Brigham and Women's Hospital
Founding Member, Mass General Brigham

What's new in irritable bowel syndrome?

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- Clinical focus: IBS, constipation, fecal incontinence, women's health
- Research focus: Epidemiology of functional GI diseases, GI manifestations of eating disorders, pathophysiology of fecal incontinence

Disclosures

Research support from Ardelyx

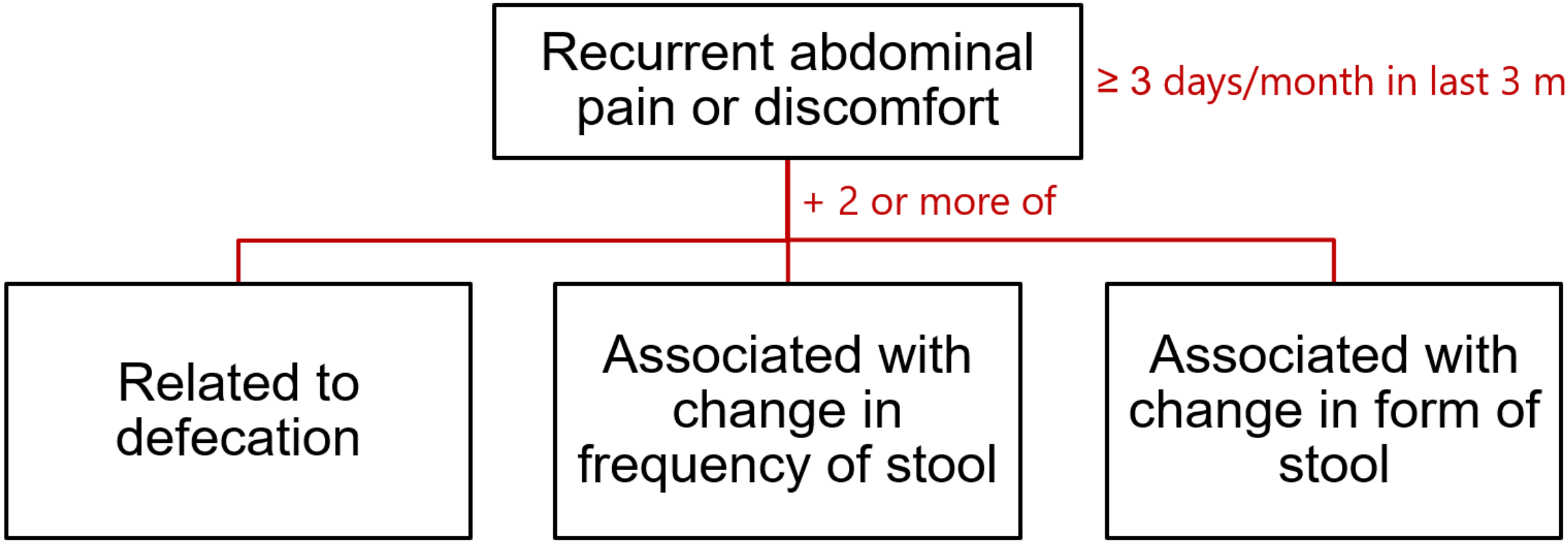
Consultant for AbbVie, Ardelyx, Atmo, Ferring, Laborie, and Takeda

Objectives

- Understand the biopsychosocial model of IBS and how it can help your patients
  - Typical IBS workup
  - Psychological overlap and neuromodulators
  - Explaining the disease to patients
- Discuss new insights/approaches in IBS with particular focus on what patients ask/care about
  - Dietary changes
  - SIBO
  - Fecal Microbiota Transplant

Defining and diagnosing irritable bowel syndrome

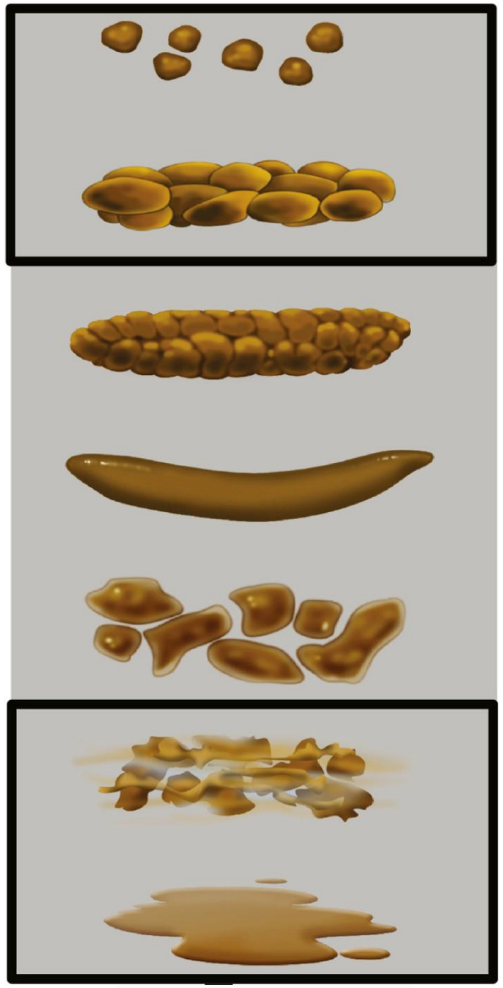
The Rome V definition of IBS is here!



Corsetti M, Shin A, *et al. Gastroenterology*. 2026 Feb 17:S0016-5085(26)00132-0.

Stool form as a surrogate for colonic transit time

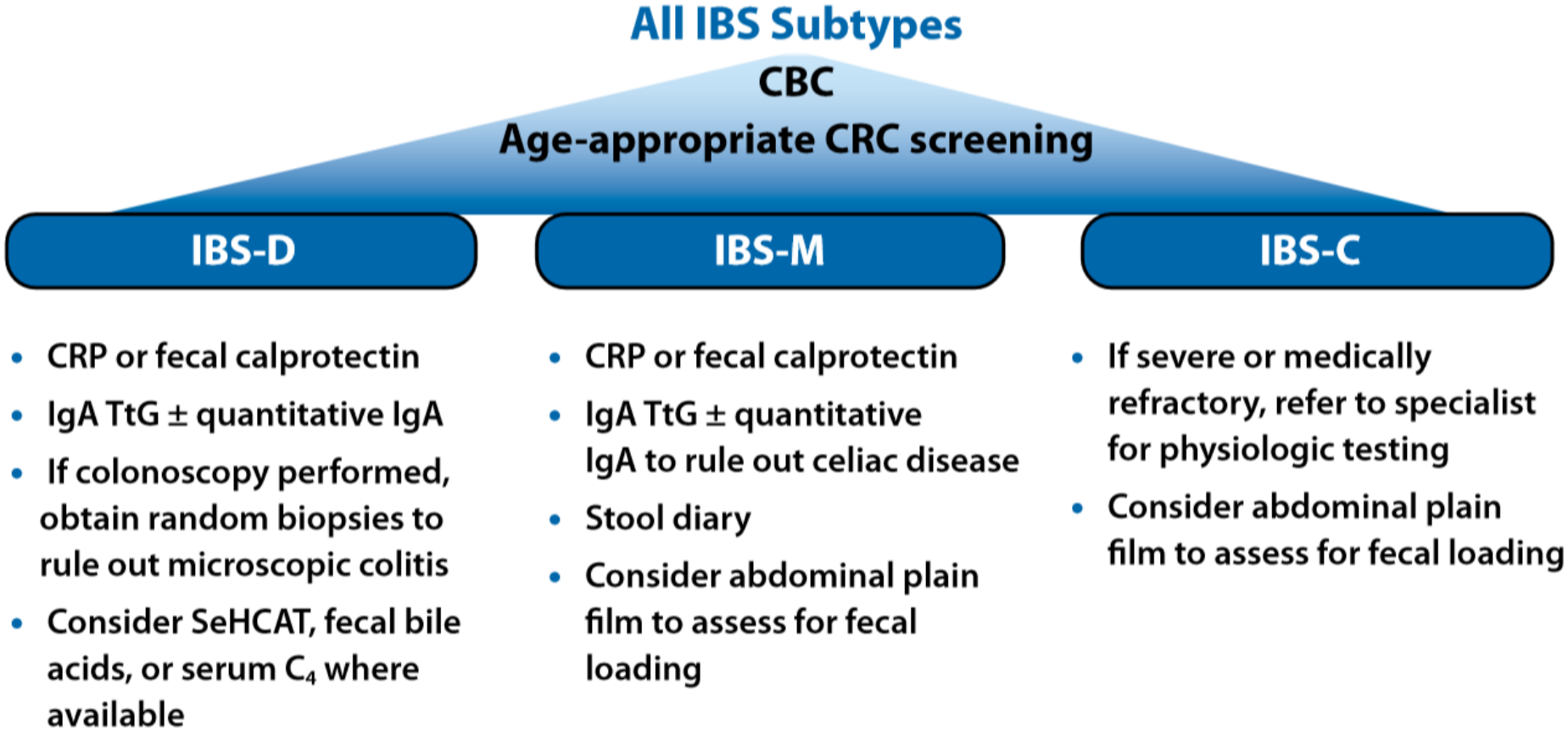
A



Type 1	Separate hard lumps, like nuts (hard to pass)
Type 2	Sausage-shaped but lumpy
Type 3	Like a sausage but with cracks on the surface
Type 4	Like a sausage or snake, smooth and soft
Type 5	Soft blobs with clear-cut edges
Type 6	Fluffy pieces with ragged edges, a mushy stool
Type 7	Watery, no solid pieces, entirely liquid

Drossman D, Hasler WL. *Gastroenterology*. 2016; 150:1393-1407.

