

Managing the Challenging IBS Patient - What's New?

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Disclosures

- ▶ I have received funding from Falk Pharma, Microba, Norgine, Nutricia, Chugai for speaking engagements

Irritable bowel syndrome

- ▶ Irritable Bowel Syndrome (IBS) is a chronic gastrointestinal disorder characterized by recurring abdominal pain and altered bowel habits, such as diarrhoea, constipation, or both, without any visible signs of damage or disease in the digestive tract

1 Rome IV diagnostic criteria for functional bowel disorders^{26,27}

Diagnosis	Criteria*
IBS	Recurrent abdominal pain; ≥ 1 day per week in the past 3 months Associated with two or more of the following criteria: - related to defecation; - associated with a change in frequency of stool; and - associated with a change in form (appearance) of stool
Functional abdominal bloating or distension	Must include both of the following: - recurrent bloating or distention occurring on average, at least one day per week; the abdominal bloating or distention predominates over other symptoms;[†] and - there are insufficient criteria for a diagnosis of irritable bowel syndrome, functional constipation, functional diarrhoea or postprandial distress syndrome
Functional diarrhoea	Loose or watery stools, without predominant abdominal pain or bothersome bloating, occurring in > 25% of stools Patients meeting criteria for diarrhoea-predominant IBS should be excluded
Functional constipation	Must include two or more of the following in > 25% of defecations: - straining; - lumpy or hard stools; - sensation of incomplete evacuation; - sensation of anorectal obstruction or blockage; - manual manoeuvres to facilitate evacuation (eg, digital evacuation or support of the pelvic floor); or - fewer than three spontaneous bowel movements per week Loose stools are rarely present without the use of laxatives Insufficient criteria for irritable bowel syndrome
Opioid-induced constipation	New, or worsening, symptoms of constipation when initiating, changing or increasing opioid therapy that must include two or more of the following in > 25% of defecations: - straining; - lumpy or hard stools; - sensation of incomplete evacuation; - sensation of anorectal obstruction or blockage; - manual manoeuvres to facilitate evacuation (eg, digital evacuation or support of the pelvic floor); or - fewer than three spontaneous bowel movements per week Loose stools are rarely present without the use of laxatives
Unspecified bowel disorders	Bowel symptoms not attributable to an organic aetiology which do not meet criteria for IBS or functional constipation, diarrhoea or abdominal bloating or distension disorders
Centrally mediated abdominal pain syndrome [‡]	Must include all of the following: - continuous or nearly continuous abdominal pain; - no or only occasional relationship of pain with physiological events (eg, eating, defecation, or menses);[§] - pain limits some aspect of daily functioning;[¶] - pain is not feigned; and - pain is not explained by another structural or functional gastrointestinal disorder or other medical condition

IBS – irritable bowel syndrome. * Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis. † Mild pain related to bloating may be present as well as minor bowel movement abnormalities. ‡ Centrally mediated abdominal pain syndrome is typically associated with psychiatric comorbidity, but there is no specific profile that can be used for diagnosis. § Some degree of gastrointestinal dysfunction may be present. ¶ Daily function could include impairments in work, intimacy, social or leisure, family life and caregiving for self or others. ♦

Linedale, E. C., & Andrews, J. M. (2017). Diagnosis and management of irritable bowel syndrome: a guide for the generalist. *The Medical journal of Australia*, 207(7), 309–315.

Traditional management of IBD paradigm

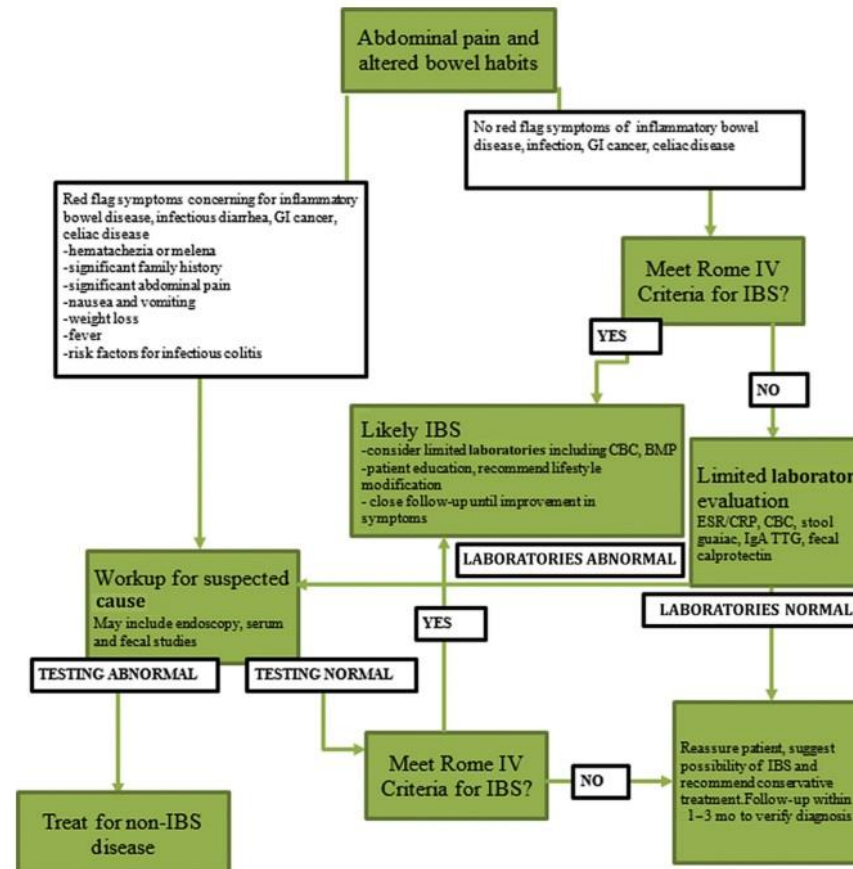


Fig. 1. Algorithm for evaluation of suspected IBS. CBC, complete blood count; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Ig, immunoglobulin.

Defrees, ND and Bailey, J. Irritable Bowel Syndrome. *Primary Care: Clinics in Office Practice*, 2017. Volume 44, Issue 4, 655 - 671

Is IBS an organic condition?

- ▶ Typically defined as a diagnosis of exclusion i.e. no organic pathology but is likely to be incorrect
- ▶ Viewed as a “functional” gut disorder



Is IBS an unexplained gut-
brain disorder?

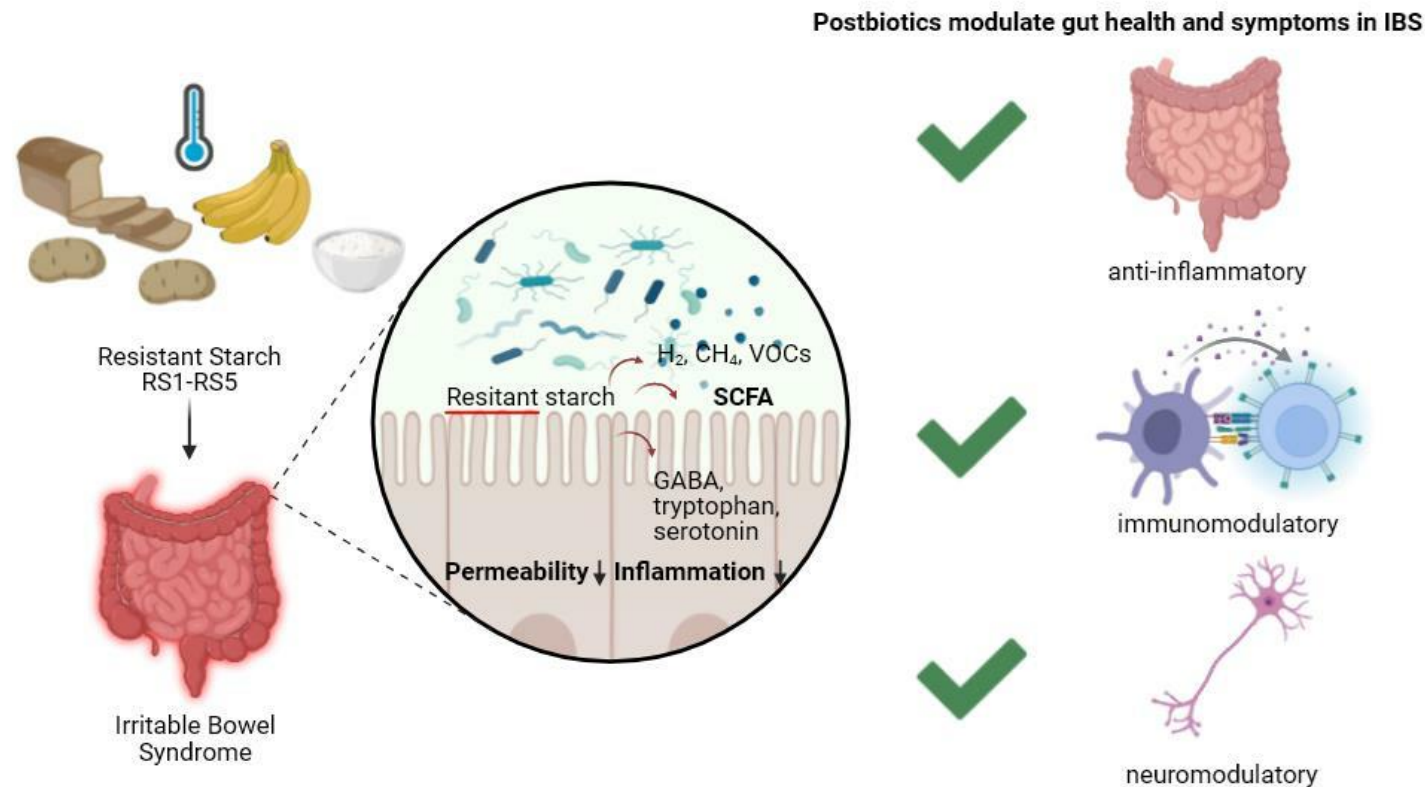
Microinflammation

- ▶ IBS subjects have increased mast cells, lymphocytes, TNF alpha, IL-6, LIF, NGF, IL-1beta in gut mucosa compared with controls, suggestive of inflammation
- ▶ Additionally, gut mucosa cells that have increased inflammation are more permeable, leading to fluid leakage into the gut

Vanner SJ, et al. Fundamentals of neurogastroenterology: basic science. *Gastroenterology* 2016;150:1280–91.

Uranga JA, Martínez V, Abalo R. Mast Cell Regulation and Irritable Bowel Syndrome: Effects of Food Components with Potential Nutraceutical Use. *Molecules*. 2020; 25(18):4314.

Modulating inflammation



Kovacs, E., Szabo, K., Varvara, R.-A., Uifălean, A., Cozma, A., Vulturar, R., Sitar-Taut, A. V., Gabbianelli, R., Myhrstad, M. C. W., Telle-Hansen, V. H., Orășan, O. H., Fodor, A., Suharoschi, R., & Hegheș, S.-C. (2025). Resistant Starch and Microbiota-Derived Secondary Metabolites: A Focus on Postbiotic Pathways in Gut Health and Irritable Bowel Syndrome. *International Journal of Molecular Sciences*, 26(16), 7753.

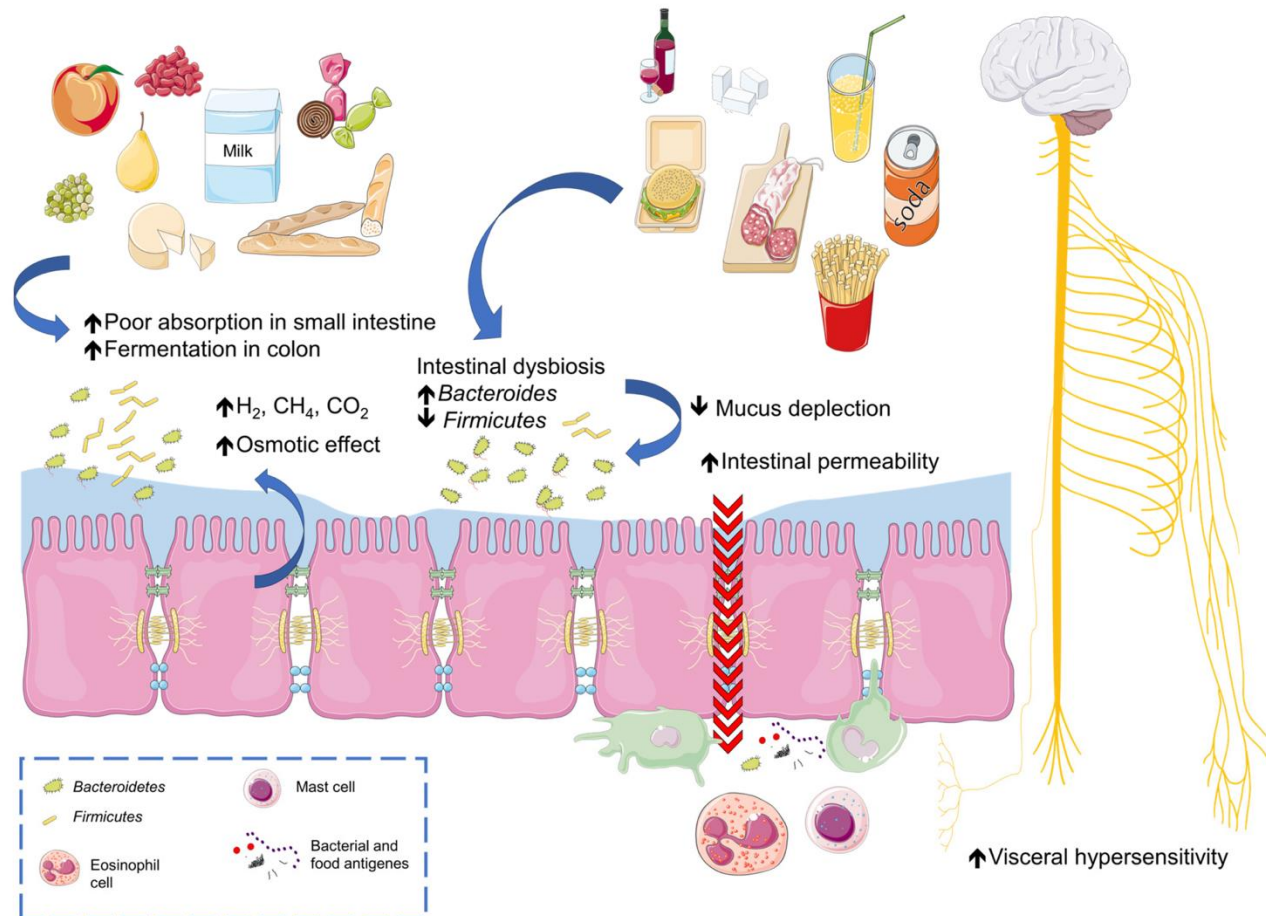
Food sensitivity

- ▶ The FODMAP diet has shown clear benefit in controlling IBS symptoms. Additionally, removal of fructose, fructans, gliadin, sorbitol, and lactose from the diet has been beneficial for some subjects
- ▶ Subjects who are biopsy-negative for coeliac disease but have elevated immunoglobulin (Ig)G antigliadin antibodies and are HLA-DQ2-positive (associated with development of celiac disease) showed improvement in IBS symptoms with a gluten-free diet

de Roest RH, Dobbs BR, Chapman BA, et al. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. *Int J Clin Pract* 2013;67(9):895–903.

