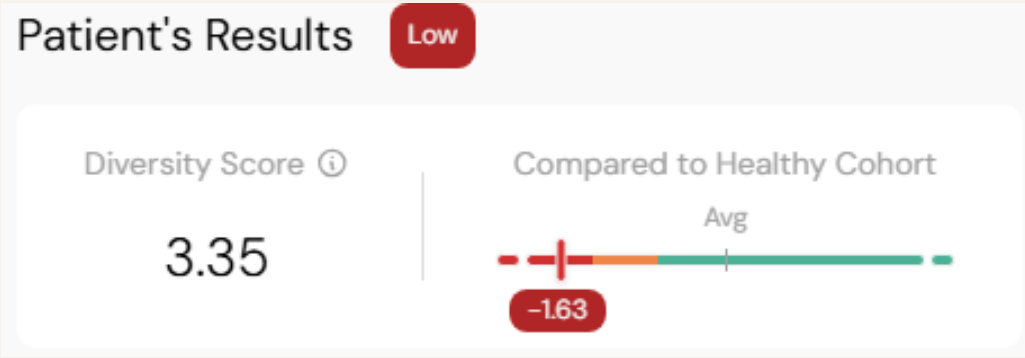
1 2 3 4 5 6

Richness and Diversity









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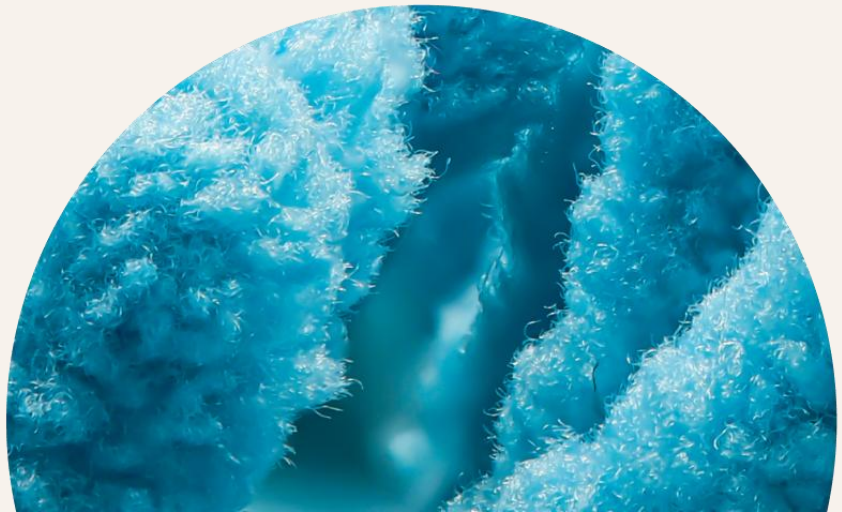
Pathogen & Pathobiont Management Framework