Diagnostic testing for patients with suspected irritable bowel syndrome and no alarm features



*Alarm features

- Age ≥50 years old
- Blood in stools
- Nocturnal symptoms
- Unintentional weight loss
- Change in symptoms
- Recent antibiotic use
- Family history of organic GI disease

CBC, complete blood count; *CRC*, colorectal screening; CRP, C-reactive protein; TTG, tissue transglutaminase.

Adapted from: Schoenfeld, PS. *Gastroenterol Hepatol (N Y)*. 2016 Aug;12(8 Suppl 3):1-11.

There are now quality indicators for IBS care: diagnosis

American Gastroenterological Association

Quality Indicators:

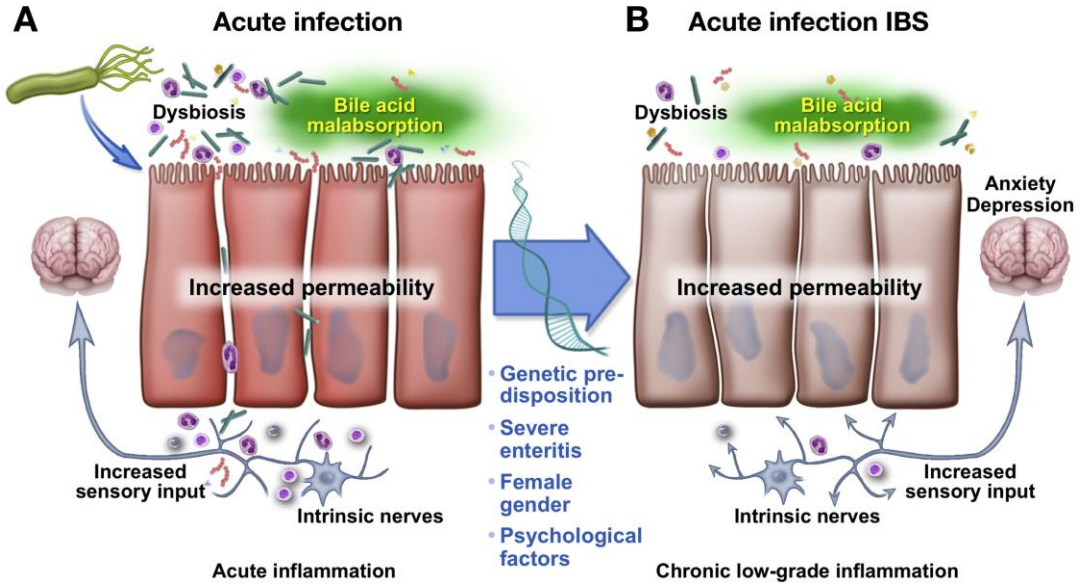
- Obtaining a detailed patient history, performing a physical examination, and providing clear communication of diagnosis to patients, including education and reassurance
- Testing for celiac disease (ie, tissue transglutaminase IgA) in patients with IBS-D or IBS-M with an alternate test (ie, tissue transglutaminase IgG or deamidated gliadin peptide IgG) for those with IgA deficiency
- Evaluation with fecal calprotectin (FCP) in individuals with IBS-D
- Avoidance of routine colonoscopy in patients with IBS who do not otherwise meet criteria for CRC screening and do not have alarm features

Hung KW, Leiman DA, *et al. Gastroenterology*. 2025 Mar;168(3):612-622.e4.

Conditions potentially associated with IBS

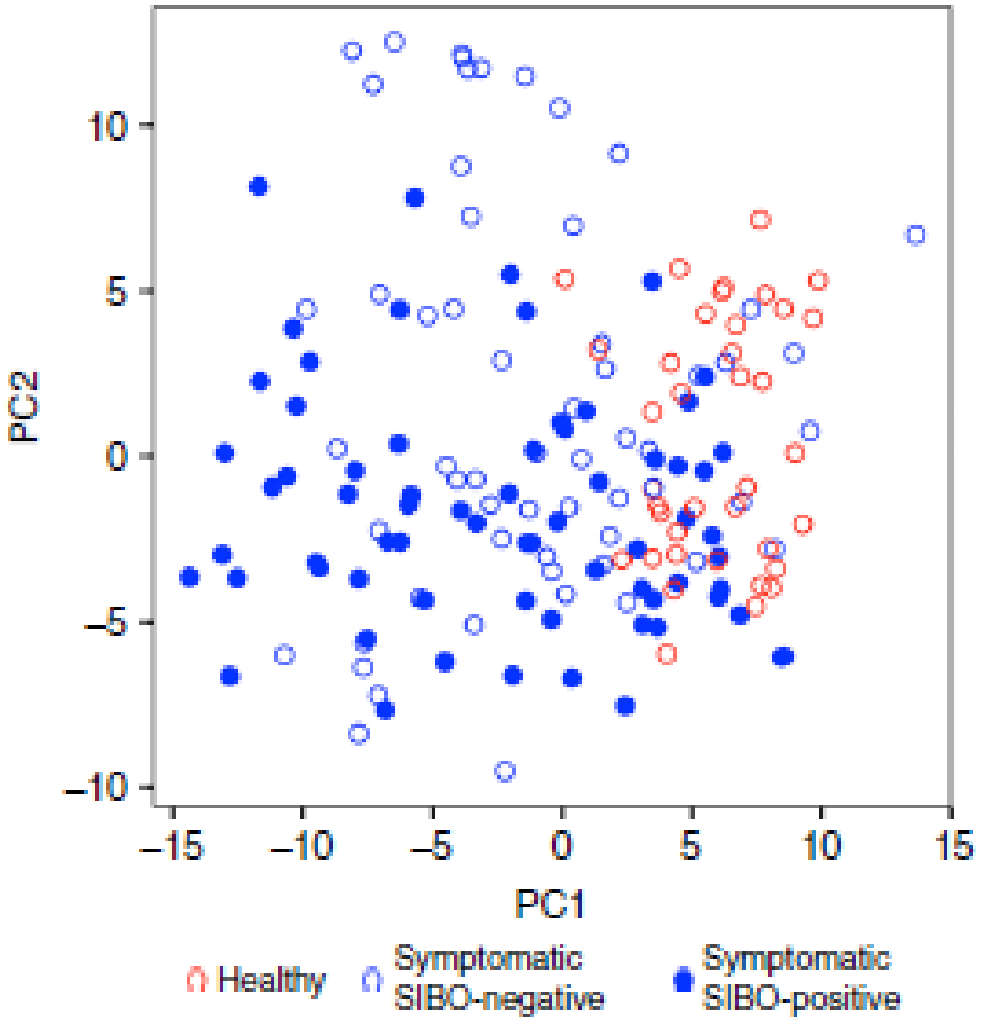
Post-infection IBS

- Post-infection IBS develops in about 10% of patients with infectious enteritis
- Risk factors:
  - Female sex
  - Younger age
  - Psychological distress during or before infection
  - Infection severity
  - Bacterial > viral infections
- Treatment does not differ but reassure that natural history suggests improvement over time



Barbara G, Grover M, *et al. Gastroenterology*. 2019 Jan;156(1):46-58.e7.