Vazquez-Roque MI, Camilleri M, Smyrk T, et al. A controlled trial of gluten-free diet in patients with irritable bowel syndrome-diarrhea: effects on bowel frequency and intestinal function. *Gastroenterology* 2013;144(5):903–11.

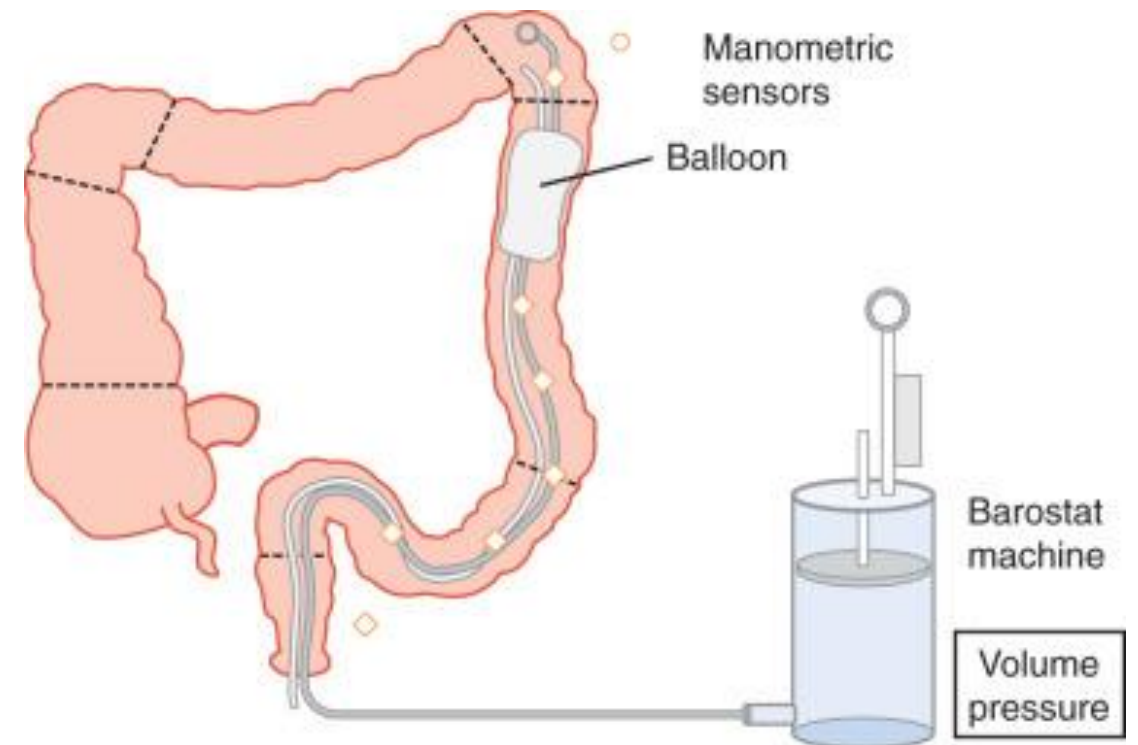
FODMAPS and processed foods



Pasta A, Formisano E, Calabrese F, Plaz Torres MC, Bodini G, Marabotto E, Pisciotta L, Giannini EG, Furnari M. Food Intolerances, Food Allergies and IBS: Lights and Shadows. *Nutrients*. 2024; 16(2):265.

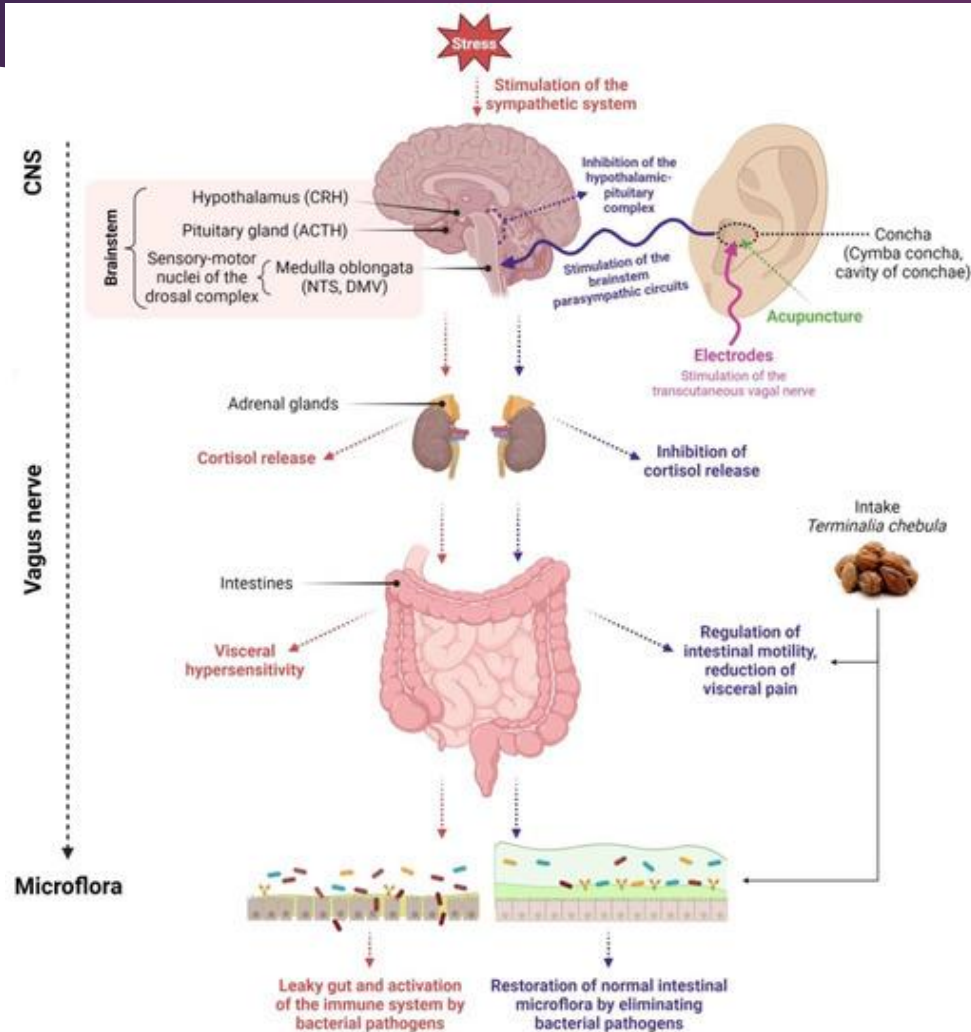
Visceral hypersensitivity

- Subjects had a colonic balloon inflated to 3.4 cm in their large intestines. 6% of controls versus 55% of IBS subjects had pain with the procedure



Mayer EA. Irritable Bowel Syndrome. *N Engl J Med* 2008;358(16):1692–9.

Visceral hypersensitivity – potential treatment pathways

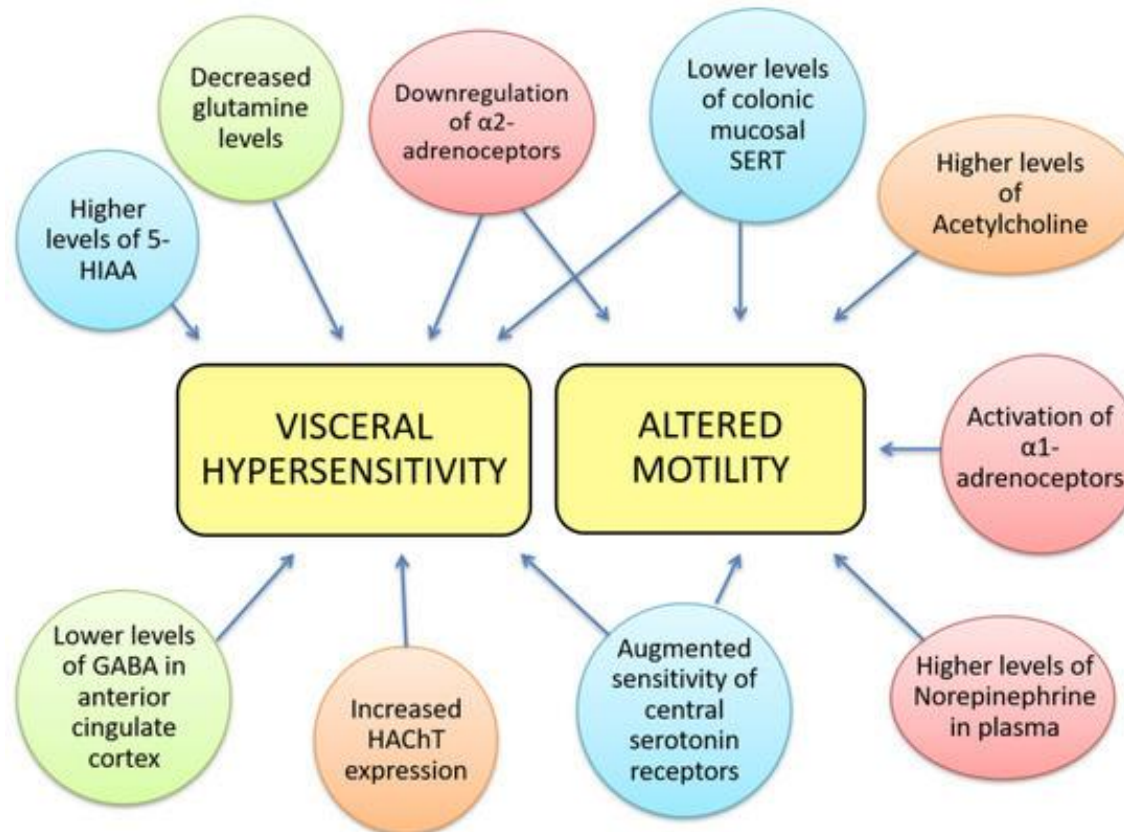


Dudzińska, E., Grabrucker, A. M., Kwiatkowski, P., Sitarz, R., & Sienkiewicz, M. (2023). The Importance of Visceral Hypersensitivity in Irritable Bowel Syndrome—Plant Metabolites in IBS Treatment. *Pharmaceuticals*, 16(10), 1405.

Dysregulation of gut motility

- ▶ Subjects with IBS received a lipid perfusion (to simulate food) and air infusion into the duodenum at a rate of 12 mL/min.
- ▶ Subjects with IBS had increased gas retention in their intestines, complained to controls, and had increased transit times of the gas from duodenum to rectum (IBS subjects had 500 cc of air in intestine vs 22 cc retention in healthy controls)

Altered gut motility



Gros M, Gros B, Mesonero JE, Latorre E. Neurotransmitter Dysfunction in Irritable Bowel Syndrome: Emerging Approaches for Management. *Journal of Clinical Medicine*. 2021; 10(15):3429.

Neurotransmitter	Drug	Receptor	Effect	Pharmacological Use
SEROTONIN	CISAPRIDE	5-HT ₄ agonist and 5-HT ₃ antagonist	Prokinetic	Use for the treatment of Gastroesophageal reflux, functional dyspepsia and gastroparesis
	TEGASEROD	5-HT ₄ agonist	Prokinetic	Use for the treatment of IBS-C
	VELUSETRAG	5-HT ₄ agonist	Prokinetic	Clinical trials have to be done for its approval
	PRUCALOPRIDE	5-HT ₄ agonist	Prokinetic	Used for the treatment of IBS-C
	ALOSETRON	5-HT ₃ antagonist	Decreases GI motility	Approved in the USA for the treatment of IBS-D
	ONDASETRON	5-HT ₃ antagonist	Antiemetic, it reduces abdominal pain	Used as antiemetic
	RAMOSETRON	5-HT ₃ antagonist	Antiemetic	Used as antiemetic in Asia
	SUMATRIPTAN	5-HT _{1B/D} agonist	Delays gastric emptying	Many side effects to be approved
GABA	PREGABALIN	GABA analogous	Analgesic and anxiolytic	Use for the treatment of neuropathic pain
	GABAPENTIN	GABA analogous	Analgesic and anxiolytic	Use for the treatment of neuropathic pain
	CGP7930	GABA-B receptor agonist	Reduces visceral pain	Clinical trials have to be done for its approval
	BACLOFEN	GABA-B receptor agonist	Reduces visceromotor response	Use for the treatment of spasticity and muscle spasms
GLUTAMATE	RILUZOLE	Glutamate reuptake activator	Improves visceral hypersensitivity	Use for the treatment of Amyotrophic Lateral Sclerosis
	MPEP	mGluR5 antagonist	Reduces allodynia	Clinical trials have to be done for its approval
	AMN082	mGluR7 agonist	Reduces visceral hypersensitivity induced by colorectal distension	Clinical trials have to be done for its approval
ACETYLCHOLINE	ZAMIFENACIN	Partially selected muscarinic M3 antagonist	Decreases colonic contractility	Clinical trials have to be done for its approval
	TOLTERODINE	Non-selective muscarinic antagonist	Induces constipation	Use for the treatment of overactive bladder syndrome
	MEBEVERINE	Muscarinic antagonist	Improves bowel transit and abdominal pain	Approved in Australia for IBS treatment

Gros M, Gros B, Mesonero JE, Latorre E. Neurotransmitter Dysfunction in Irritable Bowel Syndrome: Emerging Approaches for Management. *Journal of Clinical Medicine*. 2021; 10(15):3429.

