

The science behind Microba GI Navigator

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Executive summary

The gut microbiome and the wider gastrointestinal (GI) environment shape digestion, immune regulation and metabolic health, and disturbances in both are linked to conditions ranging from inflammatory bowel disease and colorectal cancer to irritable bowel syndrome and metabolic disease.¹⁻⁴

Yet the information practitioners need is usually scattered across separate tests – a stool culture or pathogen panel here, a calprotectin result there, a microbiome report somewhere else – each read in isolation. Bringing these layers together is where much of the clinical value lies.⁵

Microba GI Navigator is designed to close that gap. It integrates four complementary types of information within a single test ordered through a healthcare practitioner: microbial profiling and functional markers derived from shotgun metagenomics, a molecular pathogen panel using CE-marked assays, GI markers measured using CE-marked assays, and structured patient-reported information including symptoms and diet.

Rather than presenting these as isolated result sets, GI Navigator brings them together within a single report.

Every marker earns its place through an evidence-gated framework. Microbial markers must satisfy three independent tiers of evidence: a plausible mechanism of action, reproducible associations in

peer-reviewed human studies, and a statistically significant association in Microba's in-house dataset of more than 19,000 consented metagenomes.

Markers are then weighted by the strength of their link to one of 22 clinical Interpretations, and Interpretations are reported as "Evident", "Possibly Evident" or "Not Evident" using explicit, transparent logic.

The test reports 22 health Interpretations. Those rated Evident or Possibly Evident become Key Findings, each paired with ranked, evidence-graded Suggested Actions selected for practicality, safety and the strength of the supporting evidence, and graded using the Australian NHMRC framework.

Microbial results are compared against a carefully defined healthy group of 502 individuals processed through the same workflow as patient samples; certified gastrointestinal markers are interpreted against established manufacturer reference ranges.

This paper describes the scientific and technological foundations of Microba GI Navigator: how the four marker types are measured and evaluated, how raw data becomes an Interpretation, and what distinguishes this approach from legacy gut health testing.

Throughout, the emphasis is on transparency – making the evidence behind every result visible to the practitioner.

Introduction

The human gut is home to trillions of microorganisms whose collective genome encodes metabolic capabilities far exceeding those of the human genome alone.¹ Over the past two decades, large sequencing studies have shown that the composition and function of this microbial community differ between individuals and are associated with many aspects of health.²

A gut microbiome that differs from the pattern seen in healthy individuals – often described as dysbiosis – accompanies gastrointestinal, autoimmune, cardiometabolic and neurological conditions.^{2–4}

For both practitioners and the people being tested, the practical question is whether these different aspects of gut health can be measured accurately enough, and interpreted carefully enough, to provide useful clinical context. Answering that question often requires more than one type of information.

Molecular assays can detect established gastrointestinal pathogens. Stool-based GI markers can provide complementary information about intestinal inflammation, digestive function, mucosal immunity, gastrointestinal bleeding and the gut environment. Metagenomic profiling reveals which microbial species are present and the metabolic functions the community has the potential to perform. And a person's own symptoms, diet and other clinical information provide the context needed to give those measurements meaning.

Many gut health tests available today also rely on older measurement methods. Culture, quantitative PCR and 16S ribosomal RNA gene (16S) sequencing each provide only a partial view: 16S sequencing typically resolves organisms to the genus level and cannot reliably assess microbial function, while targeted panels report only a predefined list of organisms.^{6,7} Shotgun metagenomics – sequencing DNA from across the whole community rather than from a single gene – expanded what is possible, enabling species-level identification alongside analysis of the metabolic genes and pathways the community carries.^{7,8}

Microba GI Navigator builds on this foundation. It combines a CE-marked molecular pathogen panel, GI markers measured using CE-marked assays, high-resolution metagenomic profiling and structured patient information within a single test, and – importantly – it integrates them into shared Interpretations. An Interpretation is a specific state, biological process, or finding, relevant to a patient's health, that Microba reports from the overall pattern of microbial, gastrointestinal and patient markers assessed together.

This paper explains how these Interpretations are generated, how the underlying evidence is curated, and how results are translated into Suggested Actions that practitioners can use to support informed discussions with patients. As noted above, the microbiome component is for research use only; it is intended to support, not replace, clinical judgement.