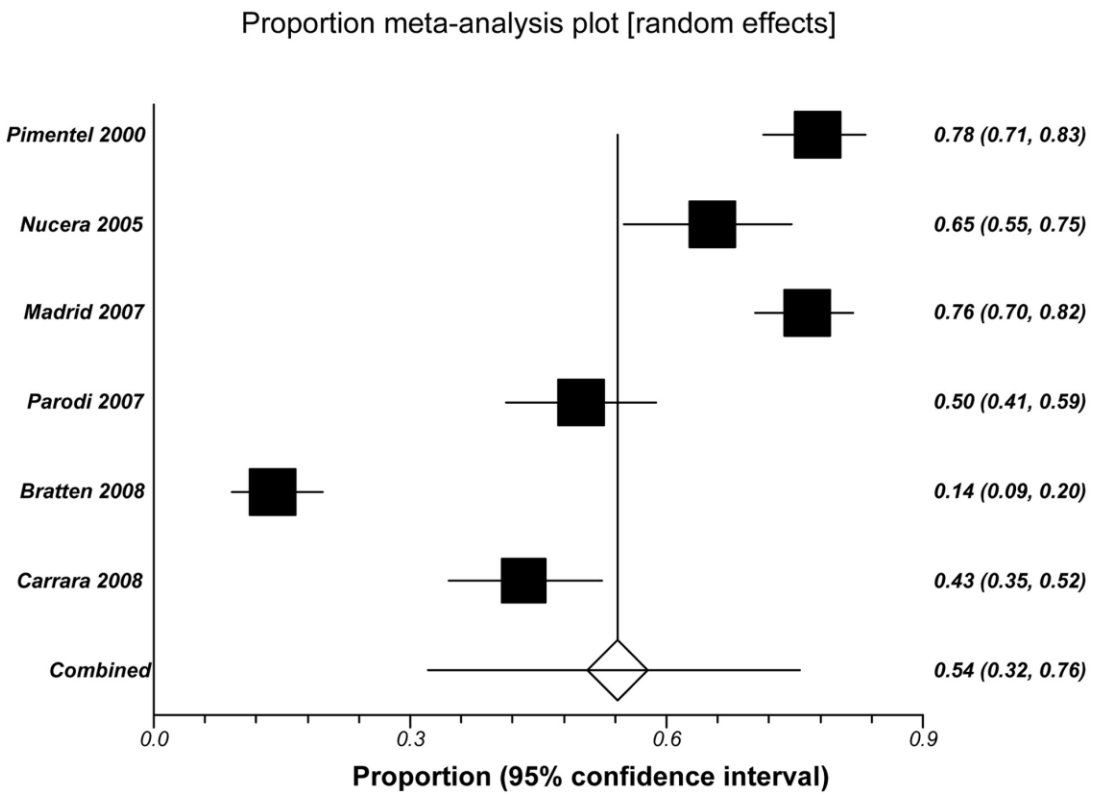
What about small intestinal bacterial overgrowth (SIBO)?



- Study of 127 patients w/ GI symptoms undergoing duodenal aspirate:
  - Small bowel flora *is* altered in symptomatic pts, but has no correlation to SIBO
  - No differences in small bowel microbiome among healthy subjects w/ and without SIBO

Saffouri GB, Shields-Cutler RR, et al. *Nat Commun*. 2019 May 1;10(1):2012.
Quigley EMM, Murray JA, et al. *Gastroenterology* 2020 Jul 15:S0016-5085(20)34928-3.

Rates of SIBO in IBS

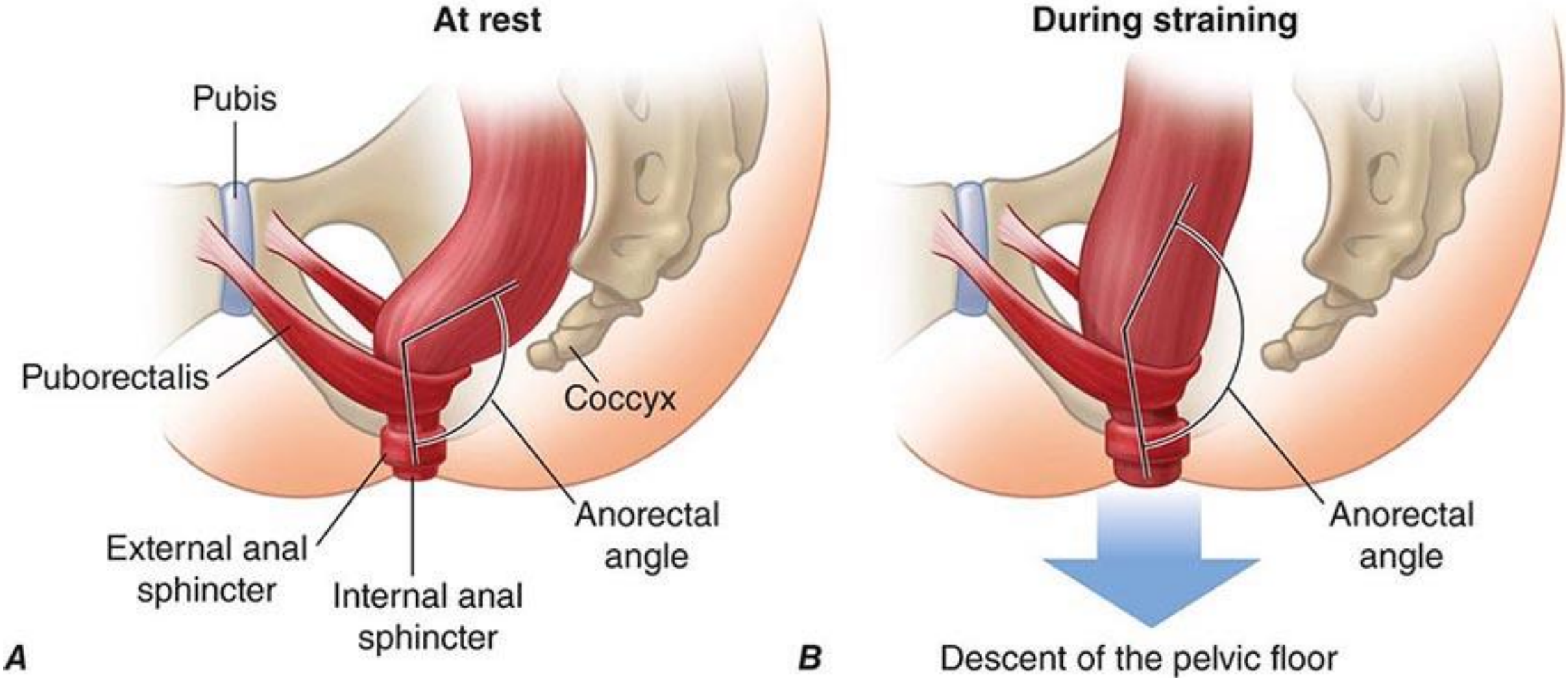


AGA Clinical Practice Update on Small Intestinal Bacterial Overgrowth: Expert Review

Eamonn M. M. Quigley,[1] Joseph A. Murray,[2] and Mark Pimentel[3]

"Relationships between SIBO and symptoms in those without obvious predisposing factors are more tenuous and symptoms are weakly predictive at best."

Pelvic floor physiology



Rectal evacuation disorders diagnosed in up 25% of constipated patients at the tertiary level

Lembo A, Camilleri M. *New England Journal of Medicine* 2003; 349(14): 1360-1368.