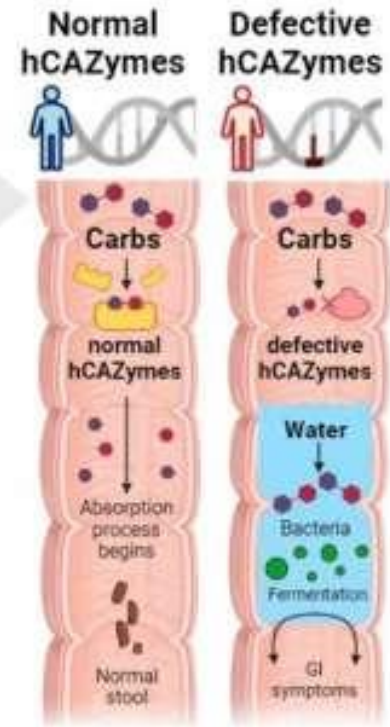
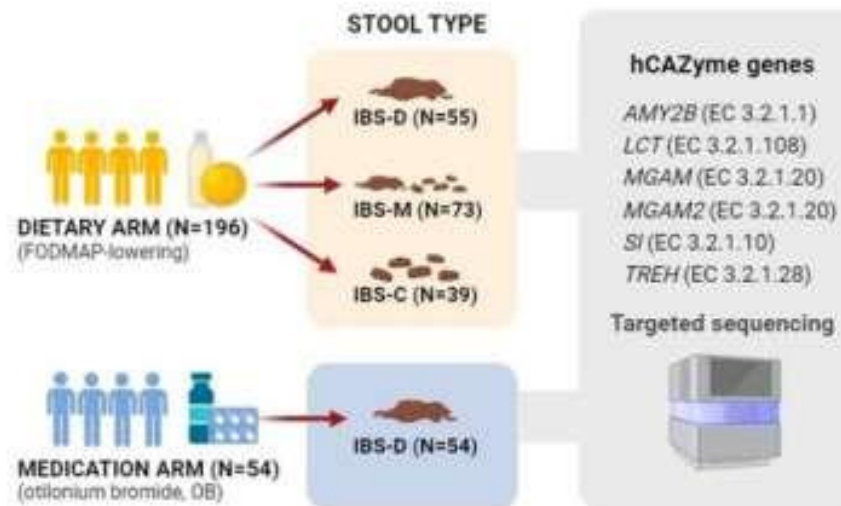
Genetics

- ▶ IBS seems to have some familial trends, though twin studies failed to show a correlation, suggesting more of an environmental or social-learning component

Mohammed I, Cherkas LF, Riley SA, et al. Genetic influences in irritable bowel syndrome: a twin study. *Am J Gastroenterol* 2005;100(6):1340.

But genetics can play a role in dietary management in IBS

Functional variation in human CAZyme genes in relation to the efficacy of a carbohydrate-restricted diet in IBS patients



Response to the carb-restricted diet



Clinical Gastroenterology and Hepatology

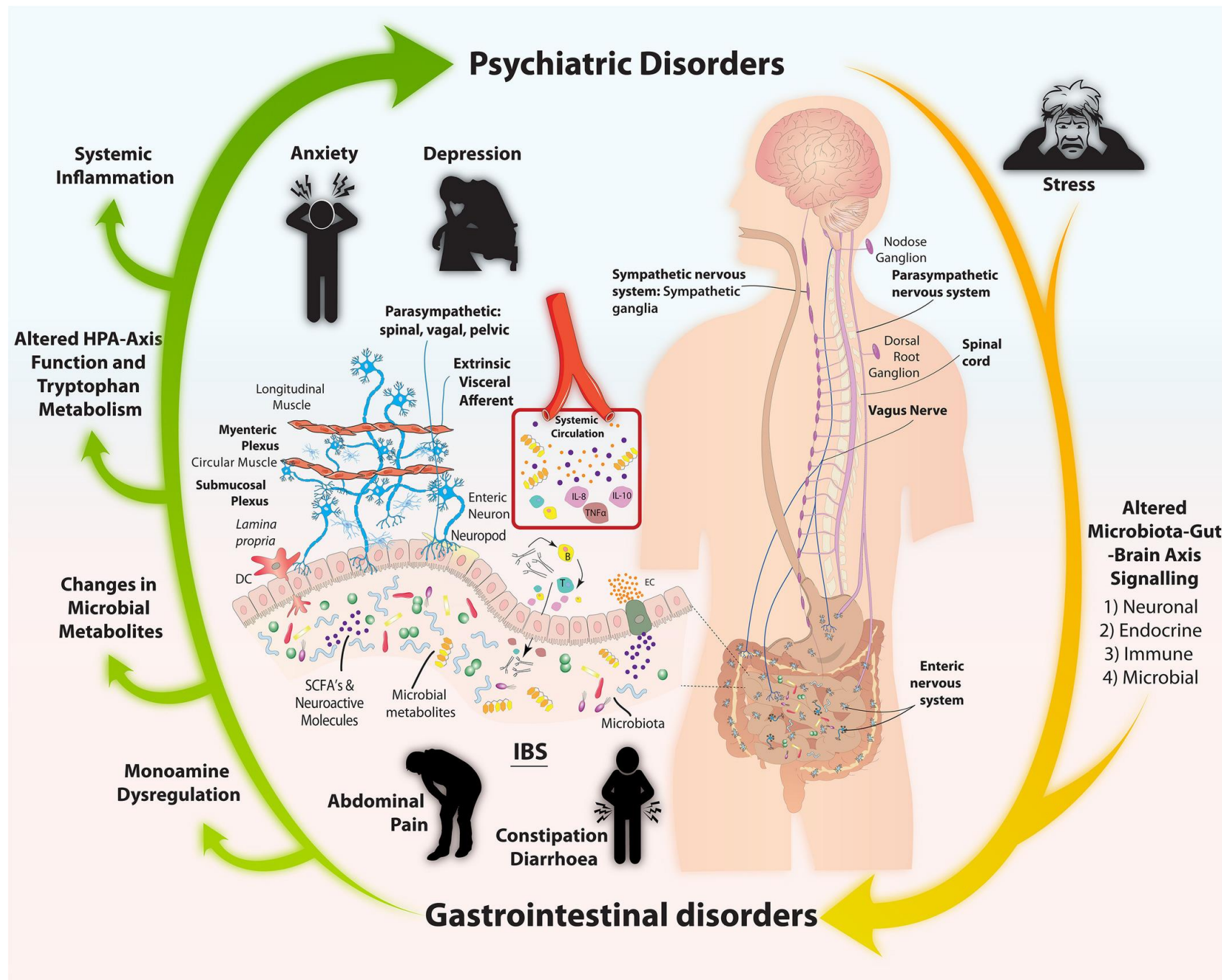
Zamfir-Taranu A, Löscher BS, Carbone F, Hoter A, Esteban Blanco C, Bozzarelli I, Torices L, Routhiaux K, Van den Houte K, Bonfiglio F, Mayr G, Corsetti M, Naim HY, Franke A, Tack J, D'Amato M. Functional Variation in Human CAZyme Genes in Relation to the Efficacy of a Carbohydrate-Restricted Diet in IBS Patients. Clin Gastroenterol Hepatol. 2025 Jun;23(7):1228-1237.e10

Mind-gut-brain axis

- ▶ Subjects with IBS take their children to the doctor more frequently than non-IBS counterparts
- ▶ Subjects with increased traumatic life events (e.g. relationship break-ups, job loss) have increased IBS symptoms; those with good social support had lower incidence of symptoms
- ▶ Subjects with IBS had higher rates of mood disorders (30%), suicidal ideation (15%–30%), hopelessness, anxiety (30%–50%), and somatization

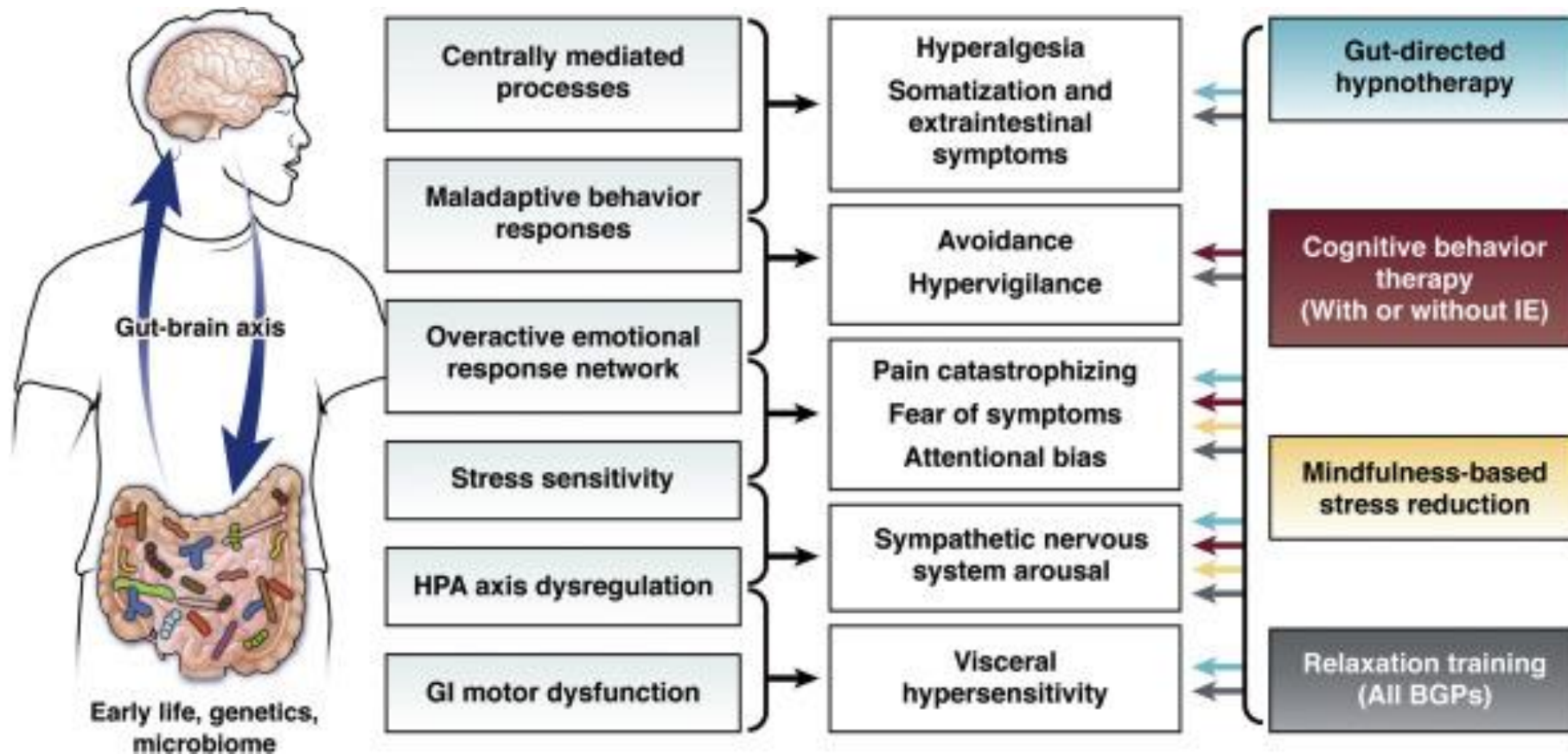
Van Oudenhove L, et al. Biopsychosocial aspects of functional gastrointestinal disorders: how central and environmental processes contribute to the development and expression of functional gastrointestinal disorders. *Gastroenterology* 2016;150:1355–67.

Wilkins T, Pepitone C, Alex B, et al. Treatment of irritable bowel syndrome in adults. *Am Fam Physician* 2012;86(5):419–26



Wilmes L, Collins JM, O'Riordan KJ, O'Mahony SM, Cryan JF, Clarke G. Of bowels, brain and behavior: A role for the gut microbiota in psychiatric comorbidities in irritable bowel syndrome. *Neurogastroenterol Motil.* 2021 Mar;33(3):e14095.

Behavioural therapy options and targets in IBS

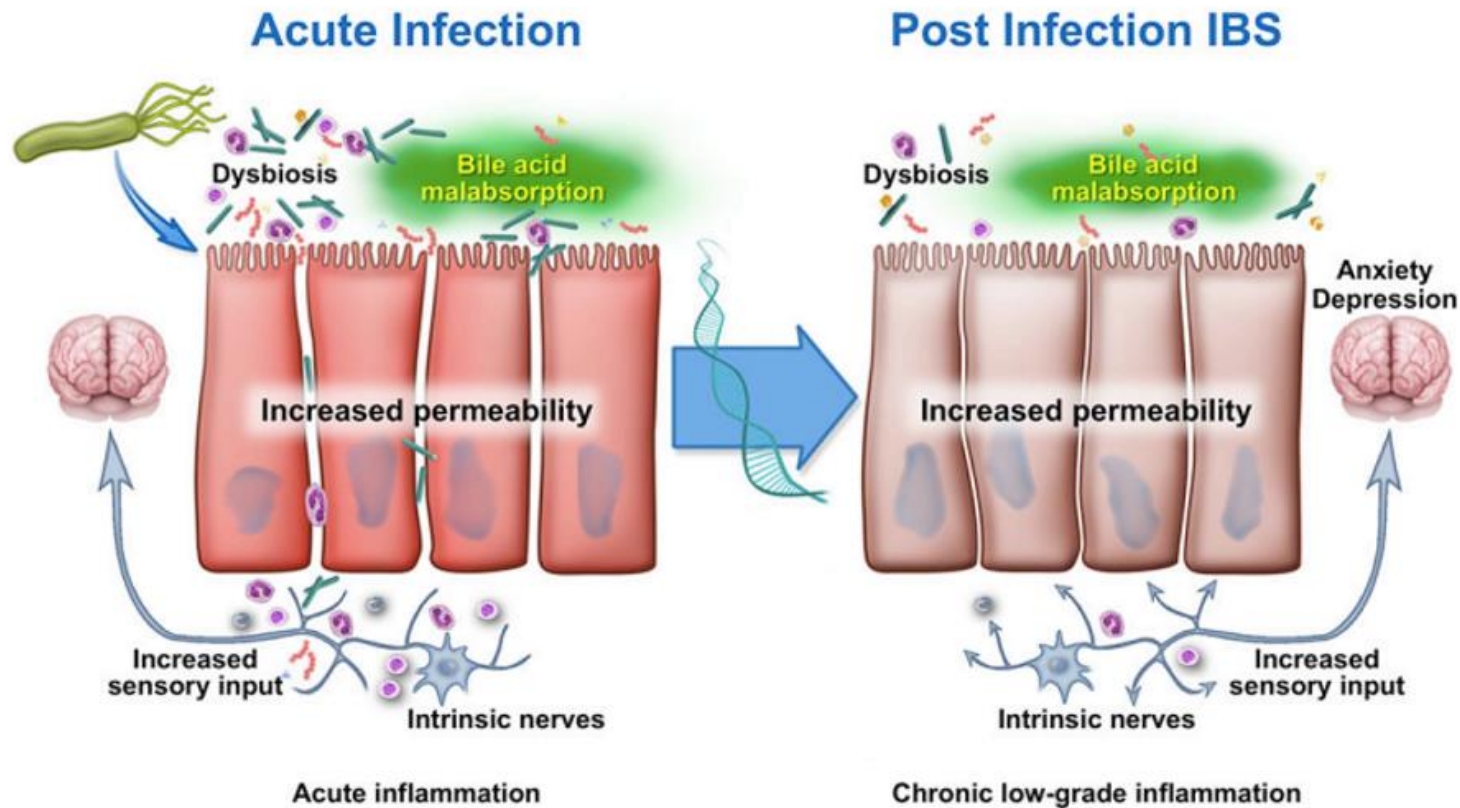


Chey WD, Keefer L, Whelan K, Gibson PR. Behavioral and Diet Therapies in Integrated Care for Patients With Irritable Bowel Syndrome. *Gastroenterology* . 2021 Jan;160(1):47-62.