A unified model for gut health: four marker types in one test

Microba GI Navigator draws on four complementary types of information. Each answers a different question, and their value increases when they are considered together.



■ MICROBIAL MARKERS

Microbial markers are derived from shotgun metagenomic sequencing of a stool sample, which provides a species-level profile of the gut microbiome together with an assessment of its functional potential.

Because different species within a single genus can play very different roles in health, species-level resolution matters clinically, and it is something genus-level 16S sequencing cannot reliably provide.⁷ Beyond identifying which organisms are present, metagenomics can assess the community's genetic potential to perform specific functions. Examples include the potential to produce butyrate, hydrogen sulphide, trimethylamine or hexa-acylated lipopolysaccharide, or to degrade mucin. These microbial markers describe what the microbial community may be capable of doing, rather than simply which organisms are present.

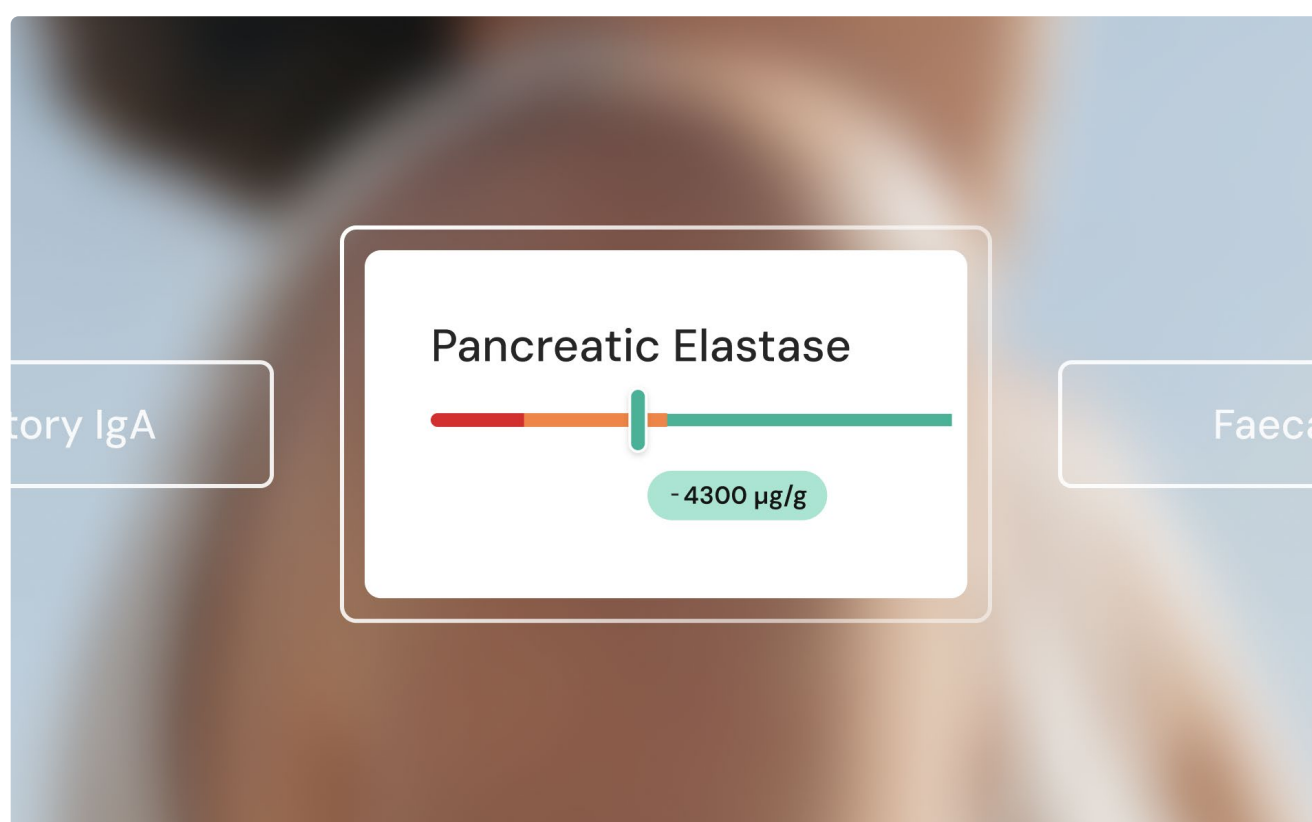
■ PATHOGEN MARKERS

Established gastrointestinal pathogens are detected using a CE-marked, PCR-based pathogen panel covering 13 common bacterial targets and virulence factors and four parasitic pathogens. Because these organisms are established causes of acute gastrointestinal illness, results are reported categorically as present, absent or indeterminate rather than compared with a healthy reference range. The same molecular panel also detects two organisms whose clinical significance remains uncertain. These are reported separately and interpreted conservatively, as described later.

