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MEDICAL POLICY – 2.04.26

Fecal Analysis in the Diagnosis of Intestinal Dysbiosis

BCBSA Ref. Policy:	2.04.26	
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Replaces:	N/A	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Intestinal dysbiosis is a condition that occurs when the microorganisms in the digestive tract are out of balance. This condition is believed to cause diseases of the digestive tract, including poor nutrient absorption, overgrowth of certain bacteria, and irritable bowel syndrome (IBS). Symptoms of these digestive problems are similar and may include: abdominal pain, excess gas, bloating, and changes in bowel movements (constipation or diarrhea, or both). One method of diagnosing digestive disorders is by testing a fecal sample. Using fecal analysis to diagnose intestinal dysbiosis, IBS, malabsorption, or small intestinal overgrowth of bacteria is unproven (investigational). More studies are needed to see if this testing improves health outcomes.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Test	Investigational
Examples: (this list may not be all inclusive) • **GI effects Comprehensive Stool Profile (Genova)** • **Comprehensive Digestive Stool Analysis 2.0 (Genova)**	**Fecal analysis of the following components is considered investigational as a diagnostic test for the evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal overgrowth of bacteria:** • Cholesterol • Chymotrypsin • Fecal secretory immunoglobulin A • Identification and quantitation of fecal yeast (including Candida albicans, Candida tropicalis, Rhodotorula, and Geotrichum) • Iso-butyrate, iso-valerate, and n-valerate • Levels of Lactobacilli, bifidobacteria, and Escherichiacoli and other "potential pathogens," including Aeromonas, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Staphylococcus aureus, and Vibrio • Long-chain fatty acids • Meat and vegetable fibers • N-butyrate • pH • Short-chain fatty acid distribution (adequate amount and proportions of the different short-chain fatty acids reflect the basic status of intestinal metabolism) • Total short-chain fatty acids • Triglycerides • β -glucuronidase

Coding

The following CPT codes may be used to identify individual components of fecal analysis

Code	Description
CPT	
82239	Bile acids; total

Code	Description
82271	Blood, occult, by peroxidase activity (e.g., guaiac), qualitative; other sources
82272	Blood, occult, by peroxidase activity (e.g., guaiac), qualitative, feces, 1-3 simultaneous determinations, performed for other than colorectal neoplasm screening
82274	Blood, occult, by fecal hemoglobin determination by immunoassay, qualitative, feces, 1-3 simultaneous determinations
82542	Column chromatography, includes mass spectrometry, if performed (e.g., HPLC, LC, LC/MS, LC/MS-MS, GC, GC/MS-MS, GC/MS, HPLC/MS), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
82656	Elastase, pancreatic (EL-1), fecal, qualitative or semi-quantitative
82710	Fat or lipids, feces; quantitative
82715	Fat differential, feces, quantitative
82725	Fatty acids, nonesterified
82784	Gammaglobulin (immunoglobulin); IgA, IgD, IgG, IgM, each
83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
83630	Lactoferrin, fecal; qualitative
83986	pH; body fluid, not otherwise specified
83993	Calprotectin, fecal
84311	Spectrophotometry, analyte not elsewhere specified
87045	Culture, bacterial; stool, aerobic, with isolation and preliminary examination (e.g., KIA, LIA), Salmonella and Shigella species
87046	Culture, bacterial; stool, aerobic, additional pathogens, isolation and presumptive identification of isolates, each plate
87075	Culture, bacterial; any source, except blood, anaerobic with isolation and presumptive identification of isolates
87102	Culture, fungi (mold or yeast) isolation, with presumptive identification of isolates; other source (except blood)
87177	Ova and parasites, direct smears, concentration and identification
87209	Smear, primary source with interpretation; complex special stain (e.g., trichrome, iron hemotoxylin) for ova and parasites
87324	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence

Code	Description
	immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Clostridium difficile toxin(s)
87427	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Shiga-like toxin
87328	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; cryptosporidium
87329	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; giardia
87336	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Entamoeba histolytica dispar group
87338	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Helicobacter pylori, stool
87449	Infectious agent antigen detection by immunoassay technique, (e.g., enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; not otherwise specified, each organism
87505	Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (e.g., Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets
87798	Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
89160	Meat fibers, feces

Related Information

Benefit Application

Due to the nonspecific nature of the Current Procedural Terminology (CPT) codes used to identify different components of fecal analysis, identification of these claims may require identification of those laboratories that specialize in the analysis for the evaluation of intestinal dysbiosis. Because there are a limited number of laboratories that provide this type of fecal analysis, these services may be provided by out-of-network providers. Also, a review of these services may be approached through a retrospective review looking for specific patterns of testing.

Evidence Review

Description

Intestinal dysbiosis may be defined as a state of disordered microbial ecology that is believed to cause disease. Laboratory analysis of fecal samples is proposed as a method of identifying individuals with intestinal dysbiosis and other gastrointestinal disorders.