Postinfectious

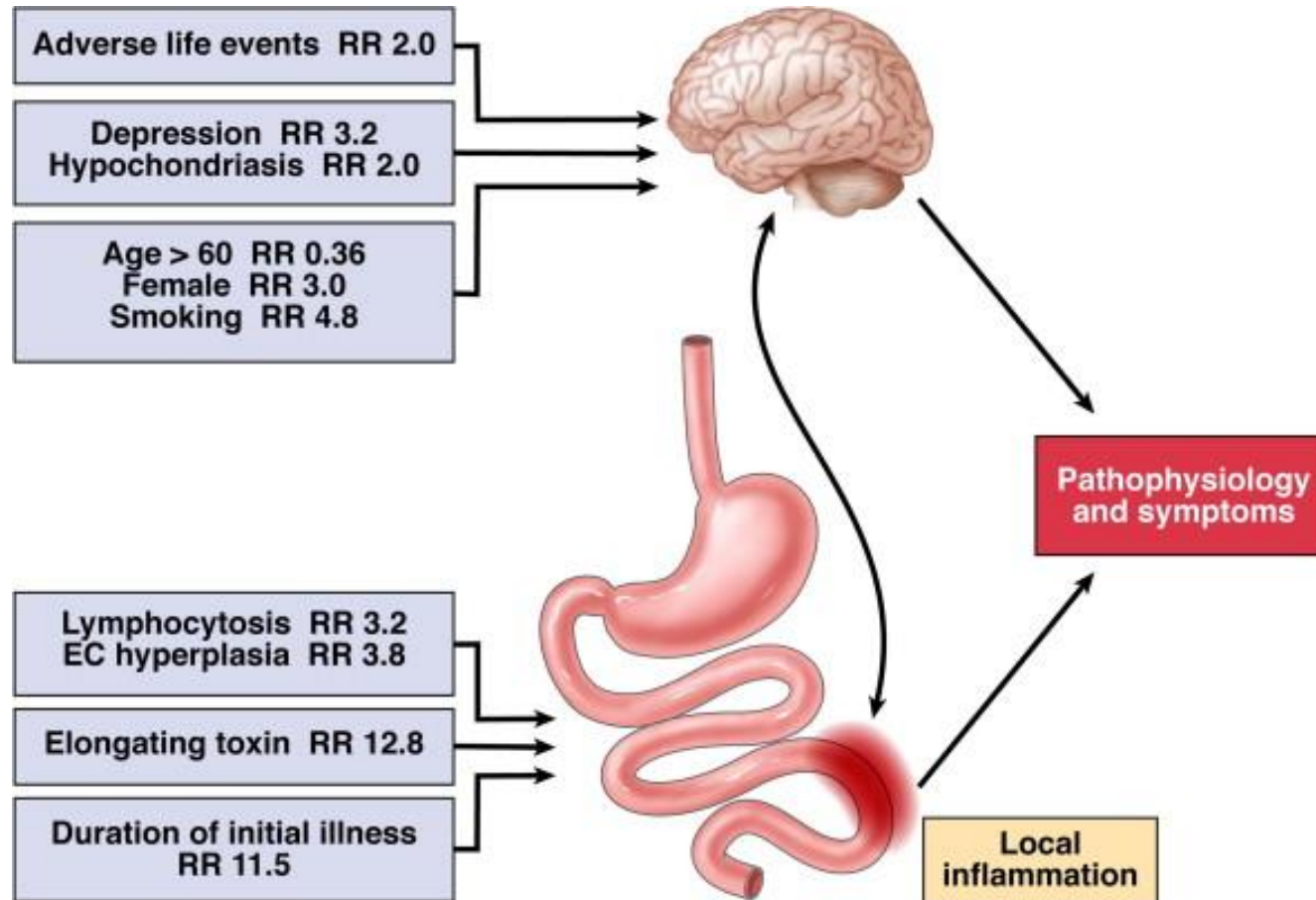
- ▶ A large cohort study showed a 6-fold increase in development of IBS after infection (bacterial, viral, helminth or protozoan)
- ▶ Risk factors included prolonged fever, prolonged infection, anxiety, depression, and younger age
- ▶ Possible causes include antibiotic usage, malabsorption (idiopathic bile acid absorption), and increased inflammation

Post-infectious IBS



<https://ibsguthealthclinic.co.uk/post-infectious-ibs-article/>

Post-infectious IBS risk factors

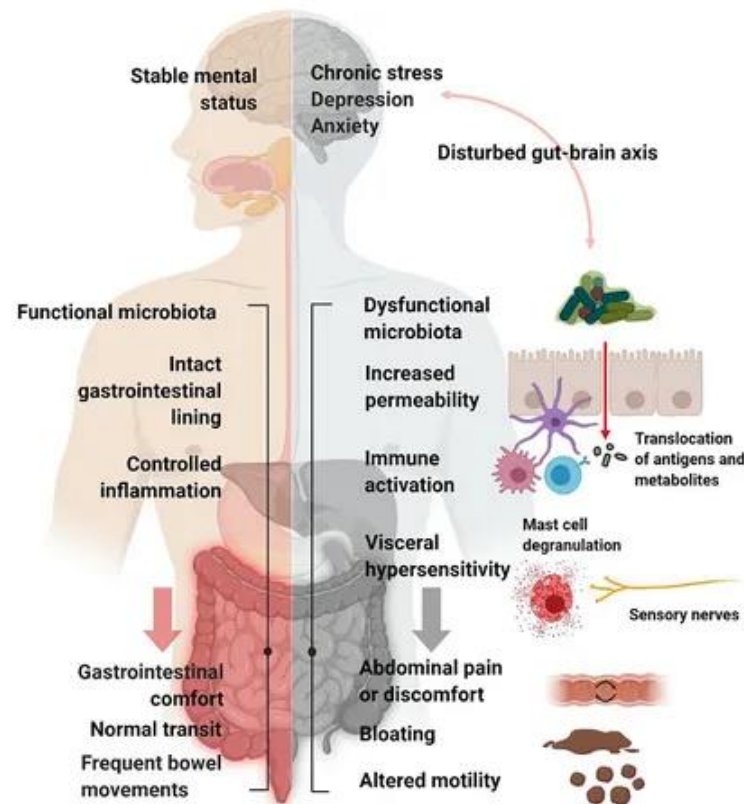


Spiller R, Garsed K.
Postinfectious irritable bowel syndrome.
Gastroenterology.
2009
May;136(6):1979-88.

Microbiome/dysbiosis

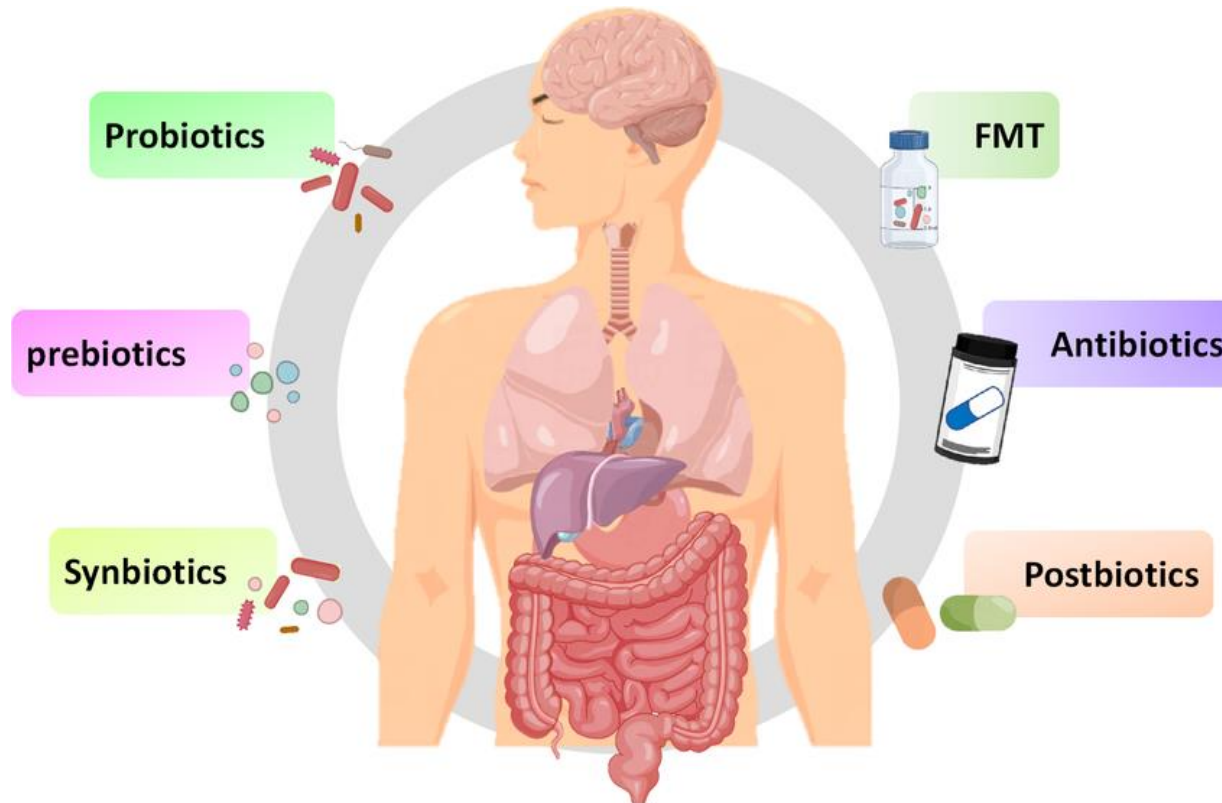
- ▶ Healthy controls have distinctly different flora than subjects with IBS, and manipulation of microbiomes with antibiotics and probiotics has been found beneficial in some studies
- ▶ Bacterial overgrowth (diagnosed with hydrogen breath tests) in some studies correlates with IBS symptoms. Improvements were observed after antibiotic treatment, though this was not demonstrated in all studies

Microbial pathogenesis of IBS



Carco C, Young W, Gearry RB, Talley NJ, McNabb WC and Roy NC (2020) Increasing Evidence That Irritable Bowel Syndrome and Functional Gastrointestinal Disorders Have a Microbial Pathogenesis. *Front. Cell. Infect. Microbiol.* 10:468.

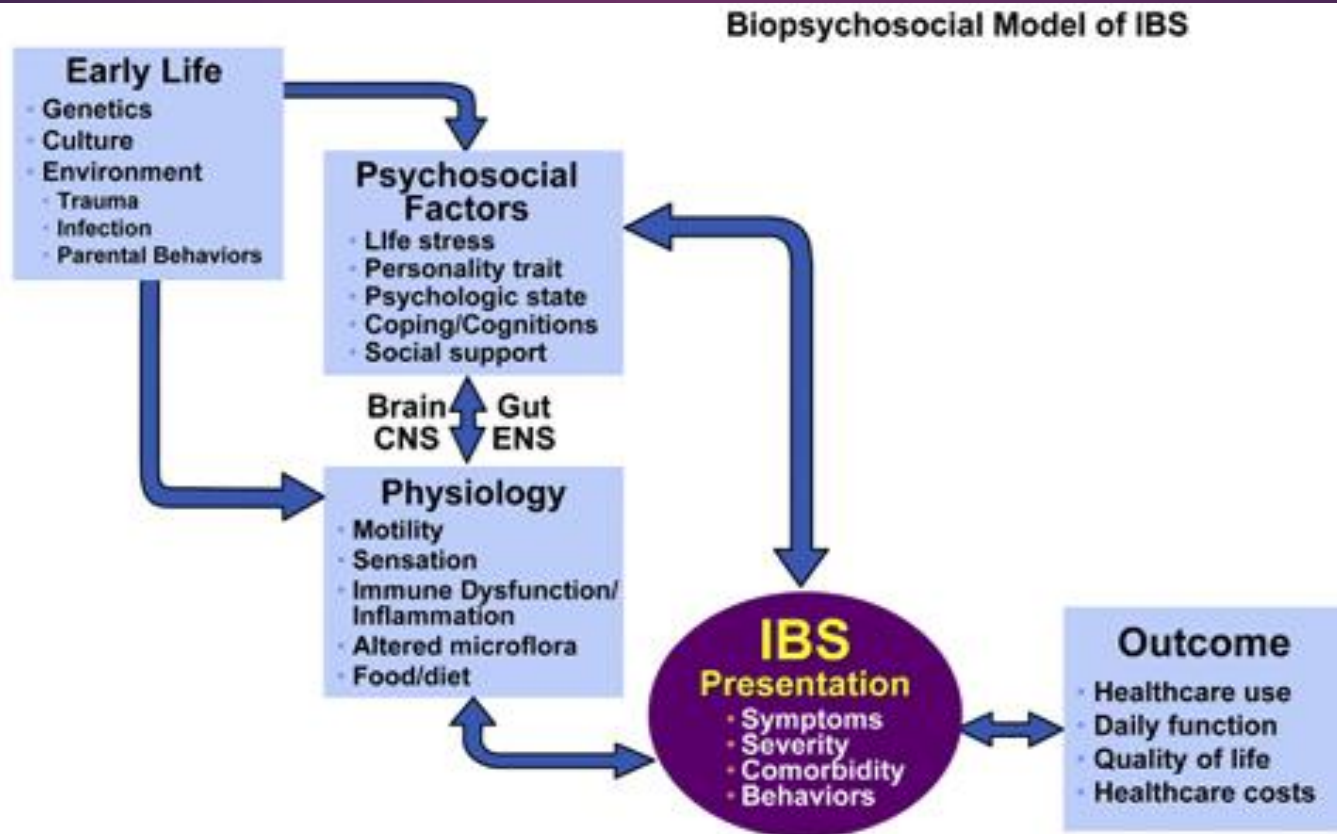
IBS microbial modulation



Yuan C, He Y, Xie K, Feng L, Gao S, Cai L. Review of microbiota gut brain axis and innate immunity in inflammatory and infective diseases. *Front Cell Infect Microbiol.* 2023 Oct 4;13:1282431