■ GASTROINTESTINAL MARKERS

Gastrointestinal markers are host-derived stool measurements that provide information about intestinal function and tissue health. These include calprotectin and lactoferrin as markers of intestinal inflammation; faecal occult blood, measured using a faecal immunochemical test (FIT), as a marker of gastrointestinal bleeding; faecal elastase-1 as a marker of pancreatic exocrine function; secretory immunoglobulin A as a marker related to mucosal immunity; and zonulin family peptides.

Most of these markers are measured using CE-marked assays within their defined intended purposes. Faecal pH is also measured as an investigative marker for research use only. Together, these measurements provide host-derived context that can be considered alongside the microbial findings.



■ PATIENT MARKERS

Patient markers capture structured information reported by the patient, including selected medical history and medication use, physical symptom burden, psychosocial health symptoms, gastrointestinal symptoms, and dietary patterns. Medical history, medications, physical symptom burden and psychosocial health symptoms are captured as present or absent. Gastrointestinal symptoms are classified as present, absent, or where applicable, partially present. Dietary markers are classified as low, moderate or high.

This information is not treated as incidental context. Symptoms are incorporated into an Interpretation according to the strength of their association with it, while dietary markers are included where evidence links them to the relevant microbial findings. In this way, the patient's symptoms and dietary context form part of the integrated Interpretation

How microbial markers earn their place: the evidence-gated framework

Not every microbial signal is clinically meaningful. To ensure that the microbial markers reported in Microba GI Navigator are supported by robust evidence, each candidate microbial marker must pass through a three-tier evidence-gated framework before it can contribute to an Interpretation. Generally, only markers that satisfy all three tiers are included, with limited and clearly disclosed exceptions.

Tier 1 – Plausible biological mechanism

There must be in-vitro, in-vivo or other mechanistic evidence providing a biologically plausible explanation for the relationship between the microbial marker and the Interpretation. The relationship may be direct, where the marker contributes to the biological process, or indirect, where the health state or gut environment helps explain why the marker is altered.

For example, the link between high levels of mucin-degrading species and a pro-inflammatory microbiome is supported by in vivo studies showing that, when dietary fibre is scarce, these microbes can increase in abundance and consume the protective mucus layer, bringing bacteria into closer contact with the gut lining and driving immune activation.^{9,10}

Tier 2 – Reproducible human associations

At least two peer-reviewed human studies must demonstrate a direct or indirect association between the microbial marker and the health state assessed in the Interpretation. Direct evidence demonstrates a correlation between the marker and a clinical measure of that state;

indirect evidence reproducibly links the marker, or a circulating metabolite derived from it to a disease associated with that state. Increased mucin-degrading capacity, for instance, has been reproducibly reported in colorectal cancer cohorts,^{11,12} a disease that is associated with intestinal inflammation.

Tier 3 – Significant association in Microba's in-house dataset

The microbial marker must show a statistically significant association (false discovery rate < 0.05) of at least a small effect size in Microba's database of more than 19,000 consented metagenomes, with a pre-defined list of diseases linked to the health state.

All analyses are controlled for age, sex, body mass index and Bristol stool index. This step confirms that a marker supported by the published literature also reproduces in a large, independent cohort processed through Microba's own laboratory and analysis pipeline.

Exceptions to this include where internal validation is not feasible due to limited numbers for a relevant disease group (e.g., marker: oxalate degradation and disease group: calcium oxalate stone formers), or where the marker is not expected to distinguish between health and disease (e.g., marker: acetate production).