Dietary treatments for irritable bowel syndrome

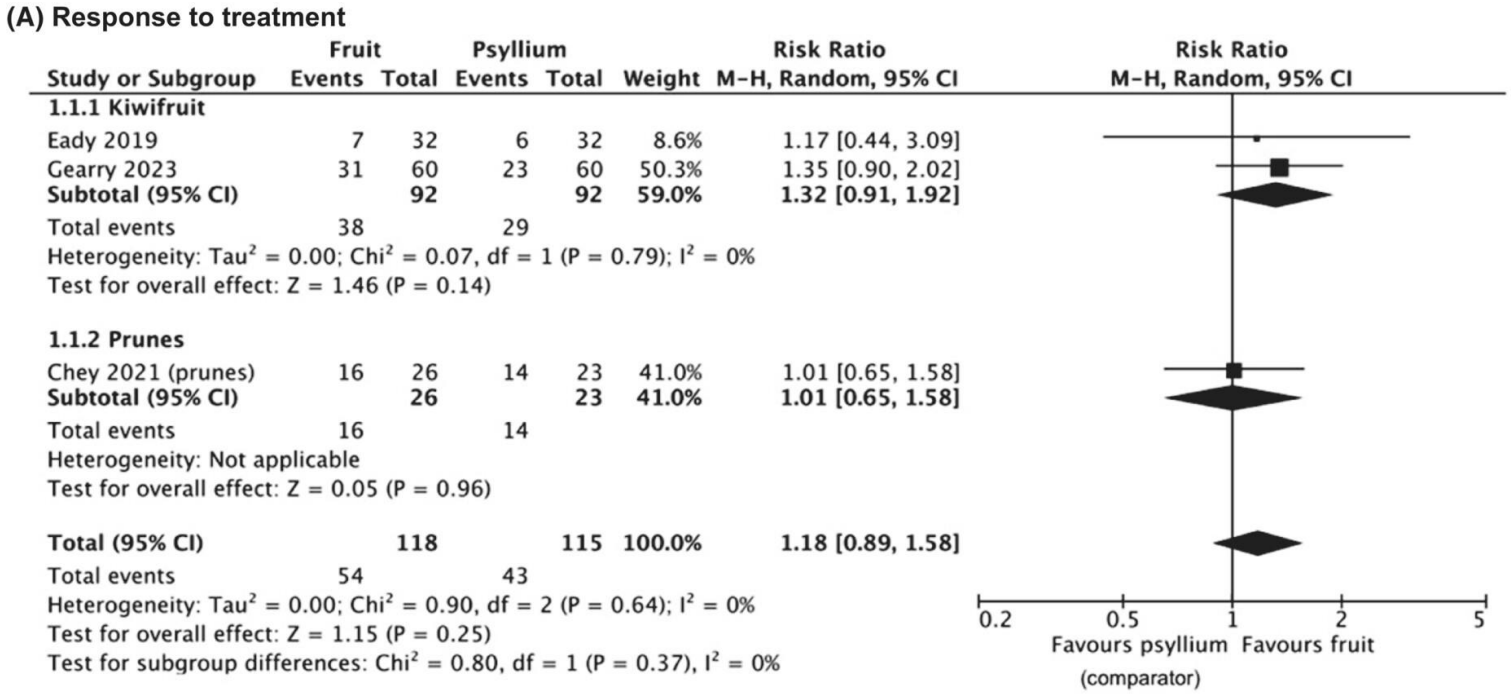
Fiber!

- Why not just eat more fiber?
- Psyllium has the best evidence in IBS for *both* diarrhea and constipation
  - ↑ stool bulk and normalizes colon transit (speeds up or slows down)
  - Slowly fermented
  - Doses: 7.5-22 g/day (1 teaspoon = 5.8g)
- Methylcellulose can be useful in constipation
  - Speeds up colonic transit, non-fermentable (less bloating)
  - Dosing: 1 tablespoon or 4 capsules = 2g
- Caution with wheat dextrin and anything that contains inulin (FODMAPs)

Eswaran S, Muir J, *et al. Am J Gastroenterol*. 2013 May;108(5):718-27.
Christodoulides S, Dimidi E, *et al. Aliment Pharmacol Ther.* 2016 Jul;44(2):103-16.

“Natural” treatments for constipation: fruits

Fruit for constipation: overall



Response to treatment:

Kiwifruit and prunes equivalent to psyllium

Van Der Schoot A, Katsirma Z, *et al*. *Aliment Pharmacol Ther*. 2024 Jan;59(2):157-174.

Fruit for constipation: practical use

- Prunes
  - Dose: 100g/day (9-10 prunes, 6g of fiber)
- Kiwifruit
  - High in soluble/insoluble fibers
  - ↑ stool water content, ?enzymes that accelerate gut motility and affect pain sensation
  - Likely less bloating relative to prunes, psyllium
  - Dose: 2 peeled, green kiwis/day (≈ 6g dietary fiber)
- No evidence that fruit has impacts on symptoms outside of bowel habits (i.e. pain)

Van Der Schoot A, Katsirma Z, *et al*. *Aliment Pharmacol Ther*. 2024 Jan;59(2):157-174.

Patient demand for dietary advice in IBS outstrips the supply of available evidence for providers

- More than 70% of IBS patients believe that food plays a role in their symptoms
- Self-reported food intolerance in IBS is associated with more severe symptom severity
- Like it or not, your patients will look to you for dietary guidance
- Evolution of concept of non-celiac gluten (wheat) sensitivity and emergence of the low-FODMAP diet

The best IBS diet for an individual is likely highly-personalized

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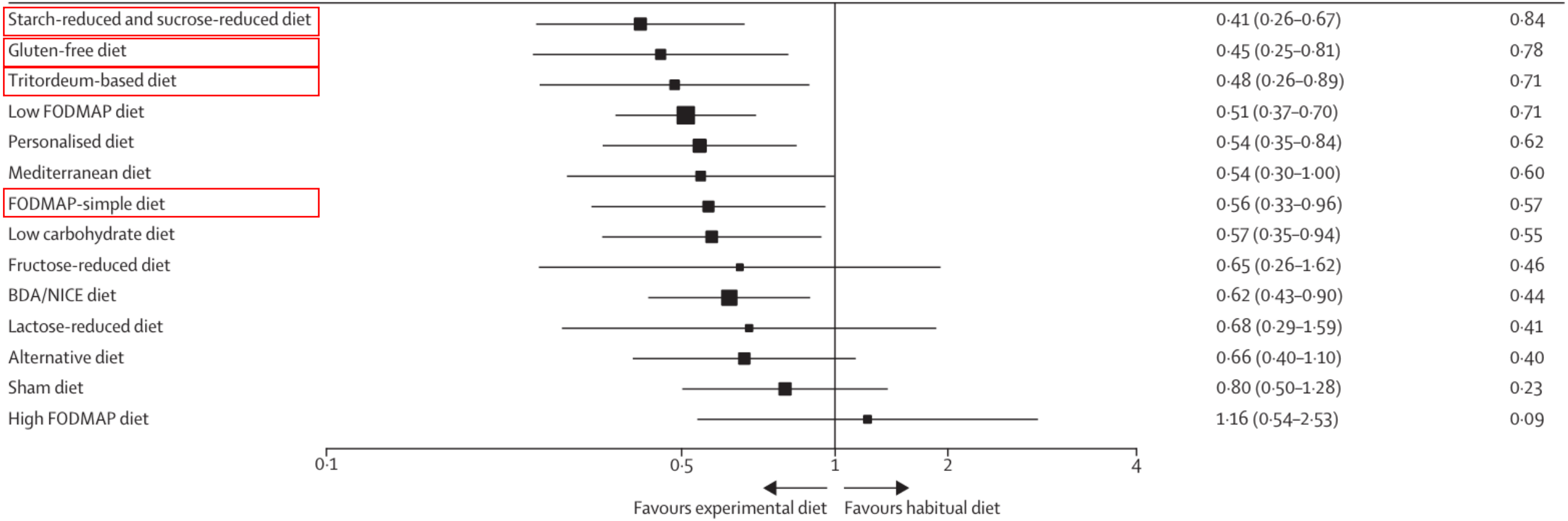


= Few studies, small numbers, consider preliminary

Cuffe MS, Staudacher HM, *et al. Lancet Gastroenterol Hepatol*. 2025 Jun;10(6):520-536.

From super restrictive to back again

- The most robust data is still for the low-FODMAP diet
- However: simplified diets gaining traction for ease, adherence, cost, and decreased risk of unnecessary restriction
  - FODMAP-gentle
  - Mediterranean
  - Gluten-free
- Fructans and mannitol most common triggers among FODMAPs

Table 2 Description of a FODMAP-gentle diet

Food group	High FODMAP foods to restrict on a FODMAP-gentle diet
Grains	Wheat and rye
Vegetables	Onion, leek, cauliflower, and mushrooms
Fruit	Apple, pear, dried fruit, stone fruit, and watermelon
Dairy	Milk and yoghurt
Meat/alternatives	Legumes

FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

Halmos EP, Gibson PR. *J Gastroenterol Hepatol*. 2019 Jul;34(7):1134-1142.
Black CJ, Staudacher HM, *et al. Gut.* 2022 Jun;71(6):1117-1126.

Caveats of dietary interventions in IBS

- Risk of bias in many dietary trials
- Effect of reintroduction/maintenance phase less certain
  - Printed handouts likely to be inadequate
  - Need a qualified dietician
- Caution in patients w/ disordered eating
  - Can reinforce harmful cognitions/ behaviors
  - Look out for ARFID and “orthorexia nervosa”
  - ARFID: Feeding and eating restriction not mediated by shape or weight concerns
  - Orthorexia Nervosa: obsessive focus on food choice with food seen as means of health>pleasure

Could targeted diets be the future of IBS?