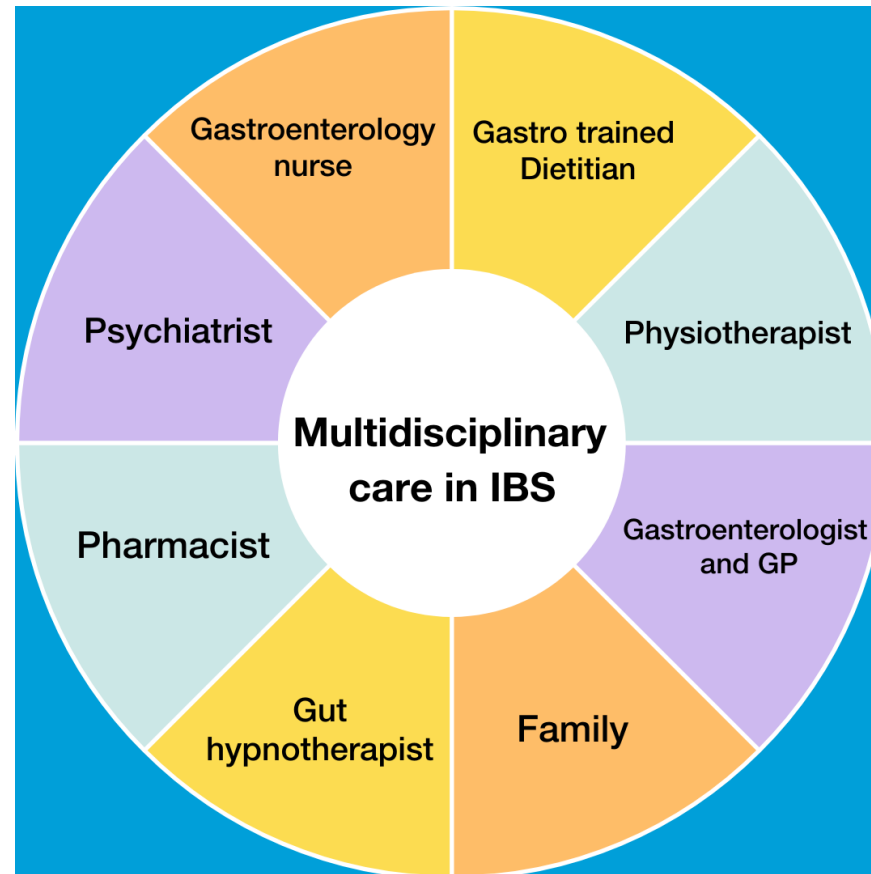
The challenging patient

Biopsychosocial model of IBS



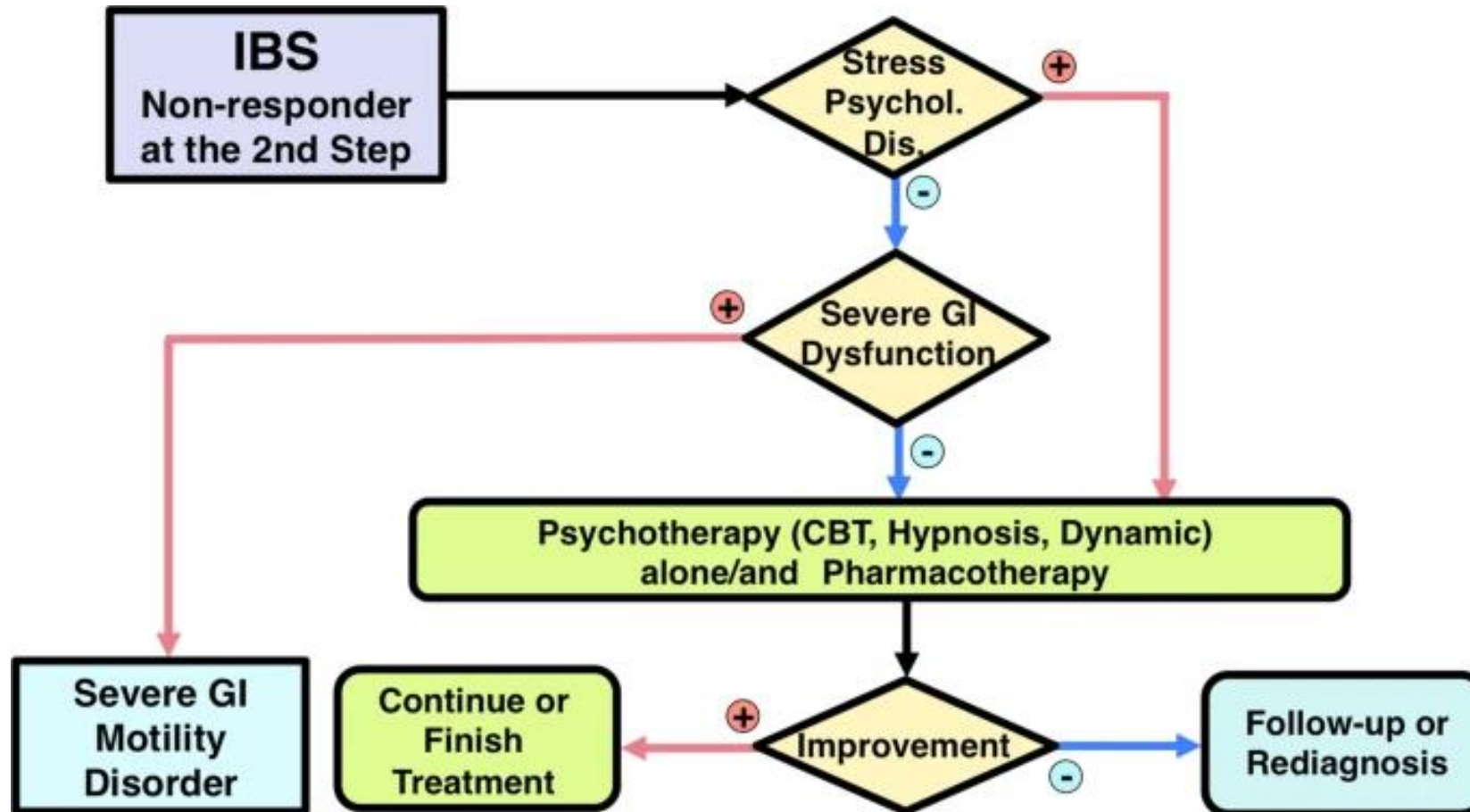
Drossman DA.
Functional
gastrointestinal
disorders: history,
pathophysiology,
clinical features
and Rome IV.
Gastroenterology
2016;150:1262–
1279.e2.

IBS and multidisciplinary care



https://www.monashfodmap.com/blog/ibs-and-multidisciplinary-care/?fbclid=IwZXh0bgNhZW0CMTAAAR3g4xaw5T2Dfwns0S2kWl8Wqip63R3NXeT4M_EGomyzrr-RV8LLn_w4PuA_aem_z70kcp2KjUk4cT_0q2-7hw

Current algorithm for refractory IBS



Fukudo, S. et al (2021). Evidence-based clinical practice guidelines for irritable bowel syndrome 2020. *Journal of gastroenterology*, 56(3), 193–217.

Some patients want a diagnostic workup

- ▶ With regards to IBS management patients expected reassurance and counselling from their doctor (mentioned by 47% and 30% of the patients, respectively), as well as pharmacotherapy (37%), **a proper diagnostic work-up** (38%) or specialist referral (39%).

Bijkerk CJ, de Wit NJ, Stalman WA, Knottnerus JA, Hoes AW, Muris JW. Irritable bowel syndrome in primary care: the patients' and doctors' views on symptoms, etiology and management. Can J Gastroenterol. 2003;17:363-368;

Patients' explanatory models for irritable bowel syndrome: symptoms and treatment more important than explaining aetiology [Get access >](#)

Rachel E Casiday, A P S Hungin, Charles S Cornford, Niek J de Wit, Mwenza T Blell

Family Practice, Volume 26, Issue 1, February 2009, Pages 40–47,

<https://doi.org/10.1093/fampra/cmn087>

Published: 14 November 2008 **Article history** ▼

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Abstract

Background. Irritable bowel syndrome (IBS) is a common condition associated with no certain organic cause, though diet and stress are widely implicated. The condition is frustrating for both sufferers and doctors, and there are problems in diagnosing and treating the condition. Eliciting explanatory models (EMs) is a useful tool for understanding how individuals relate to their illnesses and their expectations for treatment, particularly for illnesses with uncertain aetiology like IBS.

Objectives. To understand the EMs, experiences and expectations for management of patients with IBS.

Methods. Qualitative, semi-structured interviews were conducted with 51 primary care patients (31 in the UK, 20 in The Netherlands) meeting the Rome II diagnostic criteria for IBS.

Results. Although IBS often had a significant dampening effect on daily life, IBS patients made great efforts not to allow the condition to take over their lives. Triggers of symptoms were more important to patients than understanding the underlying aetiology of IBS. Diet and stress were both recognized as important triggers, but views about which foods were problematic and the extent to which stress was modifiable were inconsistent. Diagnosis and treatment were often a confusing and frustrating process, and patients often expected more diagnostic tests than they were offered before receiving a diagnosis of IBS. However, the often poor outcome of medical interventions does not, in general, appear to have a negative impact on the patient–doctor relationship.

Conclusions. Clinicians should be aware of the extensive impact of IBS on sufferers' daily life and the frustration that results from repeatedly trying treatments with little effect. Clearly explaining the guidelines for diagnosing IBS and the range of treatment options may help patients to make sense of the diagnostic and treatment processes. The personal EM should be addressed during the consultation with the IBS patient, ensuring that any successive medical interventions match with the patients' disease perception.

Casiday RE, Hungin AP, Cornford CS, de Wit NJ, Blell MT. Patients' explanatory models for irritable bowel syndrome: symptoms and treatment more important than explaining aetiology. *Fam Pract.* 2009;26:40-47.

Multidimensional clinical profile (MDCP)

MDCP Categories	Content	Comments	Examples
Category A: Categorical Rome Diagnosis	Diagnosis is based on the Rome IV criteria.	Symptom based but may include physiological criteria. Used for clinical trials but not sufficient for treatment.	IBS, functional dyspepsia, functional heartburn, functional constipation
Category B: Clinical modifier	Additional symptoms, subtypes, historical information, physical signs, laboratory or physiological studies into clinical subsets that would affect treatment planning.	Not necessarily based on evidence; follows clinical wisdom and provides for more specific treatment.	IBS-D, IBS-C, epigastric pain syndrome, postprandial distress syndrome
Category C: Impact on daily activities	Ask the patient: "Overall, how much do your symptoms currently interfere with life (work, school, social activities, self-care, concentration, and performance)?"	Quantifies the overall effect of illness perceptions, behaviors and daily functioning on treatment.	None, mild, moderate, or severe
Category D: Psychosocial modifiers	Psychosocial modifiers and comorbidities that influence patient's illness experience and may affect treatment	May be categorical (eg, DSM V diagnosis), dimensional (eg, HADS, or other scales), Rome Psychosocial red flags, or patient reports (eg, abuse) that is judged by the clinician to be clinically relevant	Anxiety, major depressive disorder, posttraumatic stress disorder, somatic symptom disorder
Category E: Physiological features and biomarkers	Laboratory or imaging studies that correlate with the physiology underlying the categorical Rome diagnosis and its subtype	Provides dimensionality for physiological or biochemical parameters of clinical relevance that enhances understanding of the diagnosis. Requires sufficient external evidence to be endorsed (eg, motility, radionuclide, biochemical). Has treatment implications (eg, degree of fecal incontinence)	Lactose tolerance test in a patient with IBS-D. Anorectal manometry and balloon expulsion consistent with dyssynergic defecation in a patient with IBS-C.

DGBI, disorder of gut-brain interaction; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; HAD, Hospital and Anxiety Depression Scale; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with predominant constipation; IBS-D, irritable bowel syndrome with predominant diarrhea; MDCP, multidimensional clinical profile.

Drossman DA, Tack J, Chang L, et al. Multidimensional clinical profile for disorders of gut-brain interaction. Raleigh, NC: Rome Foundation, 2021.



A challenging clinical case

WHAT WORKS FOR THE MASSES MAY NOT WORK FOR THE INDIVIDUAL

Ms Y

- ▶ 26 year old lady with a history of IBS diagnosed by her gastroenterologist 3 years ago
- ▶ Symptoms manifested shortly after a trip to Bali 3 years ago when she developed gastroenteritis; prior to that time was well
- ▶ Current symptoms of chronic nausea, postprandial fullness and bloating on a daily basis
- ▶ Main symptoms is that of generalised abdominal pain worsened after eating certain foods (no particular pattern)
- ▶ No vomiting
- ▶ Describes more constipation since onset of symptoms, harder stools, reduced frequency of bowel movements, often uses a laxative
- ▶ Partial relief of symptoms particularly bloating with defaecation
- ▶ No alarm symptoms such as weight loss, fever, blood in stools etc

Medical history

- ▶ Ehlers Danlos syndrome
- ▶ May-Thurner syndrome (compression left iliac vein by right iliac artery)
- ▶ Postural orthostatic tachycardia syndrome (POTS)
- ▶ Mast cell activation syndrome
- ▶ Endometriosis
- ▶ Insulin resistance
- ▶ Polycystic ovarian syndrome
- ▶ Fibromyalgia
- ▶ Anxiety and depression

Physical examination

- ▶ Overweight BMI 28
- ▶ Abdominal examination – mildly distended abdomen, soft, mild tenderness elicited on deep palpation around umbilicus
- ▶ No signs of dehydration
- ▶ Evidence of joint hypermobility

Investigations

- ▶ Normal gastroscopy and colonoscopy
- ▶ Gastric emptying study normal
- ▶ Oesophageal manometry and 24-hour pH testing unremarkable
- ▶ HIDA scan normal
- ▶ CT scan abdomen – fatty liver, small ovarian cyst, compression left iliac vein by right iliac artery
- ▶ Positive tilt table test
- ▶ ECG showed no abnormalities

Medications

- ▶ Domperidone 10 mg three times daily (partially helpful)
- ▶ Lyrica 150 mg daily
- ▶ Uses laxatives (coloxyl and senna) often
- ▶ Mirtazapine 20 mg daily
- ▶ Metformin 500 mg daily
- ▶ Ivabradine 5 mg twice daily
- ▶ Paracetamol 1g four times daily PRN
- ▶ Ondansetron PRN

Notably she has been previously trialled on multiple prokinetic drugs including erythromycin, other antidepressants including amitriptyline, endone and tapentadol (ceased), buscopan, mebeverine, iberogast, peppermint oil, multiple probiotics from her pharmacy

Dietary history

- ▶ Self trialled gluten and lactose free diet with no benefit
- ▶ Low FODMAPS diet administered by a private dietitian – minimal improvement in symptoms
- ▶ Used to have a lot of processed foods in diet
- ▶ Many solid foods make her nauseous, tolerates dry crackers well and no difficulties with liquids
- ▶ Drinks half a litre of bottled water a day
- ▶ Snacks occasionally on sweets at night

Social History

- ▶ Caucasian, single, lives at home with family – mother, father and younger brother
- ▶ University graduate works in legal industry, very health literate
- ▶ Non-smoker, non-drinker, no use of recreational drugs
- ▶ Normally quite sociable and has a group of girlfriends, active on social media; often finds difficult to go out because of her symptoms
- ▶ Work attendance has been affected by flares in her symptoms
- ▶ Accompanied by mother to appointments – very concerned and vocal about daughter's health issues

Psychological history

- ▶ Anxiety and depression since adolescence – seen a psychiatrist who prescribed mirtazapine
- ▶ No described trauma/abuse in the past
- ▶ No history of eating disorder
- ▶ Has seen a psychologist for cognitive behavioural therapy for anxiety – did not find it helpful
- ▶ Has received 6 sessions of gut hypnotherapy – not helpful

Patient concerns

- ▶ Unsatisfied with diagnosis of IBS
- ▶ No explanation as to how her symptoms came about
- ▶ Concerns around interplay of her multiple medical issues
- ▶ Not eating much – concerned about her oral intake
- ▶ Concerns around dehydration due to POTS – does describe dizziness upon standing at times especially with hot weather



Impressions?