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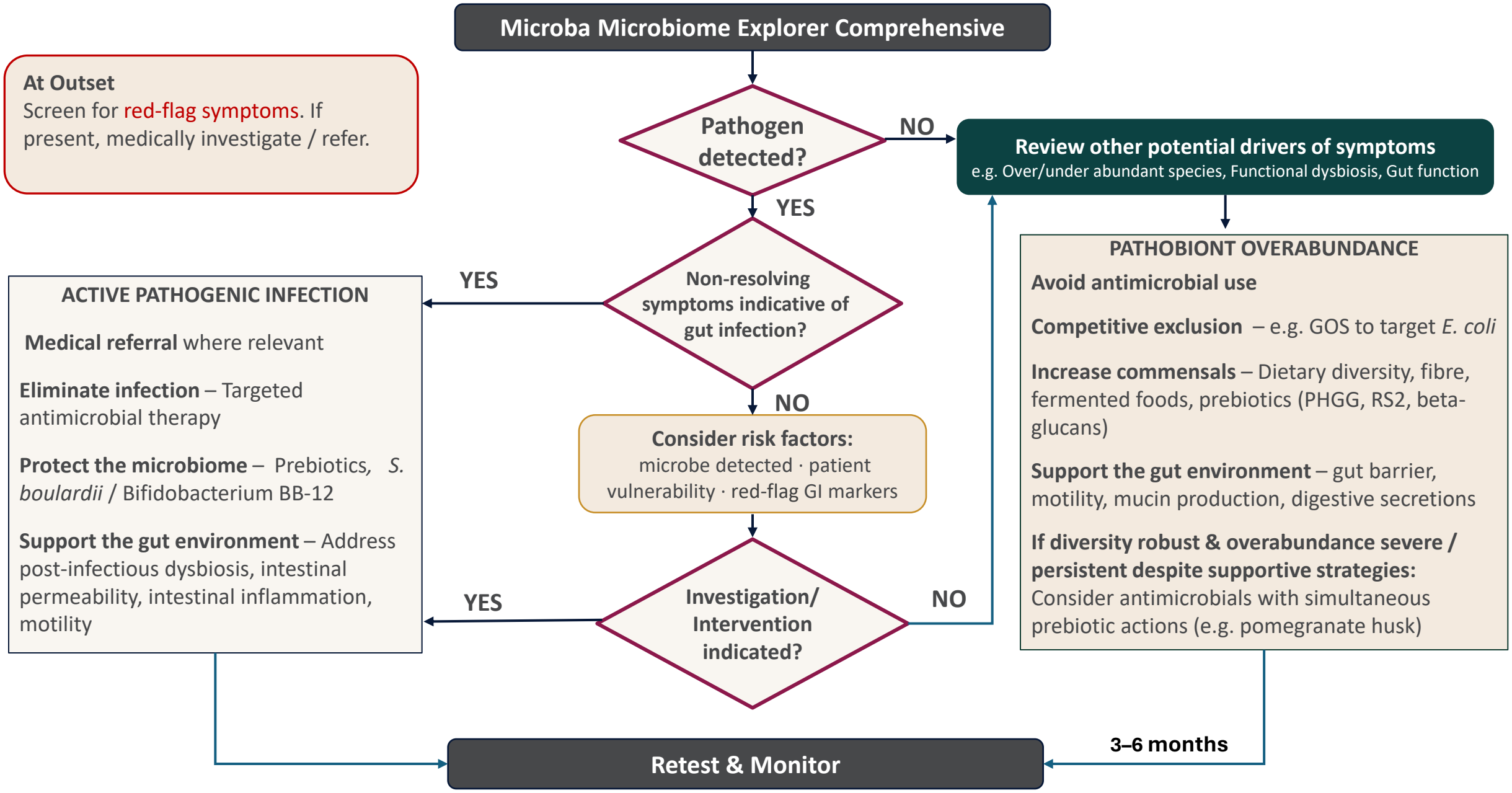
Microba Microbiome Explorer Comprehensive
At Outset
Screen for red-flag symptoms. If present, medically investigate / refer.
Pathogen detected?
NO
YES
Review other potential drivers of symptoms
e.g. Over/under abundant species, Functional dysbiosis, Gut function
PATHOBIONT OVERABUNDANCE
Avoid antimicrobial use
Competitive exclusion – e.g. GOS to target E. coli
Increase commensals – Dietary diversity, fibre, fermented foods, prebiotics (PHGG, RS2, beta-glucans)
Support the gut environment – gut barrier, motility, mucin production, digestive secretions
If diversity robust & overabundance severe / persistent despite supportive strategies: Consider antimicrobials with simultaneous prebiotic actions (e.g. pomegranate husk)
Non-resolving symptoms indicative of gut infection?
YES
ACTIVE PATHOGENIC INFECTION
Medical referral where relevant
Eliminate infection – Targeted antimicrobial therapy
Protect the microbiome – Prebiotics, S. boulardii / Bifidobacterium BB-12
Support the gut environment – Address post-infectious dysbiosis, intestinal permeability, intestinal inflammation, motility
NO
Consider risk factors:
microbe detected · patient vulnerability · red-flag GI markers
Investigation/ Intervention indicated?
YES
NO
3–6 months
Retest & Monitor
microba

Key takeaways

1. Not all pathogens, opportunistic pathogens and pathobionts need eradicating – clinical context is key

2. Test don't guess - make informed clinical decisions by assessing whole microbiome health

3. Antimicrobials may not be the best intervention option for the gut microbiome and should be carefully considered

4. If anti-microbials are necessary, take steps to protect the wider microbiome

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First, do no harm.

HIPPOCRATES

Designed to scale to clinical need

The tiered approach allows you to choose the right depth of analysis for each patient.

MICROBIOME EXPLORER COMPREHENSIVE

RRP £399

Metagenomics + GI Health Markers + Pathogen Screening

Full ecosystem mapping – A complete clinical picture from one sample.

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Microbiome and gut physiology insights – for chronic presentations once infection is ruled out.

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Thank you for listening

Any questions?