- Recent study randomized 238 people to a novel IgG blood test-guided diet vs a sham diet
- Included subjects positive for ≥1 food on an 18-food IgG assay
- Primary endpoint was a 30% reduction in abdominal pain intensity

Food	Number of subjects eliminating food in the experimental arm (N = 118)
Egg	55
Milk	44
Wheat	42
Grapefruit	38
Orange	31
Sugar	29
Lemon	27
Pineapple	27
Cabbage	23
Oat	23
Corn	22
Honey	20
Soybean	20
Cocoa	15
Black tea	14
Walnut	14
Rye	13
Yeast	13

Singh P, Chey WD, *et al*. *Gastroenterology*. 2025 Jan 31:S0016-5085(25)00328-2.

Could targeted diets be the future of IBS?

Table 2. Clinical Outcomes Between Experimental and Sham Diet Groups

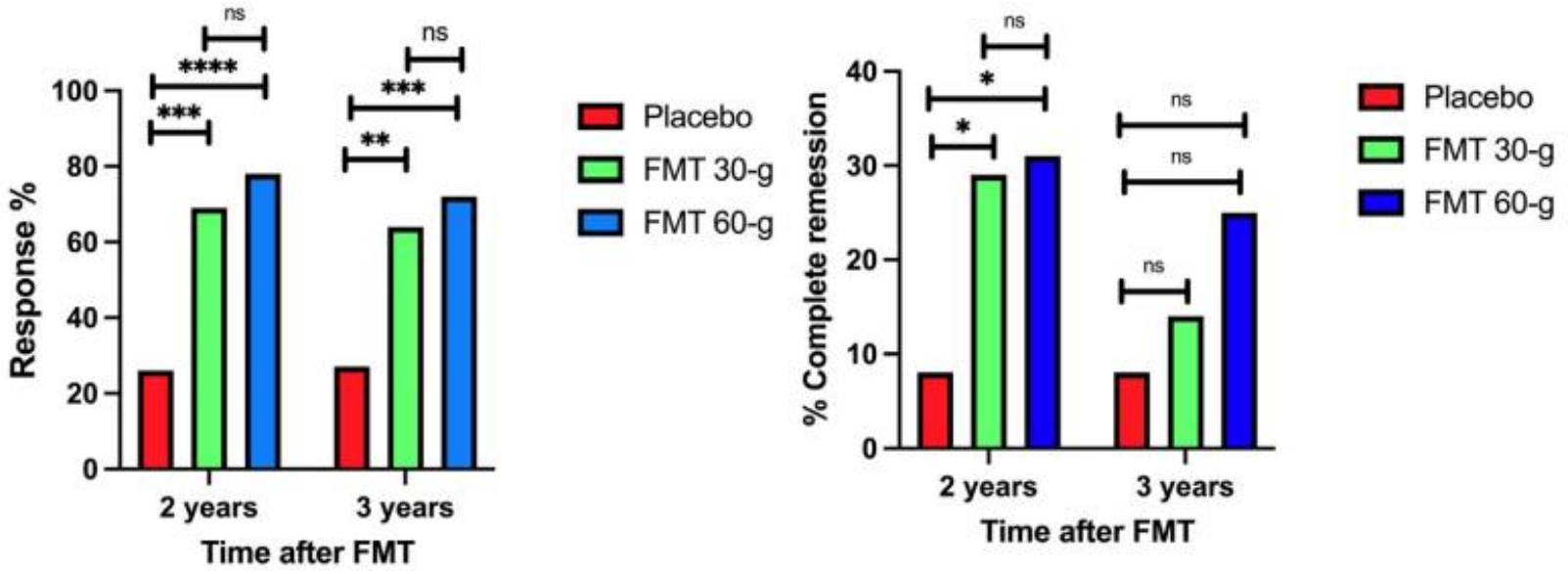
	Experimental diet (n = 118)	Sham diet (n = 105)	Δ	*P* value
		Primary outcome		
30% reduction in API	70 (59.6%)	44 (42.1%)	17.5% (2.6, 32.5)	0.02
		Secondary outcomes		
IBS-API[a]	−1.3 (0.24)	−0.9 (0.23)	−0.4 (0.24) (−0.9, 0.0)	NA
Bloating[a]	−1.2 (0.25)	−0.8 (0.25)	−0.5 (0.26) (−1.0, 0.1)	NA
IBS-SSS[a]	−84.1 (13.72)	−64.5 (13.29)	−19.6 (12.21) (−43.7, 4.5)	NA
IBS-AR	68 (57.5%)	49 (46.8%)	10.7% (−0.5, 21.9)	NA
IBS-GIS[a]	1.4 (0.20)	1.0 (0.19)	0.4 (0.17) (0.0, 0.7)	NA
SGA	21 (18.1%)	9 (8.8%)	9.3% (−270.6%, 289.2%)	NA
50-point reduction in IBS-SSS	62.9%	50.6%	12.3% (−31.9%, 56.5%)	NA
100-point reduction in IBS-SSS	22.8%	18.2%	4.6% (−315.3%, 324.5%)	NA
Days with normal bowel movement per week (BSS ≥3 and ≤5)	63.9 (54.2%)	49 (47.0%)	7.20% (−8.5%, 23.0%)	NA

Estimates are from repeated-measures models adjusted for treatment (experimental vs control), number of food sensitivities (<7, ≥7), IBS type (IBS-D, IBS-C, IBS-M), age, gender, site, baseline RPSQ, baseline IBS-SSS, time, and the time × treatment interaction was used. Random effects for subjects were used to account for the correlation among repeated measures in the same individuals.

Singh P, Chey WD, *et al*. *Gastroenterology*. 2025 Jan 31:S0016-5085(25)00328-2.

Fecal microbiota transplant for IBS

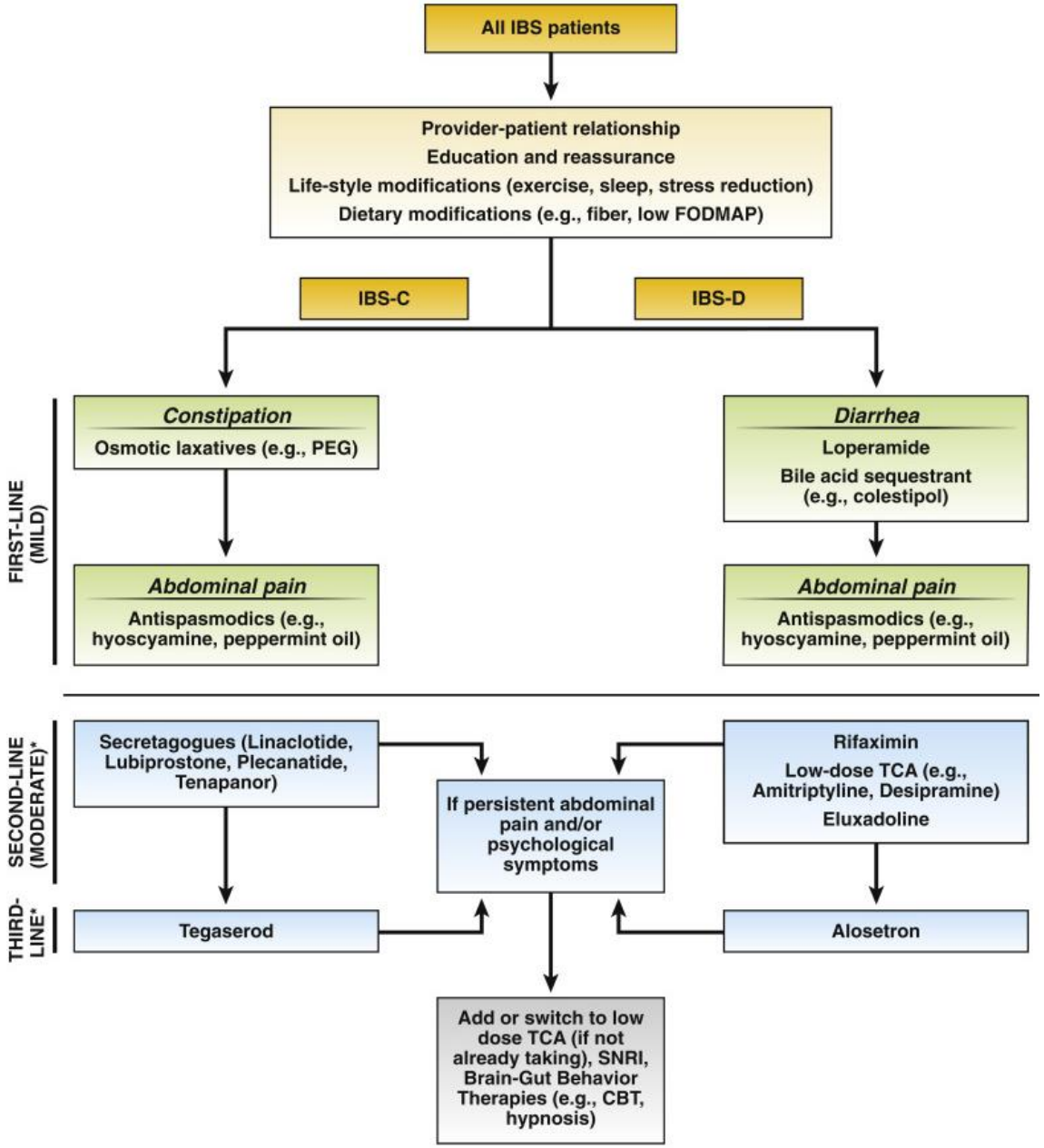
- FMT trials for IBS have been mixed
- Recent long-term trial results:
  - Patients with IBS receiving FMT continued to have fewer abdominal symptoms and fatigue and a better QOL than before procedure
  - 3 years after FMT: the response rate was 64.9% in 30g group, 71.8% in 60g group, vs. 27% in the placebo group