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Category D: Psychosocial modifiers	Psychosocial modifiers and comorbidities that influence patient's illness experience and may affect treatment	May be categorical (eg, DSM V diagnosis), dimensional (eg, HADS, or other scales), Rome Psychosocial red flags, or patient reports (eg, abuse) that is judged by the clinician to be clinically relevant	Anxiety, major depressive disorder, posttraumatic stress disorder, somatic symptom disorder
Category E: Physiological features and biomarkers	Laboratory or imaging studies that correlate with the physiology underlying the categorical Rome diagnosis and its subtype	Provides dimensionality for physiological or biochemical parameters of clinical relevance that enhances understanding of the diagnosis. Requires sufficient external evidence to be endorsed (eg, motility, radionuclide, biochemical). Has treatment implications (eg, degree of fecal incontinence)	Lactose tolerance test in a patient with IBS-D. Anorectal manometry and balloon expulsion consistent with dyssynergic defecation in a patient with IBS-C.

DGBI, disorder of gut-brain interaction; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; HAD, Hospital and Anxiety Depression Scale; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with predominant constipation; IBS-D, irritable bowel syndrome with predominant diarrhea; MDCP, multidimensional clinical profile.

Multidimensional clinical profile (MDCP) Category A – Rome diagnosis

B1. FUNCTIONAL DYSPEPSIA*

*Diagnostic criteria***

One or more of the following:

Bothersome postprandial fullness

Bothersome early satiation

Bothersome epigastric pain

Bothersome epigastric burning

AND

No evidence of structural disease
(including at upper endoscopy) that
is likely to explain the symptoms

C1. IRRITABLE BOWEL SYNDROME

*Diagnostic criteria**

Recurrent abdominal pain on
average at least 1 day/week in the last
3 months, associated with **two or
more** of the following criteria:

Related to defecation

Associated with a change in frequency
of stool

Associated with a change in form
(appearance) of stool

**Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Multidimensional clinical profile (MDCP) Category B – Clinical Modifier

- ▶ Multiple other medical issues including POTS, Ehlers Danlos Syndrome....
- ▶ Tried multiple medications and lifestyle recommendations including dietary interventions without much improvement in symptoms

Multidimensional clinical profile (MDCP) Category C – Impact on daily activities

- ▶ Moderate impact on quality of life
- ▶ Affects attendance at work, affects socialising with friends

Multidimensional clinical profile (MDCP) Category D – Psychosocial modifiers

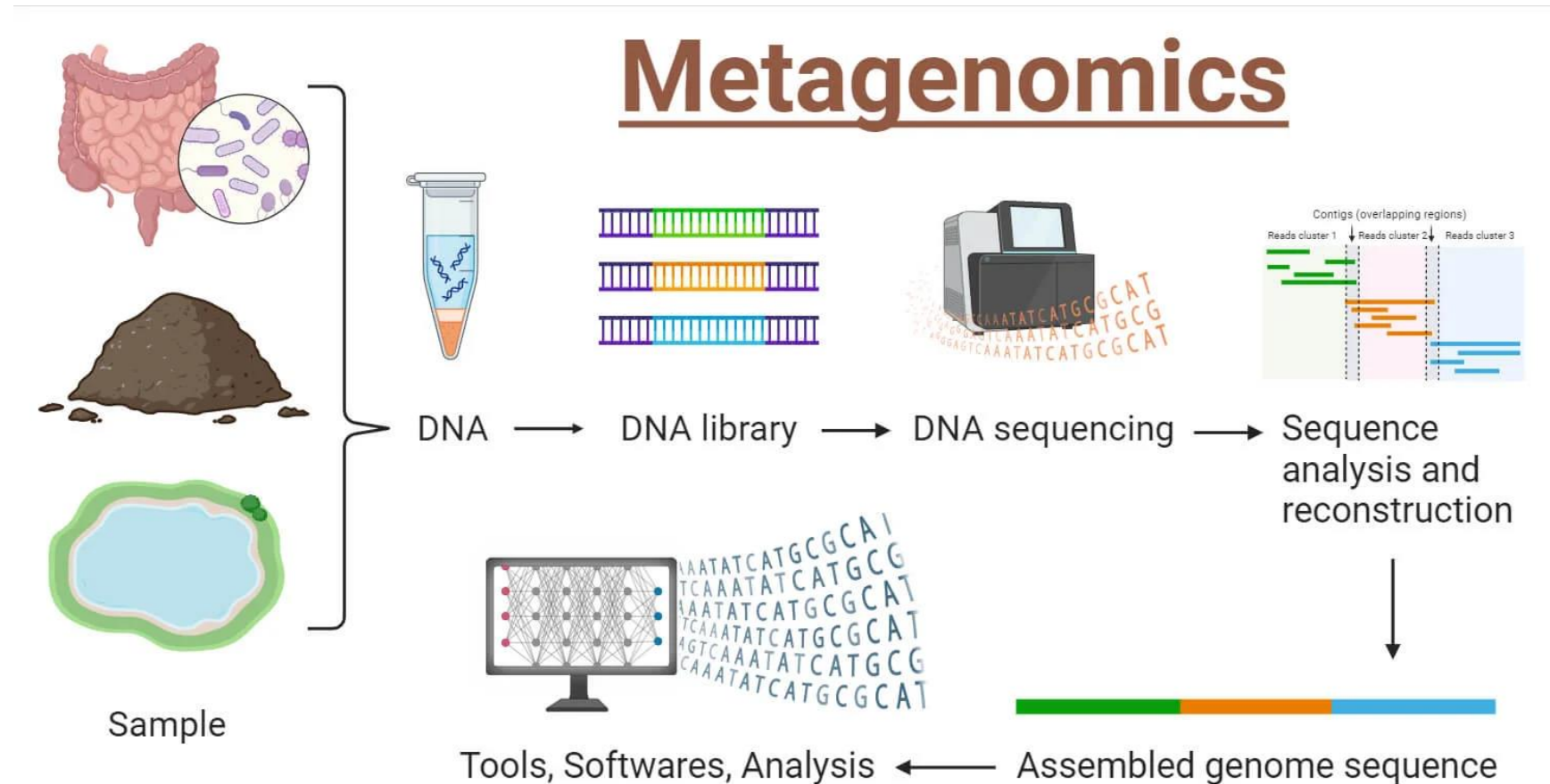
- ▶ Diagnosed anxiety and depression
- ▶ On antidepressant treatment prescribed by psychiatrist
- ▶ No background of eating disorder
- ▶ Already tried interventions such as gut hypnotherapy
- ▶ Very involved mother

Multidimensional clinical profile (MDCP) Category E – Physiological features and biomarkers

MDCP Categories	Content	Comments	Examples
Category A: Categorical Rome Diagnosis	Diagnosis is based on the Rome IV criteria.	Symptom based but may include physiological criteria. Used for clinical trials but not sufficient for treatment.	IBS, functional dyspepsia, functional heartburn, functional constipation
Category B: Clinical modifier	Additional symptoms, subtypes, historical information, physical signs, laboratory or physiological studies into clinical subsets that would affect treatment planning.	Not necessarily based on evidence; follows clinical wisdom and provides for more specific treatment.	IBS-D, IBS-C, epigastric pain syndrome, postprandial distress syndrome
Category C: Impact on daily activities	Ask the patient: "Overall, how much do your symptoms currently interfere with life (work, school, social activities, self-care, concentration, and performance)?"	Quantifies the overall effect of illness perceptions, behaviors and daily functioning on treatment.	None, mild, moderate, or severe
Category D: Psychosocial modifiers	Psychosocial modifiers and comorbidities that influence patient's illness experience and may affect treatment	May be categorical (eg, DSM V diagnosis), dimensional (eg, HADS, or other scales), Rome Psychosocial red flags, or patient reports (eg, abuse) that is judged by the clinician to be clinically relevant	Anxiety, major depressive disorder, posttraumatic stress disorder, somatic symptom disorder
Category E: Physiological features and biomarkers	Laboratory or imaging studies that correlate with the physiology underlying the categorical Rome diagnosis and its subtype	Provides dimensionality for physiological or biochemical parameters of clinical relevance that enhances understanding of the diagnosis. Requires sufficient external evidence to be endorsed (eg, motility, radionuclide, biochemical). Has treatment implications (eg, degree of fecal incontinence)	Lactose tolerance test in a patient with IBS-D. Anorectal manometry and balloon expulsion consistent with dyssynergic defecation in a patient with IBS-C.

DGBI, disorder of gut-brain interaction; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; HAD, Hospital and Anxiety Depression Scale; IBS, irritable bowel syndrome; IBS-C, irritable bowel syndrome with predominant constipation; IBS-D, irritable bowel syndrome with predominant diarrhea; MDCP, multidimensional clinical profile.

Metagenomic studies



Example of metagenomic sequencing test – Faecal Metapanel

MetaPanel™

Metagenomic GI pathogen assay

Clinical history

Undifferentiated GI symptoms. H/O gastroparesis with recent hospitalisation for the above and gut bug.

Overall interpretation

1 Pathogen

No pathogens detected.

2 Antimicrobial resistance

AmpC beta-lactam resistance gene, blaMIR group detected.

Overall recommendation

The detection of a gene conferring resistance to beta lactams is suggestive of increased prior antibiotic use or recent travel to countries with higher antimicrobial resistance.

In the setting of future Gram-negative sepsis, empiric therapy with an aminoglycoside or cefepime is likely to be effective.

Low microbial diversity and richness noted. Consumption of a diverse predominantly plant-based diet that includes fermented foods and avoids ultraprocessed foods, combined with regular exercise, is recommended to promote a healthy gut microbiome which may in turn provide colonisation resistance against bacteria harbouring resistance genes.

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Final Associated Report ID
R125050014931_R

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Microbial Diversity

Microbial diversity is a measure that accounts for the number of different species (richness) and their relative abundance (evenness). This is assessed using the Shannon Index, a measure widely used by the scientific community. Low microbial diversity could reflect low numbers of species (low richness) or that certain species dominate the microbiome (low evenness). Low microbial diversity may be associated with microbiome instability, systemic inflammation and faster gut transit time.



Species Richness

Richness refers to the number of different species present in a particular ecological community, habitat, or defined area. It's a simple count of species and does not consider the abundance of each species or their relative proportions. In essence, species richness provides a measure of the variety of species in a given area but doesn't tell you anything about their distribution or evenness. It is one of the most basic and commonly used metrics in ecological and biodiversity studies. Generally, the higher the richness, the greater the diversity.



The Atmo Gas Capsule System

Clinician Portal used to review data and create Motility Study Report(s)



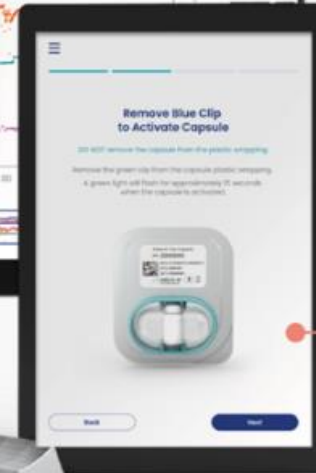
Receiver stores data received wirelessly from the Capsule

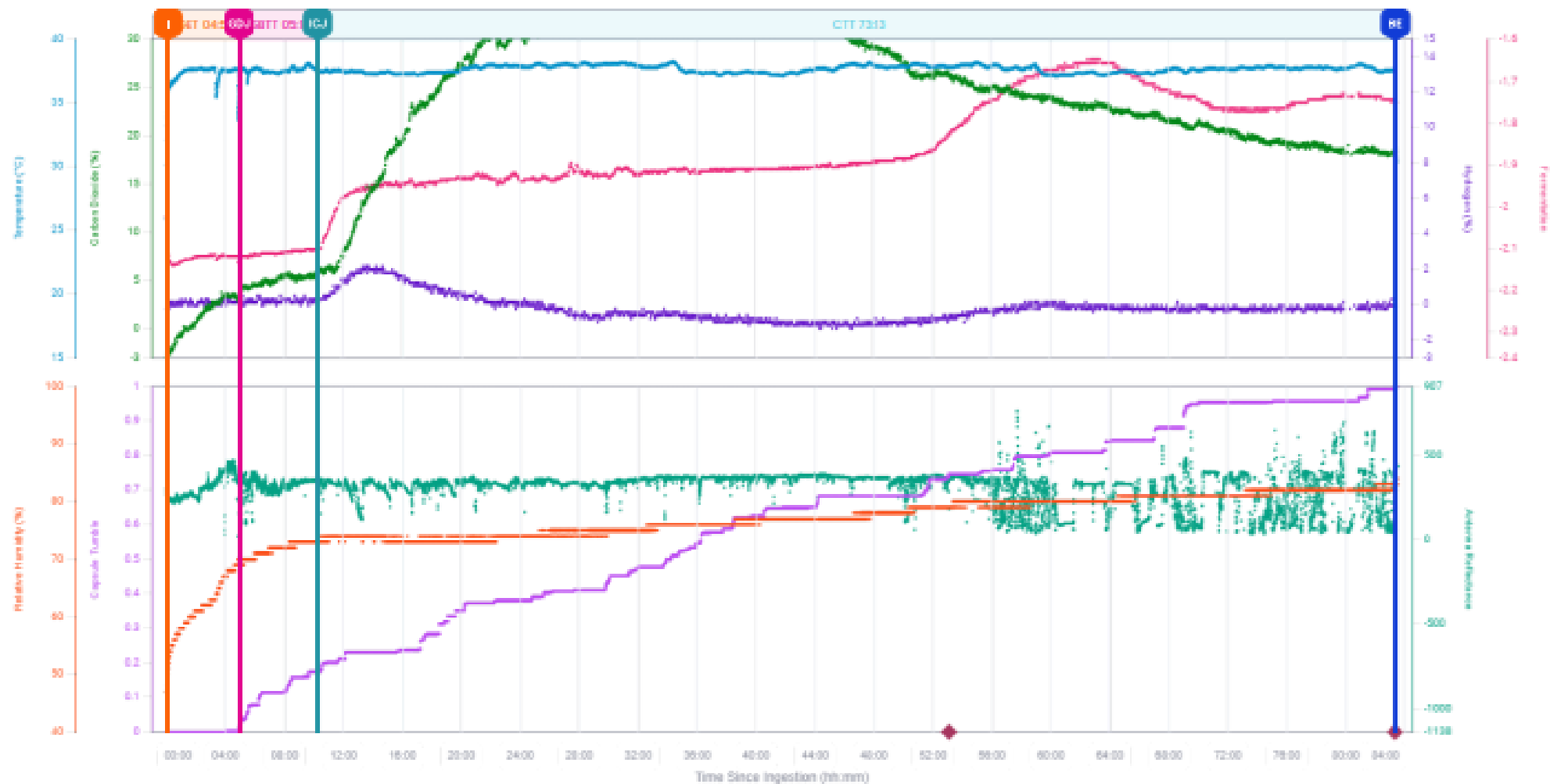
Patient Belt holds the Receiver on the patient