Once a microbial marker qualifies, its contribution to a given Interpretation is weighted by the strength of the evidence linking the two. This produces four marker–strength tiers:

- **Strong** – the marker is associated with a human clinical measure that directly reflects the Interpretation (e.g., methane producer abundance is positively correlated with gut transit as measured by radio-opaque markers) or the marker itself is the Interpretation (e.g., microbial diversity).
- **Moderate** – a circulating form of the marker, or a related metabolite, is associated with a clinical measure that directly reflects the Interpretation (e.g., plasma trimethylamine-N-oxide is positively correlated with plasma HsCRP).
- **Weak** – the marker is linked only indirectly through associated health conditions, or it is a GI marker not validated for assessing that specific Interpretation (e.g., faecal occult blood used in the context of inflammation).
- **Borderline** – a Strong, Moderate or Weak marker is present at a borderline level.



Evidence for non-microbial markers

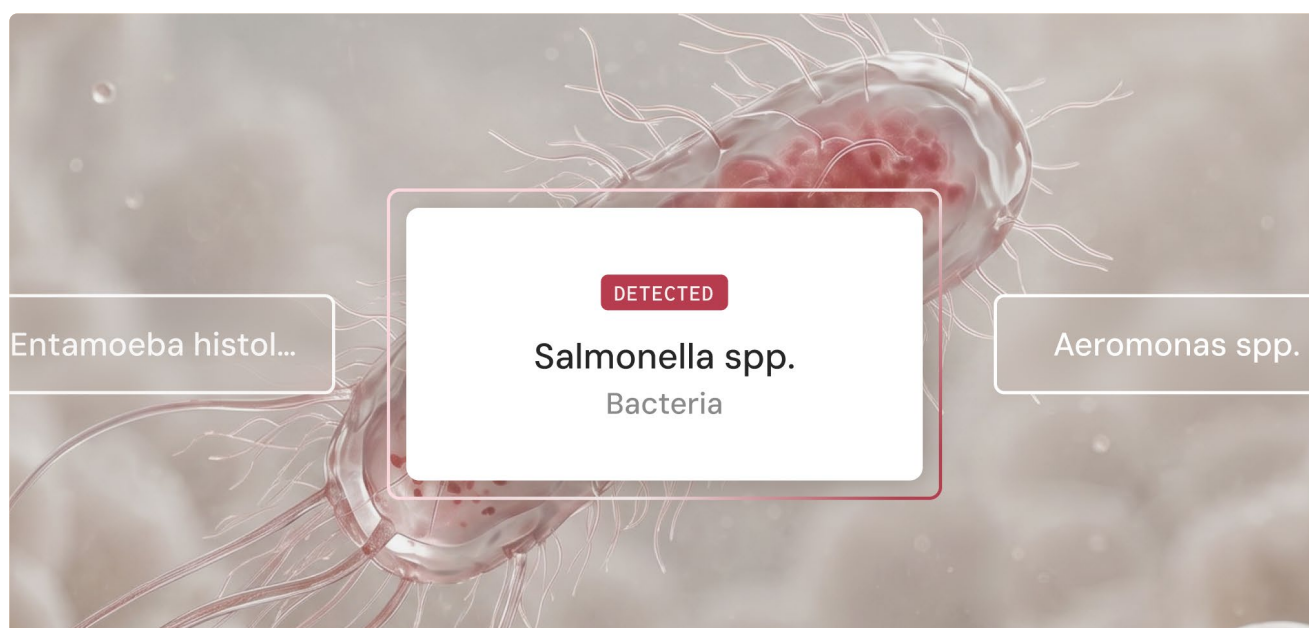
Gastrointestinal, pathogen and patient markers are evaluated using principles appropriate to each marker type. GI markers are generally included in the Interpretations that align with their validated intended purpose.

In rare cases, a GI marker may also contribute to an additional Interpretation where there is both a biologically plausible mechanism and supporting published evidence. At present, this applies only to faecal occult blood in relation to gut inflammation and pH in relation to slower colonic transit.

GI markers are also weighted according to the strength of evidence linking them to each Interpretation. A **strong GI marker** is measured using a certified assay and is used within its validated clinical purpose for the Interpretation in which it appears. Where a GI marker is not clinically validated for that specific Interpretation, but is supported by mechanistic and published evidence, it is treated as a **weak GI marker**.

Pathogen markers are established potentially pathogenic organisms tested with a validated, certified assay.

Patient symptom, medical history, medication and psychosocial risk markers are weighted by the strength of their association with the Interpretation using the NHMRC framework, and dietary markers are included where they are linked to the microbial markers in that Interpretation.