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder that affects 10% to 20% of the general population in the US and worldwide. Symptoms include abdominal pain and/or bloating associated with disordered bowel habit (constipation, diarrhea, or both). Pathophysiology is poorly understood but may be related to chronic low-grade mucosal inflammation and disturbances in GI flora. Recommended treatments include dietary restriction and pharmacologic symptom control. As living microorganisms that promote health when administered to a host in therapeutic doses, probiotics are being investigated as a treatment for IBS. Several systematic reviews of randomized controlled trials have found evidence to support efficacy but results from recent randomized controlled trials have been mixed. This discrepancy may be due in part to the differential effects of different probiotic strains and doses.

Background

Fecal Markers of Dysbiosis

Laboratory analysis of both stool and urine has been investigated as markers of dysbiosis. Commercial laboratories may offer testing for comprehensive panels or individual components of various aspects of digestion, absorption, microbiology, and metabolic markers. Representative components of fecal dysbiosis testing are summarized in **Table 1**.

Table 1. Components of the Fecal Dysbiosis Marker Analysis

Markers	Analytes
Digestion	• Triglycerides • Chymotrypsin • Iso-butyrate, iso-valerate, and n-valerate • Meat and vegetable fibers
Absorption	• Long-chain fatty acids • Cholesterol • Total fecal fat • Total short-chain fatty acids
Microbiology	• Levels of Lactobacilli, bifidobacteria, and Escherichiacoli and other "potential pathogens," including Aeromonas, Bacillus cereus, Campylobacter, Citrobacter, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Staphylococcus aureus, and Vibrio • Identification and quantitation of fecal yeast (including Candida albicans, Candida tropicalis, Rhodotorula, and Geotrichum) (optional viral and/or parasitology components)
Metabolic	• N-butyrate (considered key energy source for colonic epithelial cells) • β-glucuronidase • pH • Short-chain fatty acid distribution (adequate amount and proportions of the different short-chain fatty acids reflect the basic status of intestinal metabolism)
Immunology	• Fecal secretory immunoglobulin A (as a measure of luminal immunologic function) • Calprotectin[a]

[a] Fecal calprotectin as a stand-alone test is not addressed in this policy.

Fecal Testing for Intestinal Dysbiosis

The gastrointestinal tract is colonized by a large number and a variety of microorganisms including bacteria, fungi, and archaea. The concept of intestinal dysbiosis rests on the assumption that abnormal patterns of intestinal flora, such as overgrowth of some commonly found microorganisms, have an impact on human health. Symptoms and conditions attributed to intestinal dysbiosis in addition to gastrointestinal disorders include chronic disorders (e.g., irritable bowel syndrome [IBS], inflammatory or autoimmune disorders, food allergy, atopic eczema, unexplained fatigue, arthritis, ankylosing spondylitis), malnutrition, or neuropsychiatric symptoms or neurodevelopmental conditions (e.g., autism), and breast and colon cancer.

The gastrointestinal tract symptoms attributed to intestinal dysbiosis (i.e., bloating, flatulence, diarrhea, constipation) overlap in part with either IBS or small intestinal bacterial overgrowth (SIBO) syndrome. The diagnosis of IBS is typically made clinically, based on a set of criteria referred to as the Rome criteria. The small intestine normally contains a limited number of bacteria, at least as compared with the large intestine. SIBO may occur due to altered motility (including blind loops), decreased acidity, exposure to antibiotics, or surgical resection of the small bowel. Symptoms include malabsorption, diarrhea, fatigue, and lethargy. The laboratory criterion standard for diagnosis consists of the culture of a jejunal fluid sample, but this requires invasive testing. Hydrogen breath tests, commonly used to evaluate lactose intolerance, have been adapted for use in diagnosing SIBO.

Summary of Evidence

For individuals with gastrointestinal conditions such as suspected intestinal dysbiosis, IBS, malabsorption, or SIBO who receive fecal analysis testing, the evidence includes several cohort and case-control studies comparing fecal microbiota in individuals who had a known disease with healthy controls. Relevant outcomes are test validity, symptoms, and functional outcomes. The available retrospective cohort studies on fecal analysis have suggested that some components of the fecal microbiome and inflammatory markers may differ across individuals with IBS subtypes. No studies were identified on the diagnostic accuracy of fecal analysis versus another diagnostic approach or that compared health outcomes in individuals managed with and without fecal analysis tests. No studies were identified that directly informed the use of fecal analysis in the evaluation of intestinal dysbiosis, malabsorption, or SIBO. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

No studies were identified that assessed the accuracy of the GI Effects fecal panel for diagnosing IBS or for documenting "gut health," a concept that may be difficult to define given large interindividual variability in gut flora. Evidence for the clinical validity and utility of the GI Effects Comprehensive Stool Profile is lacking. Because probiotics are not currently a standard treatment of IBS, the impact of test results on disease management is uncertain; i.e., a chain of evidence for clinical utility of the test cannot be established.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in **Table 2**.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02839317	Comparison of MicroBiota Between Patients With Early and Late Crohn's Disease and Relationship With Different Genetic and Serological Profiles	300	May 2024
NCT05619055	Intestinal Dysbacteriosis in the Pathogenesis of Necrotizing Enterocolitis	30	Mar 2025

NCT: National Clinical Trial Identifier

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strengths of evidence ratios, and include a description of management of conflict of interest.