Atmo® Motility Bar
Standardised Meal Option
eg. Atmo Motility Bar
Ingested with the Capsule¹

Atmo® Gas Capsule
The ingestible component
with onboard sensors

Mobile Device used to initiate study and upload results via the Clinic App





Traces

- Temperature
- Carbon Dioxide
- Hydrogen
- Fermentation
- Relative Humidity
- Capsule Tumble
- Antenna Reflectance
- Bowel Movement

Transit metrics

Transit range	Time (h:min)	Normal range (h)
Gastric Emptying Time (GET)	4:53	< 5 hours
Small Bowel Transit Time (SBTT)	5:18	> 2 and < 6
Orocecal Transit Time (OCTT)	10:11	> 3 and < 10
Colonic Transit Time (CTT)	73:13	< 59
Small and Large Bowel Transit Time (SLBTT)	78:32	< 64
Whole Gut Transit Time (WGTT)	83:25	< 73

Alimetry (electrogastrography)



Gastric Alimetry[®] Test Interpretation in Gastroduodenal Disorders: Review and Recommendations

Daphne Foong ¹, Stefan Calder ^{2 3 4}, Chris Varghese ², Gabriel Schamberg ^{3 4}, William Xu ², Charlotte Daker ⁵, Vincent Ho ^{1 6}, Christopher N Andrews ⁷, Armen A Gharibans ^{2 3 4}, Greg O'Grady ^{2 3 4}

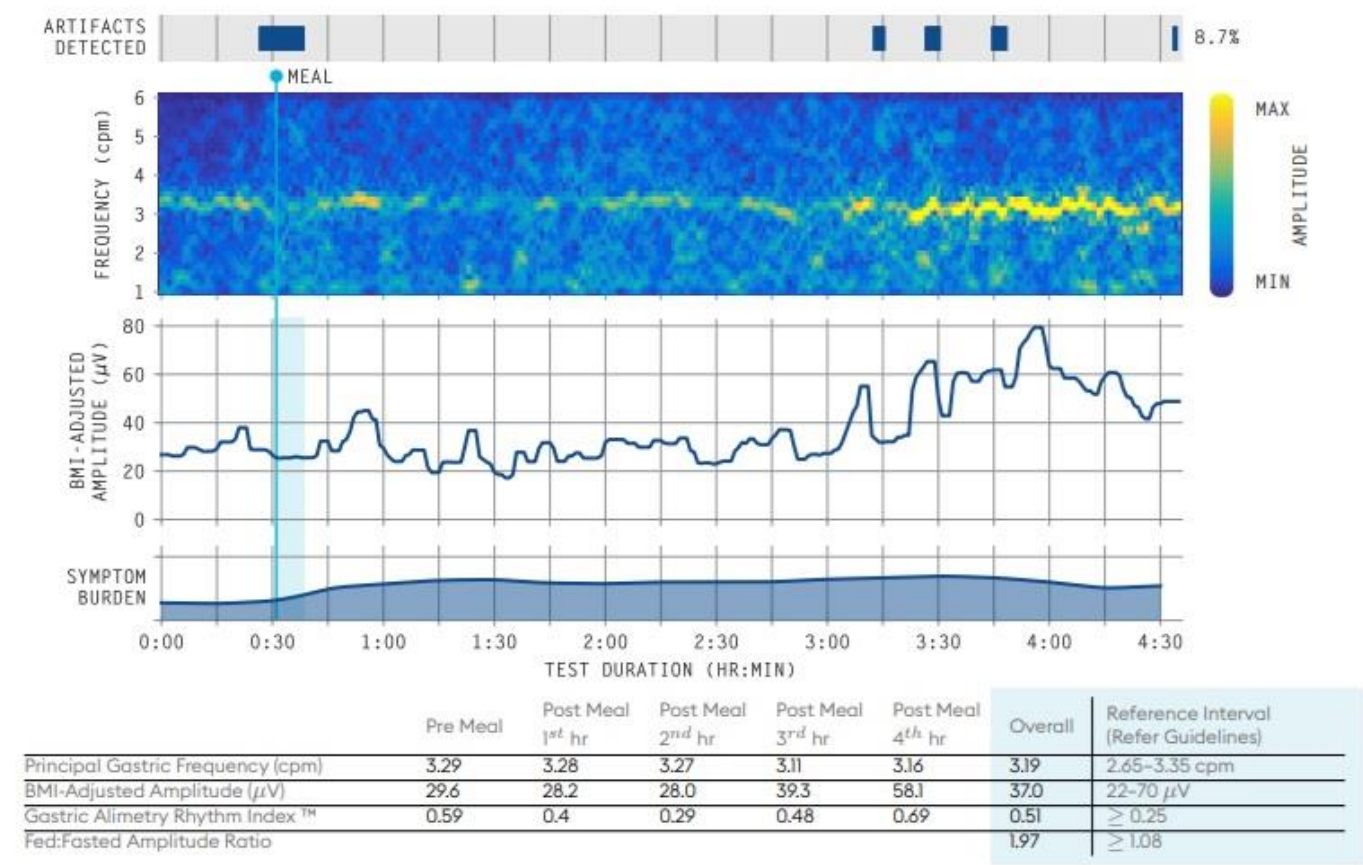
Affiliations + expand

PMID: 37892572 PMCID: PMC10607701 DOI: 10.3390/jcm12206436

Abstract

Chronic gastroduodenal symptoms are prevalent worldwide, and there is a need for new diagnostic and treatment approaches. Several overlapping processes may contribute to these symptoms, including gastric dysmotility, hypersensitivity, gut-brain axis disorders, gastric outflow resistance, and duodenal inflammation. Gastric Alimetry[®] (Alimetry, New Zealand) is a non-invasive test for evaluating gastric function that combines body surface gastric mapping (high-resolution electrophysiology) with validated symptom profiling. Together, these complementary data streams enable important new clinical insights into gastric disorders and their symptom correlations, with emerging therapeutic implications. A comprehensive database has been established, currently comprising > 2000 Gastric Alimetry tests, including both controls and patients with various gastroduodenal disorders. From studies employing this database, this paper presents a systematic methodology for Gastric Alimetry test interpretation, together with an extensive supporting literature review. Reporting is grouped into four sections: Test Quality, Spectral Analysis, Symptoms, and Conclusions. This review compiles, assesses, and evaluates each of these aspects of test assessment, with discussion of relevant evidence, example cases, limitations, and areas for future work. The resultant interpretation methodology is recommended for use in clinical practice and research to assist clinicians in their use of Gastric Alimetry as a diagnostic aid and is expected to continue to evolve with further development.

Keywords: body surface gastric mapping; chronic nausea and vomiting; disorders of gut brain interaction; functional dyspepsia; gastroparesis; motility disorders.



Clinical Comments

Test Quality: Pass. Impedance was good. Mild artifacts (8.7%). 100% of standard meal completed. But had about 3 vomiting episodes after the meal until the end of the test.

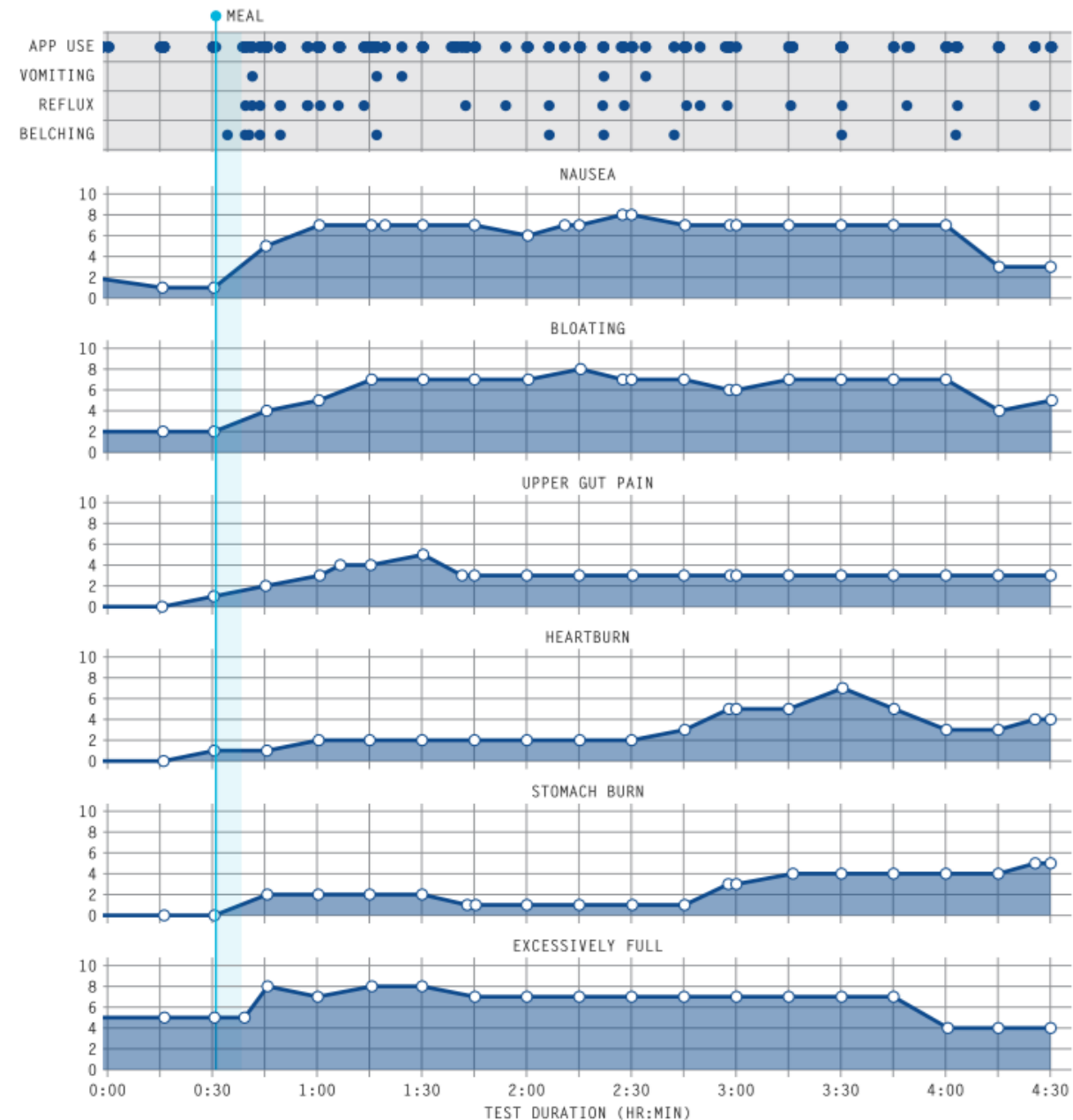
Spectral analysis: Overall Principal Gastric Frequency was normal at 3.19 cpm. The GA-RI was stable at 0.51. The BMI-adjusted amplitude is normal at 37μV. The meal response is present (Fed:Fasted Amplitude Ratio = 1.97). No transient abnormalities identified.

Symptoms: Symptoms were "less than usual" on the day of testing. The Total Symptom Burden Score was 31/70. There was mild early satiation (3/10) noted after the meal. Baseline symptoms were nausea, bloating, upper gut pain, heartburn and excessive fullness. Bloating, excessive fullness, and nausea were highly severe except for upper gut pain and all appears meal responsive. Heart burn and stomach burn appeared towards the end of the test. There was 1 belching, and no reflux events recorded. Heartburn and stomach burn were correlated with gastric amplitude (0.5).

Gut-Brain Well-Being: The AGBW score was at 27/40. Depressive symptoms were scored at 13/16, stress symptoms scored at 7/12, and anxiety symptoms were scored at 7/12.

Conclusion: Overall abnormal Gastric Alimetry spectral analysis with a long lag to the meal response. Symptom profile appears to be post-prandial distress with a meal responsive and post gastric phenotype. Consider the hypersensitivity and/or disordered accommodation, with symptoms correlating with gastric activity, and lagged meal response with delayed gastric emptying and possible issues with postprandial accommodation, as per patient's clinical context.

Symptom Graph



Summary of additional diagnostic tests

- ▶ Rome 4 diagnostic criteria for IBS and functional dyspepsia
- ▶ Post-infectious aetiology
- ▶ Dysbiosis
- ▶ Slow transit constipation
- ▶ Visceral hypersensitivity

Treatment on a pathophysiological basis

- ▶ Seen along with mother and clearly conveyed the results of tests and how they relate to pathophysiology
- ▶ Presented the research literature to mother and daughter and asked them to further investigate
- ▶ Expectant improvement in symptoms but not complete amelioration

[nature](#) > [scientific reports](#) > [articles](#) > articleArticle | [Open access](#) | Published: 19 October 2017

Evidence for long-term sensitization of the bowel in patients with post-infectious-IBS

[D. Balemans](#), [S. U. Mondelaers](#), [V. Cibert-Goton](#), [N. Stakenborg](#), [J. Aguilera-Lizarraga](#), [J. Dooley](#), [A. Liston](#),
[D. C. Bulmer](#), [P. Vanden Berghe](#), [G. E. Boeckxstaens](#)  & [M. M. Wouters](#)

[Scientific Reports](#) **7**, Article number: 13606 (2017) | [Cite this article](#)

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Abstract

Post-infectious irritable bowel syndrome (PI-IBS) is a common gastrointestinal disorder characterized by persistent abdominal pain despite recovery from acute gastroenteritis. The underlying mechanisms are unclear, although long-term changes in neuronal function, and low grade inflammation of the bowel have been hypothesized. We investigated the presence and mechanism of neuronal sensitization in a unique cohort of individuals who developed PI-IBS following exposure to contaminated drinking water 7 years ago. We provide direct evidence of ongoing sensitization of neuronal signaling in the bowel of patients with PI-IBS. These changes occur in the absence of any detectable tissue inflammation, and instead appear to be driven by pro-nociceptive changes in the gut micro-environment. This is evidenced by the activation of murine colonic afferents, and sensitization responses to capsaicin in dorsal root ganglia (DRGs) following application of supernatants generated from tissue biopsy of patients with PI-IBS. We demonstrate that neuronal signaling within the bowel of PI-IBS patients is sensitized 2 years after the initial infection has resolved. This sensitization appears to be mediated by a persistent pro-nociceptive change in the gut micro-environment, that has the capacity to stimulate visceral afferents and facilitate neuronal TRPV1 signaling.