From markers to Interpretations

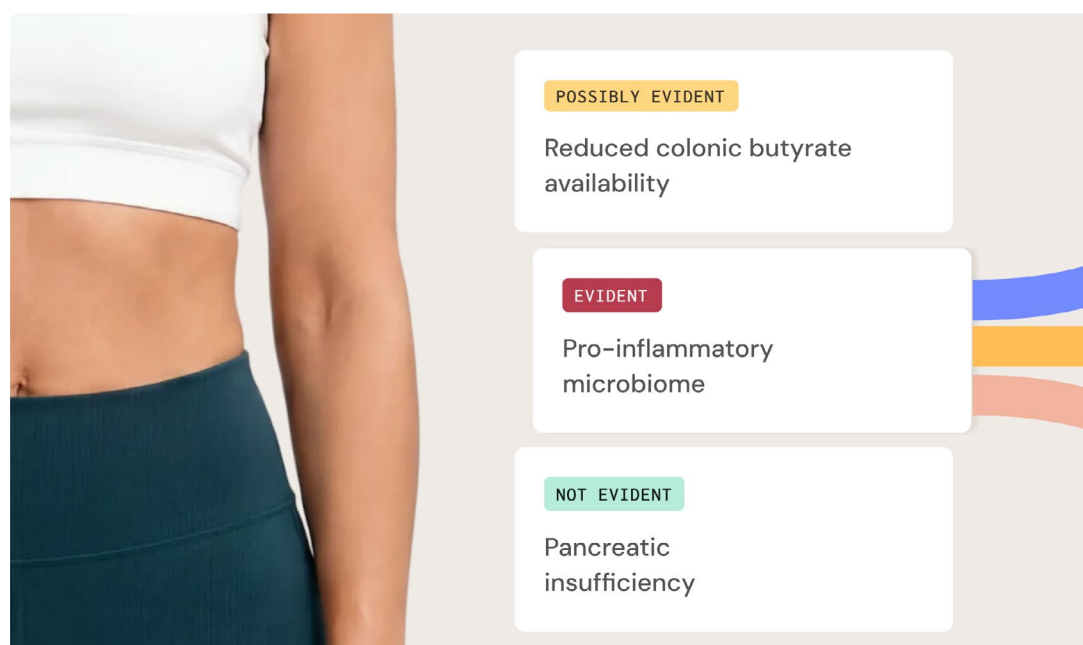
Generating accurate data is necessary but not sufficient. For gut health testing to be useful, the data must be translated into information that can support practitioners in their evaluation of the patient.

Microba GI Navigator does this by organising relevant markers into health Interpretations. Each Interpretation is a specific state, biological process, or finding, relevant to a patient's health, that Microba reports from the overall pattern of microbial, gastrointestinal and/or patient markers assessed together.

Examples of Interpretations include: a pro-inflammatory microbiome, slower colonic transit or visceral hypersensitivity. Related Interpretations are then grouped into broader health categories.

Within each Interpretation, the relevant microbial, gastrointestinal and patient markers are assessed collectively. The Interpretation is rated using predefined logic that considers both the number of markers that are out of range and the strength of evidence linking each marker to the Interpretation. Each Interpretation is reported as one of three outcomes:

- **Evident** – the combination of findings meets the predefined threshold for demonstrating there is evidence to support the Interpretation.
- **Possibly Evident** – some findings support the Interpretation, but the threshold for Evident is not met.
- **Not Evident** – the available findings provide insufficient support for the Interpretation.



These ratings indicate the degree to which the results support a particular Interpretation. They do not independently diagnose a condition or confirm that a specific physiological process is occurring.

In total, Microba GI Navigator reports 22 Interpretations. Nineteen draw on microbial, gastrointestinal and/or pathogen markers, often in combination with patient-reported information. A further three—dietary gaps, psychosocial risk and lower gastrointestinal symptoms—are derived from patient-reported symptoms and dietary information alone. The full set of Interpretations is summarised in Table 1. A couple of worked examples illustrate how different marker types are integrated.

■ WORKED EXAMPLE: SLOWER COLONIC TRANSIT

This Interpretation combines a microbial marker, a gastrointestinal marker and several patient markers.