El-Salhy, M, Winkel R, et al. Gastroenterology. 2022 Oct;163(4):982-994.e14.

Thinking about pharmacologic treatments for IBS

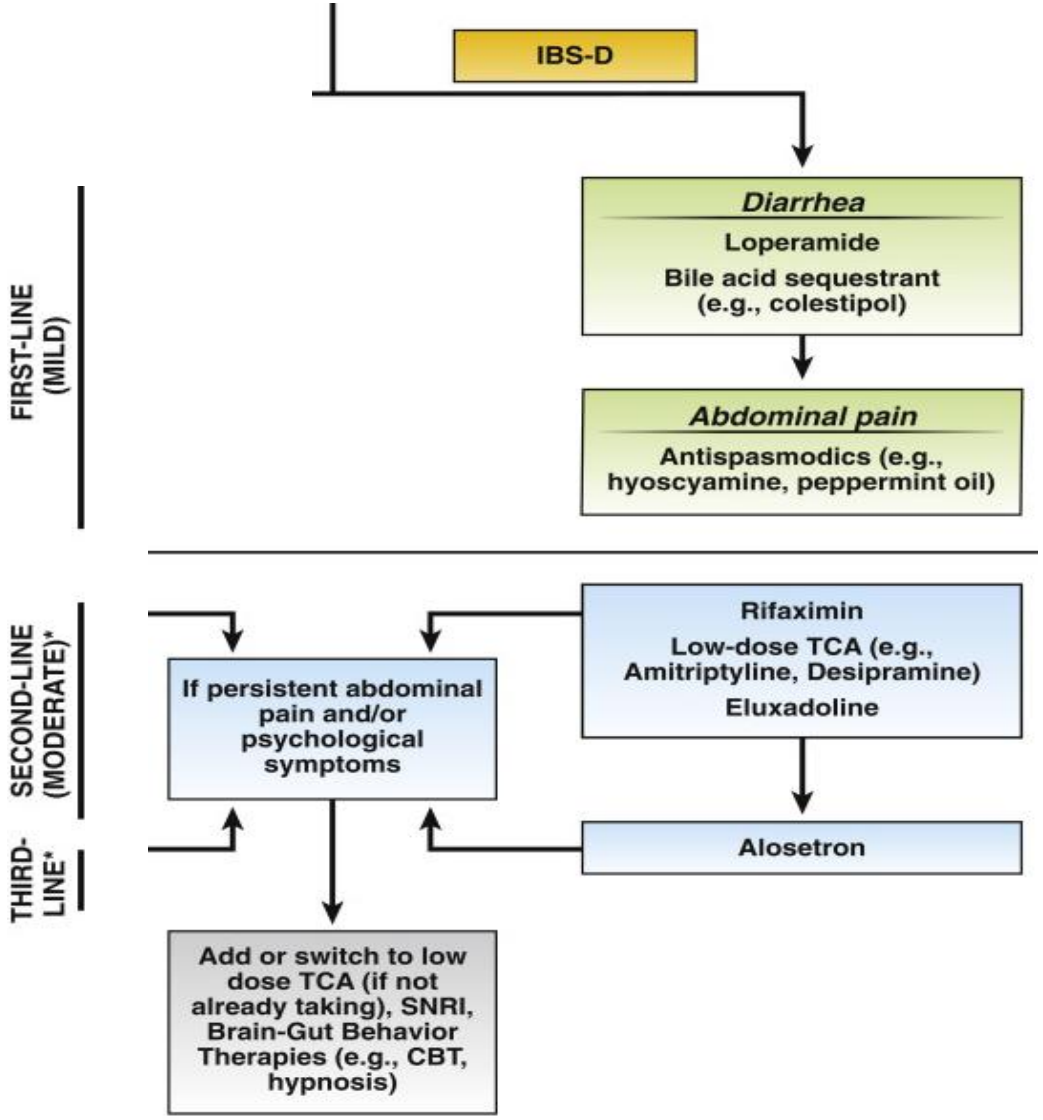
https://gastro.org/clinical-guidance/pharmacological-management-of-irritable-bowel-syndrome-with-diarrhea-ibs-d/



*Selection of the medication should be based on the clinical features and needs of the patient.

TCA, tricyclic antidepressant; SNRI, serotonin-norepinephrine reuptake inhibitor; PEG, polyethylene glycol; CBT, cognitive behavioral therapy

Latest US guidelines for the pharmacologic treatment of IBS-D



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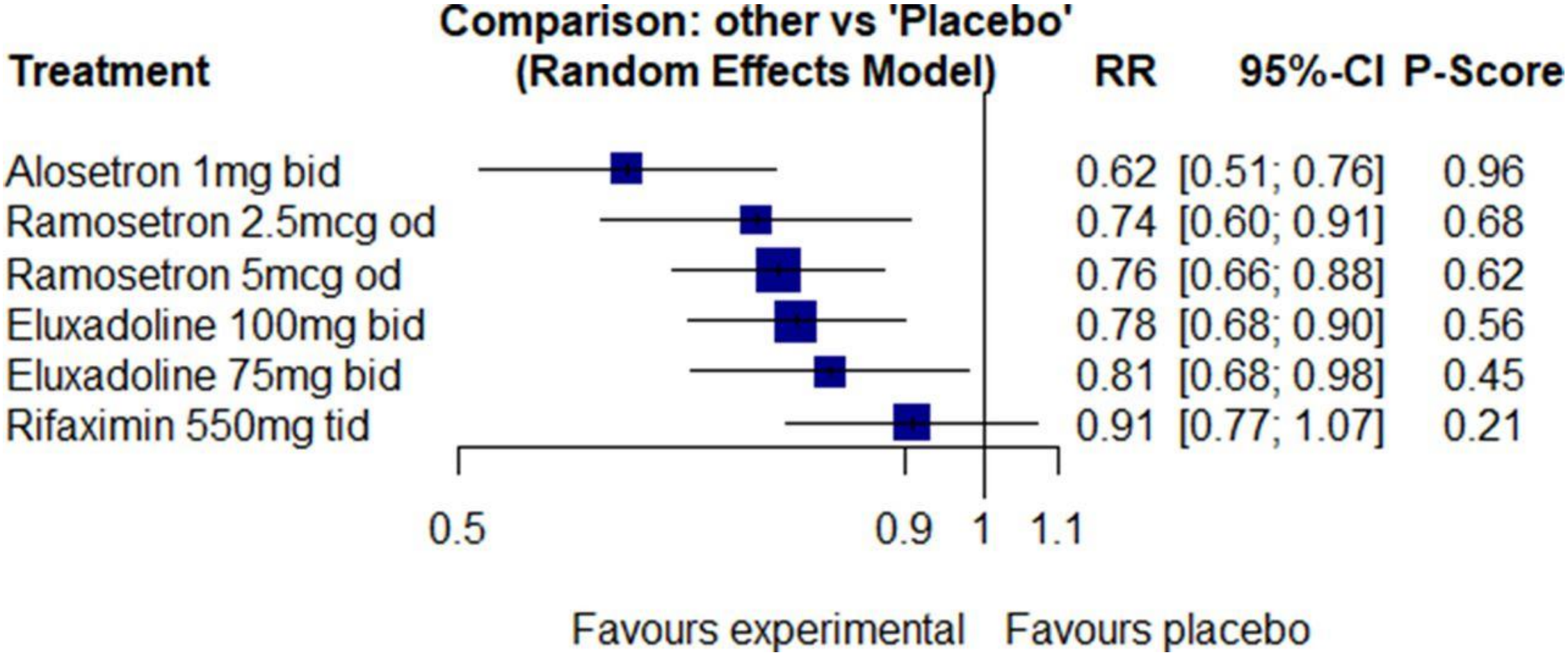
TCA, tricyclic antidepressant; SNRI, serotonin-norepinephrine reuptake inhibitor; PEG, polyethylene glycol; CBT, cognitive behavioral therapy