American Gastroenterological Association

The American Gastroenterological Association (AGA) published clinical practice guidelines (2019) on laboratory evaluation of functional diarrhea and diarrhea-predominant IBS in adults.[9] Related to fecal analysis, the AGA suggests the use of fecal calprotectin or fecal lactoferrin to screen for IBS in individuals presenting with chronic diarrhea (conditional recommendation; low-quality evidence).

In 2020, the AGA published a clinical practice update on SIBO.[10] On the topic of fecal analysis, the guideline states, "there is insufficient evidence to support the use of inflammatory markers, such as fecal calprotectin to detect SIBO." No other fecal markers are explicitly mentioned.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the US Food and Drug Administration has chosen not to require any regulatory review of comprehensive testing for fecal dysbiosis.

Some US commercially available fecal dysbiosis tests are listed below in **Table 3**.

Table 3. Commercially Available Fecal Dysbiosis Tests by CLIA Certified Laboratories

Device	Manufacturer	Indications
GI Effects	Genova Diagnostics	Assessment of complete gut health, assessing the root cause of many GI complaints; includes the utilization of stool profiles

CLIA: Clinical Laboratory Improvement Amendments

References

1. Emmanuel A, Landis D, Peucker M, et al. Faecal biomarker patterns in patients with symptoms of irritable bowel syndrome. Frontline Gastroenterol. Oct 2016; 7(4): 275-282. PMID 27761231
2. Genova Diagnostics. 2024; **https://www.gdx.net/tests/prep/gi-stool-profiles**. Accessed January 14, 2025.
3. Goepp J, Fowler E, McBride T, et al. Frequency of abnormal fecal biomarkers in irritable bowel syndrome. Glob Adv Health Med. May 2014; 3(3): 9-15. PMID 24891989
4. Jeffery IB, Das A, O'Herlihy E, et al. Differences in Fecal Microbiomes and Metabolomes of People With vs Without Irritable Bowel Syndrome and Bile Acid Malabsorption. Gastroenterology. Mar 2020; 158(4): 1016-1028.e8. PMID 31843589
5. Andoh A, Kuzuoka H, Tsujikawa T, et al. Multicenter analysis of fecal microbiota profiles in Japanese patients with Crohn's disease. J Gastroenterol. Dec 2012; 47(12): 1298-307. PMID 22576027
6. Sobhani I, Tap J, Roudot-Thoraval F, et al. Microbial dysbiosis in colorectal cancer (CRC) patients. PLoS One. Jan 27 2011; 6(1): e16393. PMID 21297998
7. Joossens M, Huys G, Cnockaert M, et al. Dysbiosis of the faecal microbiota in patients with Crohn's disease and their unaffected relatives. Gut. May 2011; 60(5): 631-7. PMID 21209126
8. Langhorst J, Elsenbruch S, Koelzer J, et al. Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel diseases: performance of fecal lactoferrin, calprotectin, and PMN-elastase, CRP, and clinical indices. Am J Gastroenterol. Jan 2008; 103(1): 162-9. PMID 17916108
9. Smalley W, Falck-Ytter C, Carrasco-Labra A, et al. AGA Clinical Practice Guidelines on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable Bowel Syndrome in Adults (IBS-D). Gastroenterology. Sep 2019; 157(3): 851-854. PMID 31302098
10. Quigley EMM, Murray JA, Pimentel M. AGA Clinical Practice Update on Small Intestinal Bacterial Overgrowth: Expert Review. Gastroenterology. Oct 2020; 159(4): 1526-1532. PMID 32679220

History

Date	Comments
07/01/21	New policy, approved June 8, 2021. Fecal analysis in the diagnosis of intestinal dysbiosis and irritable bowel syndrome is considered investigational.
03/01/22	Annual Review, approved February 7, 2022. Policy updated with literature review through October 15, 2021; reference added. Policy statement unchanged.
02/01/23	Annual Review, approved January 23, 2023. Policy updated with literature review through October 26, 2022; references added. Policy statements unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.

Date	Comments
03/01/24	Annual Review, approved February 12, 2024. Policy updated with literature review through October 24, 2023; no references added. Policy statements unchanged.
03/01/25	Annual Review, approved February 10, 2025. Policy updated with literature review through October 22, 2024; Policy title changed from "Fecal Analysis in the Diagnosis of Intestinal Dysbiosis and Irritable Bowel Syndrome" to "Fecal Analysis in the Diagnosis of Intestinal Dysbiosis "No references added. Policy statements unchanged.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.