The primary microbial signal is methane production potential, a strong marker carried predominantly by methanogenic archaea such as *Methanobrevibacter smithii*. Experimental studies indicate that methane can alter intestinal motility and slow transit, while human studies consistently report higher methanogen abundance and methane production with constipation, particularly constipation-predominant irritable bowel syndrome.¹³

Faecal pH contributes as a supporting, weak gastrointestinal marker. Slower colonic transit is generally associated with higher faecal pH and lower short chain fatty acid concentrations, alongside a shift from carbohydrate towards protein fermentation.^{14,15}

Relevant patient markers include hard or lumpy stools, lower frequency of bowel motions, symptoms consistent with constipation or IBS-C, laxative use and known redundant colon.

An Evident rating requires either the Strong microbial marker—methane-production potential—together with at least one relevant patient marker, or the Weak gastrointestinal marker—faecal pH—together with the highest-graded patient marker, hard or lumpy stools.

A **Possibly Evident** rating is assigned where there is less supporting evidence: faecal pH together with any relevant patient marker; two or more patient markers by themselves; or hard or lumpy stools alone.

■ WORKED EXAMPLE: VISCERAL HYPERSENSITIVITY

This Interpretation is driven primarily by microbial markers considered alongside patient-reported symptoms.

Histamine-production potential is a moderate strength microbial marker. Histamine receptors, including H1 and H4 receptors, are expressed on neural and immune cells within the human gut. Activation of these pathways can sensitise visceral afferent nerves and amplify pain signalling.¹⁶ In one study, gut bacteria from a subgroup of patients with irritable bowel syndrome produced high levels of histamine and induced visceral hyperalgesia when transferred into mice. This effect was reduced by blocking the histamine H4 receptor.¹⁷

Hexa-acylated lipopolysaccharide production potential is another moderate strength marker. It can promote visceral sensitisation through TLR4-driven proinflammatory signalling.¹⁸

Butyrate production potential is a weak strength marker and may support reduced visceral sensitivity in humans.¹⁹

These markers are interpreted alongside relevant patient markers such as IBS symptoms, chronic visceral pain conditions and the degree of physical symptom burden.

An Evident rating requires either high histamine-production potential or high hexa-acylated LPS-production potential with at least two supporting patient markers.

A **Possibly Evident** rating is assigned where there is less supporting evidence: one microbial marker together with one patient marker; the highest-ranked patient marker alone (IBS symptoms); or any two supporting patient markers.

TABLE 1

The 22 Interpretations reported by Microba GI Navigator, grouped by health category.

HEALTH CATEGORY	INTERPRETATION	MARKER TYPES
Gut environment	Altered mucosal immunity	GI
Gut environment	Blood in stool	GI
Gut environment	Gut inflammation	GI
Gut environment	Pro-inflammatory microbiome	Microbial, Patient
Gut barrier	Colonic butyrate availability	Microbial, Patient
Gut barrier	Mucus-disrupting microbiome	Microbial
Gut barrier	Intestinal permeability link	Microbial, Patient
Gut function	Pancreatic insufficiency	GI, Patient
Gut function	Slower colonic transit	Microbial, GI, Patient
Gut-brain axis	Abdominal pain link	Microbial, Patient
Gut-brain axis	Visceral hypersensitivity	Microbial, Patient
Gut infection	Bacterial pathogens	Pathogen
Gut infection	Parasitic pathogens	Pathogen
Microbiome balance	Impaired detoxification	Microbial
Microbiome balance	Low microbiome diversity	Microbial
Microbiome balance	Organisms of uncertain significance	Pathogen
Microbiome balance	Putrefactive microbiome	Microbial, Patient

HEALTH CATEGORY	INTERPRETATION	MARKER TYPES
Microbiome balance	Systemic inflammation link	Microbial
Microbiome balance	Unbalanced SCFA producers	Microbial, Patient
Clinical context	Dietary gaps	Patient
Clinical context	Lower GI symptoms	Patient
Clinical context	Psychosocial risk	Patient

Key findings and suggested actions

Interpretations rated Evident or Possibly Evident are surfaced as Key Findings – the results most likely to warrant a practitioner's attention. Each Key Finding is paired with one or more evidence-graded Suggested Actions, so that the report not only describes the finding but presents available evidence for what may be done in response.