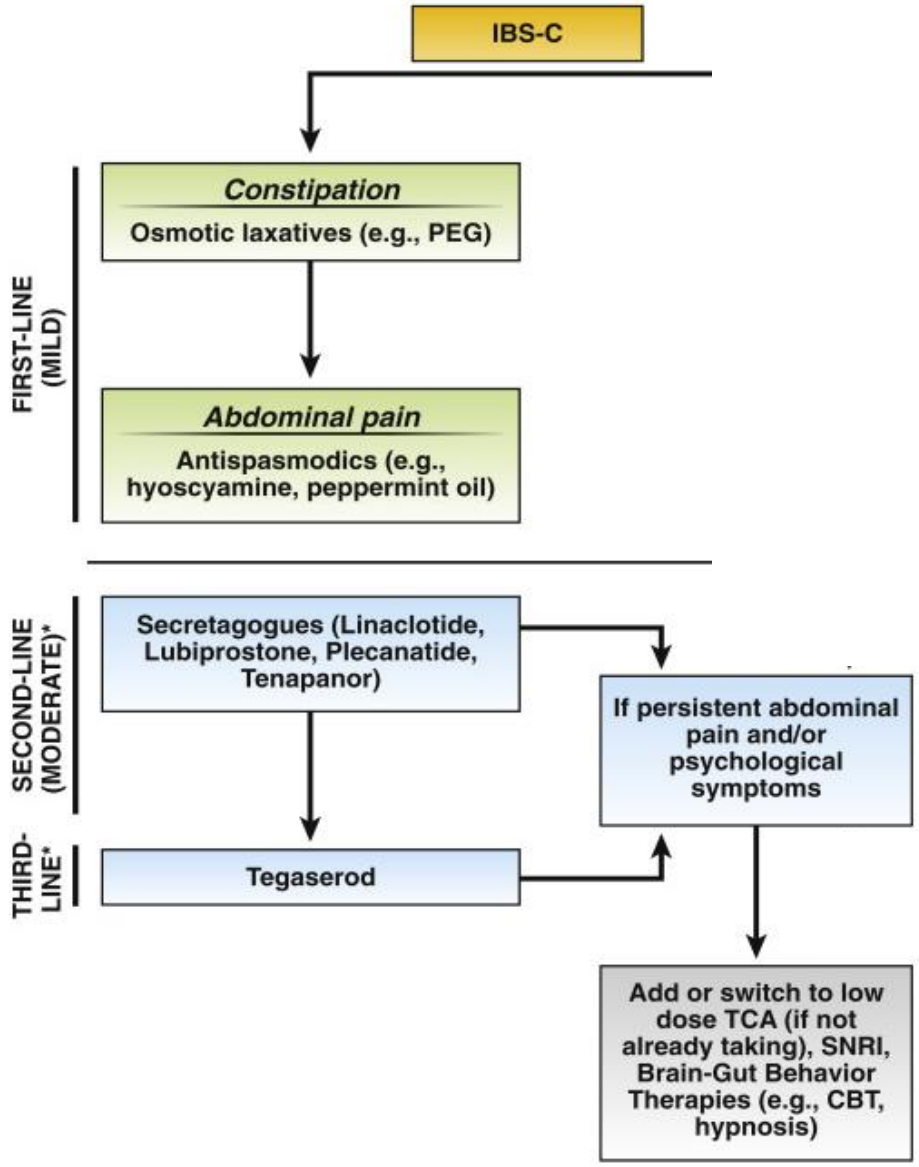
https://gastro.org/clinical-guidance/pharmacological-management-of-irritable-bowel-syndrome-with-diarrhea-ibs-d/

Comparative evidence of approved IBS-D therapies



Black CJ, Burr NE, et al. *Gut*. 2020 Jan;69(1):74-82.

Latest US guidelines for the pharmacologic treatment of IBS-C

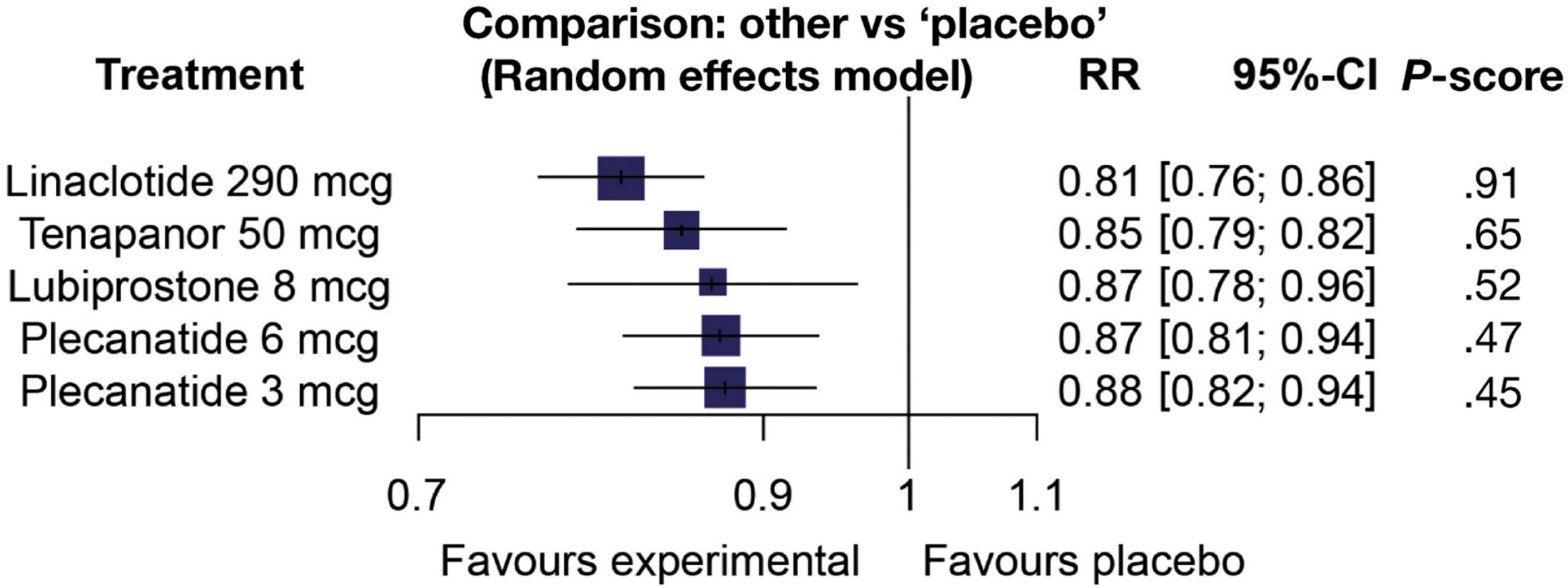


*Selection of the medication should be based on the clinical features and needs of the patient.

TCA, tricyclic antidepressant; SNRI, serotonin-norepinephrine reuptake inhibitor; PEG, polyethylene glycol; CBT, cognitive behavioral therapy

https://gastro.org/clinical-guidance/pharmacological-management-of-irritable-bowel-syndrome-with-diarrhea-ibs-d/

Comparative evidence of approved IBS-C therapies



Black CJ, Burr NE, et al. *Gastroenterology.* 2018 Dec;155(6):1753-1763.