Dysbiosis

Randomized Controlled Trial > Korean J Gastroenterol. 2006 Jun;47(6):413-9.

[The effects of probiotics on symptoms of irritable bowel syndrome]

[Article in Korean]

Young Gyun Kim ¹, Jong Tae Moon, Kuen Man Lee, Nu Ri Chon, Hyojin Park

Affiliations + expand

PMID: 16809947

Abstract

Background/aims: Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) tract disorder that has heterogeneous clinical presentations such as abdominal pain, diarrhea, constipation, and abdominal distension. It is known that several mechanisms are involved in the pathogenesis of IBS. Probiotics may target one or more pathophysiologic pathways in IBS and may improve the symptoms of IBS. However, the results of studies about probiotics on IBS are controversial. Therefore, the aim of this study was to evaluate the effect of probiotics on GI symptoms and intestinal gas volume changes in patients with IBS.

Methods: Forty patients were randomly allocated to be treated with Medilac DS (Bacillus subtilis, Streptococcus faecium) (n=20) or placebo (n=20) in a double-blind, prospective manner. The change in intestinal gas volume and symptom scores after 4-week treatment were evaluated for the efficacy.

Results: There was no significant difference in bloating, frequency of gas expulsion, frequency of defecation, and hardness of stool before and after the treatment. However, the severity of abdominal pain and the frequency of abdominal pain decreased significantly in Medilac DS group (2.4+/-1.3 cm/day --> 1.6+/-1.6 cm/day, 1.7+/-1.3/day --> 1.0+/-1.0/day) (p=0.044, p=0.038), but not in placebo group (2.1+/-2.0 cm/day --> 1.8+/-2.1 cm/day, 1.3+/-1.2/day --> 1.4+/-1.9/day). In both groups, intestinal gas volume at baseline, after 2-week treatment, and after 4-week treatment did not show significant change. Medilac DS was well tolerated without adverse events.

Conclusions: Medilac DS is a safe and useful probiotic agent for the treatment of abdominal pain in patients with IBS.

ese



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Clinical Trial > Am J Gastroenterol. 2014 Jun;109(6):887-94. doi: 10.1038/ajg.2014.74.

Epub 2014 Apr 15.

Prucalopride improves bowel function and colonic transit time in patients with chronic constipation: an integrated analysis

Anton Emmanuel¹, Marina Cools², Lieve Vandeplasseche², René Kerstens²

Affiliations + expand

PMID: 24732867 PMCID: PMC4050523 DOI: 10.1038/ajg.2014.74

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Abstract

Objectives: Constipation is often characterized by slow colonic transit, but the relationship between colonic transit time (CTT) and symptoms is unclear. The aims of this study were to investigate the effect of prucalopride, a 5-hydroxytryptamine receptor-4 agonist, on CTT and assess the relationship between CTT and symptoms.

Methods: This was an integrated analysis of three randomized, placebo-controlled, phase 2 dose-finding trials of prucalopride in patients with chronic constipation (ClinicalTrials.gov identifiers: NCT00617513; NCT00631813; and NCT00596596). Measurements of CTT were analyzed using radio-opaque markers at the start and end (4 or 12 weeks) of treatment. At these visits, patients assessed the presence and severity of their symptoms.

Results: In total, 280 patients had CTT measurements before and at the end of treatment and were included in the analysis. Their mean age was 43 years, 93% were women, and mean duration of constipation was 19 years. After a once daily treatment with prucalopride 2 mg (n=98) and 4 mg (n=70), CTT was reduced by 12.0 h (95% confidence interval (CI): -18.9, -5.1) and 13.9 h (95% CI: -20.5, -7.4), respectively; CTT increased by 0.5 h (95% CI: -4.5, 5.5) with placebo (n=112). At the end of the trial, symptoms including bloating/flatulence/distension and straining were rated as severe or very severe by a higher proportion of patients with slow or very slow CTT (>48 h) than by those with normal CTT.

Conclusions: There was a clear relationship between increased CTT and increased symptom severity in patients with chronic constipation. Treatment with prucalopride accelerated CTT in these individuals.



> World J Gastroenterol. 2007 Sep 21;13(35):4771-4775. doi: [10.3748/wjg.v13.i35.4771](https://doi.org/10.3748/wjg.v13.i35.4771)

Increasing dietary fiber intake in terms of kiwifruit improves constipation in Chinese patients

Annie On On Chan¹, Gigi Leung¹, Teresa Tong¹, Nina YH Wong¹

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PMCID: PMC4611199 PMID: [17729399](https://pubmed.ncbi.nlm.nih.gov/17729399/)

Abstract

AIM: To investigate if increased dietary fiber, in terms of kiwifruit, is effective in Chinese constipated patients.

METHODS: 33 constipated patients and 20 healthy volunteers were recruited for a 4-wk treatment of kiwi fruit twice daily. Response during wk 1-4 was defined as an increase in complete spontaneous bowel motion (CSBM) ≥ 1 /wk. Secondary efficacy included response during wk 1-4, individual symptoms and scores of bowel habits and constipation. Responses were compared with the baseline run-in period. Colonic transit time and anorectal manometry were performed before and after treatment.

RESULTS: Responder rate was 54.5% in the constipated group. The mean CSBM increased after treatment (2.2 ± 2.6 vs 4.4 ± 4.6 , $P = 0.013$). There was also improvement in the scores for bothersomeness of constipation ($P = 0.02$), and satisfaction of bowel habit ($P = 0.001$), and decreased in days of laxative used ($P = 0.003$). There was also improvement in transit time ($P = 0.003$) and rectal sensation ($P < 0.05$). However, there was no change in the bowel symptoms or anorectal physiology in the healthy subjects.

CONCLUSION: Increasing dietary fiber intake is effective in relieving chronic constipation in Chinese population.

The efficacy and neural mechanism of acupuncture therapy in the treatment of visceral hypersensitivity in irritable bowel syndrome

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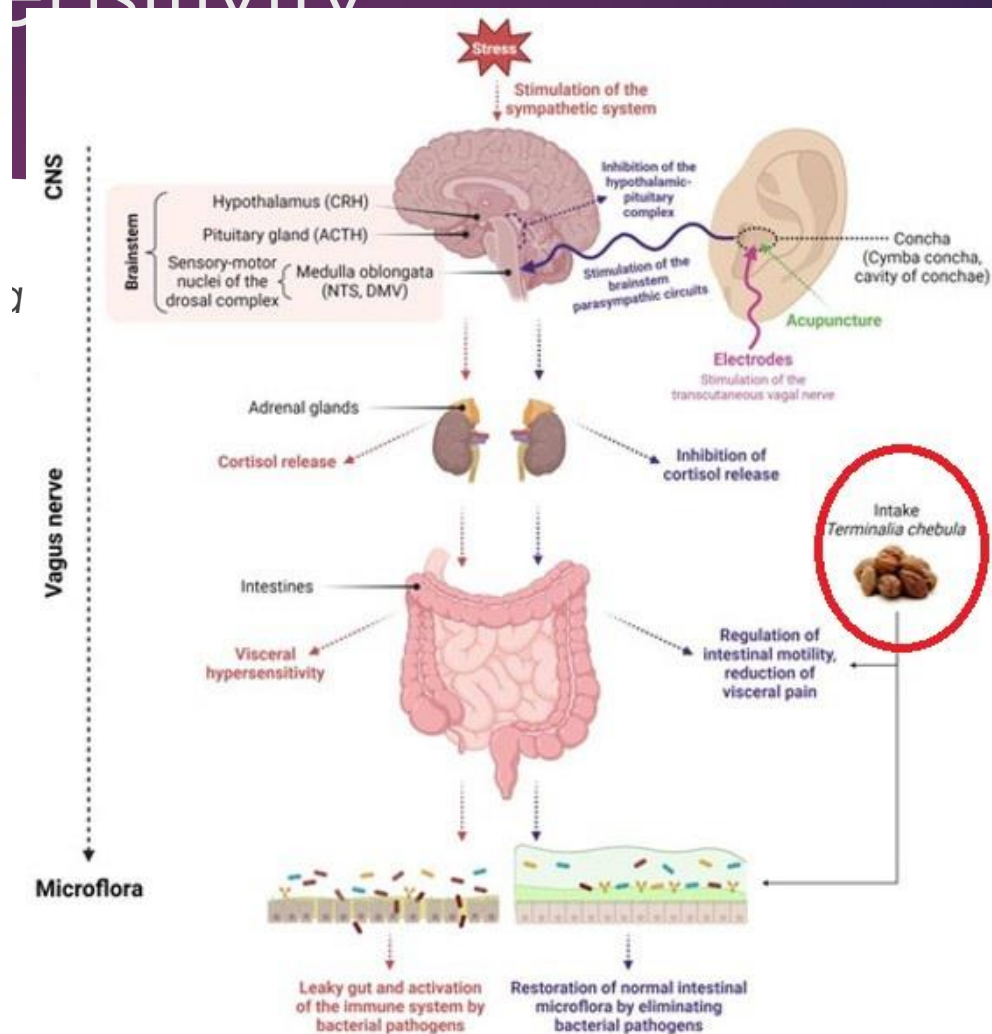
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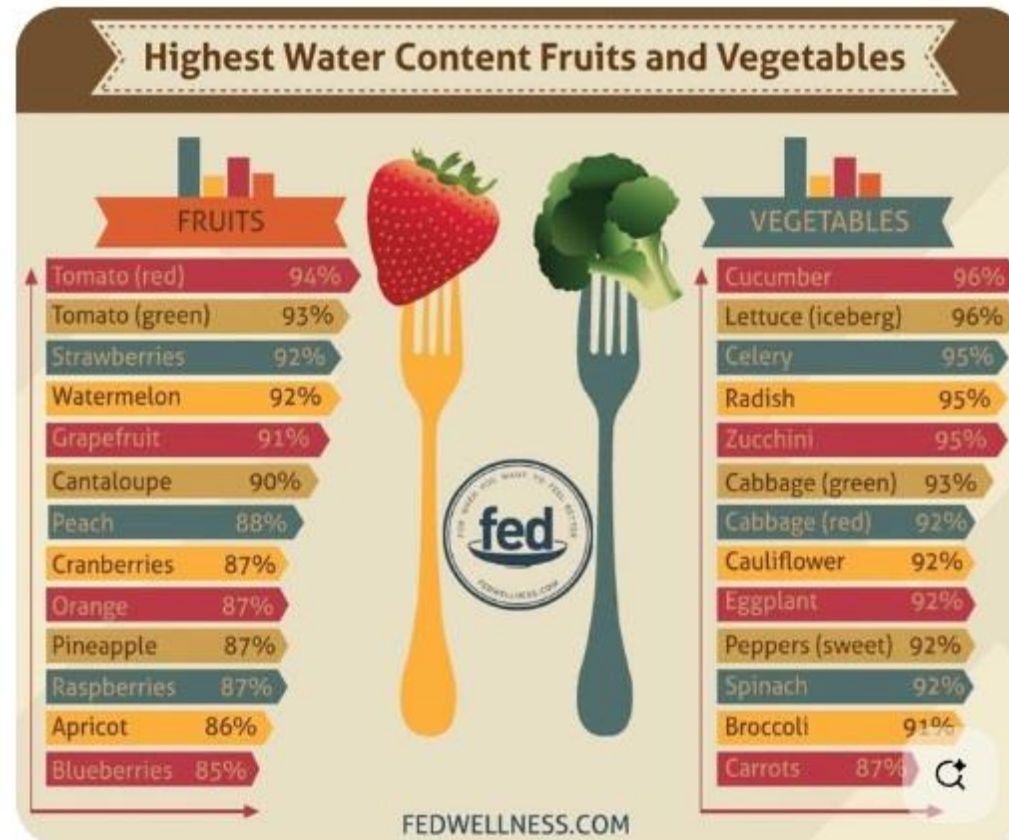
Abstract

Irritable Bowel Syndrome (IBS) is a complex functional gastrointestinal disorder primarily characterized by chronic abdominal pain, bloating, and altered bowel habits. Chronic abdominal pain caused by visceral Hypersensitivity (VH) is the main reason why patients with IBS seek medication. Significant research effort has been devoted to the efficacy of acupuncture as a non-drug alternative therapy for visceral-hyperalgesia-induced IBS. Herein, we examined the central and peripheral analgesic mechanisms of acupuncture in IBS treatment. Acupuncture can improve inflammation and relieve pain by reducing 5-hydroxytryptamine and 5-HT_{3A} receptor expression and increasing 5-HT₄ receptor expression in peripheral intestinal sensory endings. Moreover, acupuncture can also activate the transient receptor potential vanillin 1 channel, block the activity of intestinal glial cells, and reduce the secretion of local pain-related neurotransmitters, thereby weakening peripheral sensitization. Moreover, by inhibiting the activation of *N*-methyl-D-aspartate receptor ion channels in the dorsal horn of the spinal cord and anterior cingulate cortex or releasing opioids, acupuncture can block excessive stimulation of abnormal pain signals in the brain and spinal cord. It can also stimulate glial cells (through the P2X7 and prokinetic protein pathways) to block VH pain perception and cognition. Furthermore, acupuncture can regulate the emotional components of IBS by targeting hypothalamic-pituitary-adrenal axis-related hormones and neurotransmitters via relevant brain nuclei, hence improving the IBS-induced VH response. These findings provide a scientific basis for acupuncture as an effective clinical adjuvant therapy for IBS pain.

Sensitivity



Hydration



Patient outcome

- ▶ Very happy that there was a diagnostic process where the underlying mechanisms behind her IBS was uncovered
- ▶ 80% improvement in her symptoms
- ▶ Allowed her to return back fully to work and engage better socially



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