Suggested Actions are selected using a structured, evidence-based process. For each Key Finding, the report first identifies the out-of-range microbial marker with the strongest evidence of association with that Interpretation. Candidate suggested actions for that marker are then prioritised against a defined set of criteria, including:

- whether the action involves medical referral, medication or another intervention requiring medical oversight;
- its feasibility and suitability for real-world clinical practice;
- tolerability – whether it is likely to provoke or aggravate GI symptoms; and
- the strength and relevance of the supporting evidence.

The evidence assessment considers the consistency and magnitude of the observed effect, the NHMRC Grade of Recommendation, whether the studies measured the same outcome as the report or a related outcome, and the study sample sizes.

All candidate suggested actions are ranked against these criteria. In the Key Findings and Suggested Actions view, only the highest-ranked action is shown initially. In future versions of the report, the remaining actions will also be available for viewing in ranked order. All Suggested Actions include a "Reasoning" section that provides the NHMRC evidence grade and hyperlinks to the studies used to inform the grade.

This layered approach—combining mechanistic plausibility, reproducible human evidence, internal validation and transparent, evidence-graded Suggested Actions—provides practitioners with a clear rationale for each finding and an evidence-based foundation for discussions with their patients.

Benchmarking results: comparison groups

A result only means something relative to an appropriate comparator, and the right comparator differs by marker type. Microba GI Navigator is explicit about which is used for each (Table 2).

Microbial markers are compared against Microba's healthy group: metagenomic profiles from 502 individuals who met strict criteria for health. These criteria include no major medical conditions; no or minimal gastrointestinal symptoms; mild or no stress, anxiety and depression; no recent use of medications known to have a strong impact on the gut microbiome, and lifestyle factors consistent with general health, such as a body mass index below 30, no smoking, daily fruit and vegetable intake, and low-to-moderate alcohol consumption.

Crucially, every healthy sample was collected and processed using the same workflow as patient samples. This removes a common and underappreciated source of bias: tests that compare patient results against public datasets, or against their own entire database regardless of health status, introduce variability from differences in collection, processing, analysis and/or health status.

Gastrointestinal markers are interpreted against the established reference ranges provided by the assay manufacturers, consistent with their CE-marked intended use.

Patient and pathogen markers are not compared against a reference group. Patient markers are graded as present, partially present or not present, or as low, moderate or high (dietary patient markers), while pathogens are reported as detected, not detected or indeterminate. This categorical reporting reflects the nature of the underlying information.

TABLE 2

Comparison basis for each marker type in Microba GI Navigator.

MARKER TYPE	COMPARISON BASIS	HOW RESULTS ARE REPORTED
Microbial	Microba healthy group (n = 502)	Within or outside the healthy range
Pathogen panel (CE-marked)	No comparison group	Detected, not detected or indeterminate
Gastrointestinal (CE-marked)	Established manufacturer reference ranges	Within or outside the reference range
Patient – symptoms	No comparison group	Present, partially present or not present
Patient – diet	No comparison group	Low, moderate or high

Technology and quality foundations

The Interpretations described above are only as reliable as the data that underpin them. Microba's GI Navigator is built on the same validated technology platform used across Microba's microbiome testing. This platform is described in detail in the companion Microba Microbiome Explorer white paper, with its key elements summarised below.

SAMPLE PRESERVATION.

Stool samples remain biologically active after collection, meaning microbial composition can change if the sample is not adequately preserved. Microba uses a swab-based active-drying collection tube that was benchmarked against commonly used room-temperature preservation methods in a peer-reviewed study.

It showed the best overall performance among the methods tested for technical reproducibility and compositional stability and maintained its performance across a range of storage temperatures, supporting its suitability for postal collection.²⁰

ACCREDITED, AUTOMATED LABORATORY.

Sequencing, gastrointestinal marker assays and pathogen panels are performed in a NATA-accredited medical laboratory operating to ISO 15189 standards. The laboratory uses a high level of automation, supported by an automated quality-control pipeline that monitors each sample throughout processing.

The software used to analyse and interpret the sequencing data has been benchmarked by Parks et al. 2021²¹ and are developed under an ISO 13485 quality management system for software as a medical device.

SHOTGUN METAGENOMICS AND THE MICROBA COMMUNITY PROFILER.

Shotgun metagenomic sequencing analyses DNA extracted from a stool sample, providing a comprehensive and relatively unbiased profile of the microbial community.⁸

Sequencing reads are classified using the Microba Community Profiler, Microba's proprietary whole-genome alignment tool. In a peer-reviewed benchmarking study, the profiler was compared with nine widely used academic classifiers across 140 simulated microbial communities.

It achieved the highest combined precision and recall among the classifiers evaluated, while maintaining very high precision and substantially reducing false-positive species calls.²¹ Accurate species identification is important because false-positive detections can lead to misleading interpretations of an individual microbiome profile.

What distinguishes Microba GI Navigator

Several features distinguish Microba GI Navigator from conventional gut microbiome tests.

- **Integration across four data types.** Microbial, pathogen, gastrointestinal and patient information are combined into shared Interpretations rather than presented as separate, disconnected result sets. This allows the report to identify potentially meaningful relationships across data layers—for example, the combined patterns of methane, faecal pH and patient symptoms associated with slower colonic transit.
- **High-resolution metagenomics.** Species-level shotgun metagenomic profiling and whole-community assessment of functional potential provide substantially greater resolution than the predominantly genus-level information generated by conventional 16S sequencing or the predefined targets included in qPCR panels.⁷
- **Evidence-gated marker curation.** Markers are reported only where supported by mechanistic plausibility, reproducible human evidence and internal validation, with limited, scientifically justified exceptions. This limits the inclusion of scores or Interpretations with insufficient scientific support.
- **Transparent, evidence-graded actions.** Suggested Actions are ranked using explicit criteria, assigned NHMRC Grades of Recommendation and linked directly to the studies used in their assessment.
- **Restraint where the evidence is uncertain.** Organisms of uncertain clinical significance are reported separately, in line with current guidance, helping to reduce the risk of overinterpretation and unnecessary treatment.^{22,23}
- **Like-for-like benchmarking and dual accreditation.** Microbial results are compared with a healthy reference cohort whose samples were collected, processed and analysed using the same workflow. Testing is performed within a NATA-accredited medical laboratory operating to ISO 15189 standards, while software used to analyse and interpret metagenomic data is developed under an ISO 13485-certified quality management system.

Limitations and future directions

Transparency about limitations is essential for the responsible interpretation of microbiome results.

The metagenomic microbiome component of Microba GI Navigator is for research use only and is not a diagnostic test. Results should be interpreted by qualified practitioners alongside the patient's clinical history, symptoms and other relevant findings. They are not intended to diagnose, treat or prevent disease. The clinically validated pathogen panel and gastrointestinal markers may be used within their defined intended purposes.

Shotgun metagenomics measures microbial DNA in a stool sample. It provides information about microbial composition and the genetic capacity of the community to perform particular functions, but does not directly measure gene expression, metabolite production, host exposure or clinical effect. Stool also represents one sampled compartment of the gastrointestinal microbial community and may not reflect microbes associated with other intestinal locations.

Like all sequencing-based microbiome tests, the metagenomic profile is compositional. It measures the relative proportions of microbial species rather than their absolute quantities, meaning that a change in one organism can influence the apparent relative abundance of others.

The scientific framework is designed to evolve as the evidence develops. Microbial markers are generally selected on the basis of mechanistic plausibility, reproducible human evidence and validation in Microba's internal dataset, with a small number of clearly disclosed exceptions. Associations do not necessarily establish causation, and the clinical relevance of a finding depends on the wider microbial and patient context. Microba continues to review and refine the test as microbiome science advances.

Conclusion

Microba GI Navigator represents a considered step towards more integrated gut health testing. By bringing together a CE-marked pathogen panel, gastrointestinal markers measured using CE-marked assays, high-resolution metagenomic profiling and structured patient information—and integrating these data within a single report — it provides a more comprehensive view than any one layer can provide alone.

The approach is designed to support robust and transparent interpretation: an evidence-gated framework that prioritises well-supported markers, considered logic that evaluates all markers within an Interpretation, evidence-graded Suggested Actions linked to their supporting studies, and comparison with a healthy group processed using the same workflow.

The metagenomic microbiome component is provided for research use and is intended to add information for a healthcare practitioner to consider alongside the person's history, symptoms and other clinical findings. It is not intended to replace clinical judgement. As microbiome science advances, Microba is committed to continually reviewing the evidence and responsibly incorporating well-supported advances into its testing and interpretation framework.

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