There are now quality indicators for IBS care: treatment

Quality Indicators:

- Treatment with alosetron, eluxadoline, rifaximin, or tricyclic antidepressants (TCAs) should be considered in patients with IBS-D
- Treatment with linaclotide, lubiprostone, plecanatide, tenapanor, or TCAs should be considered in patients with IBS-C
- Avoidance of centrally acting opioids for IBS-related pain
- Recognition of the brain–gut axis and performance or referral for brain–gut behavior therapies, such as cognitive behavioral therapy or gut-directed hypnotherapy
- Dietary counseling (eg, increased soluble fiber or low fermentable oligo-, di-, mono-saccharide and polyol [FODMAP] diet) or referral to a dietitian

Hung KW, Leiman DA, *et al. Gastroenterology*. 2025 Mar;168(3):612-622.e4.

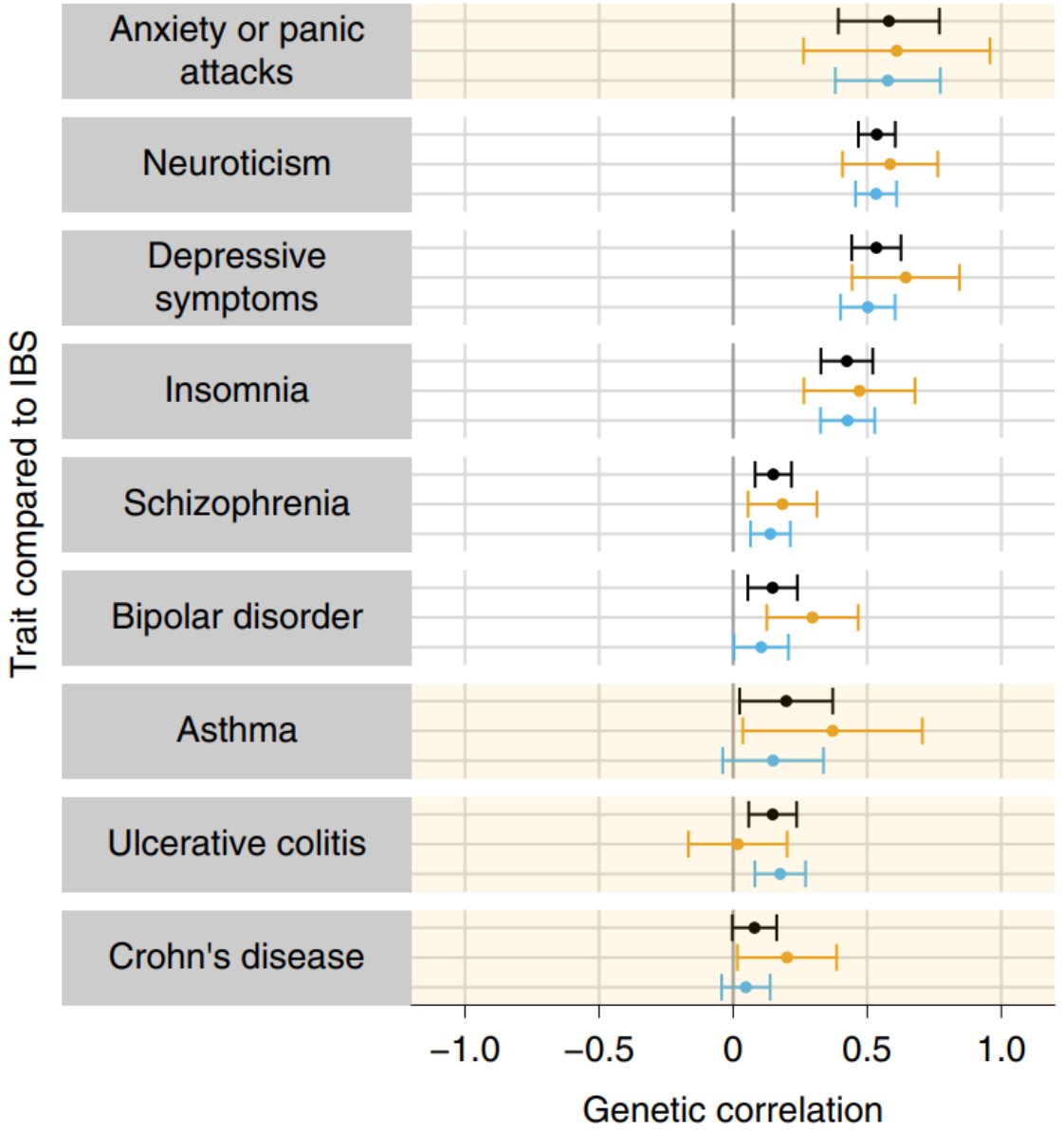
Rationale and use of neuromodulators

IBS and psychological disease: chicken or egg?

Genetic correlation between IBS and anxiety

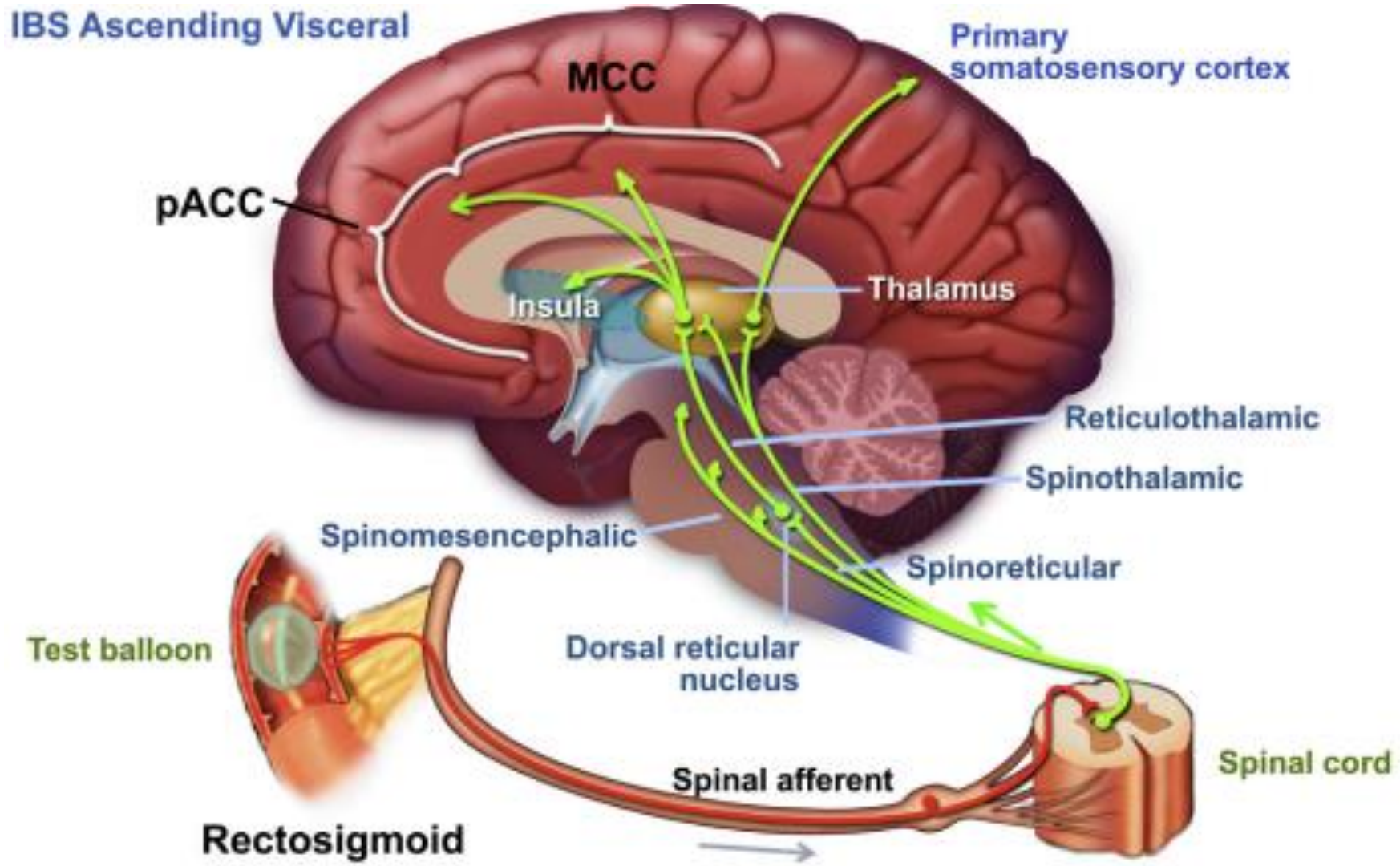
Association remained even after removing those with overlap

Suggests shared etiology rather than one condition causing the other



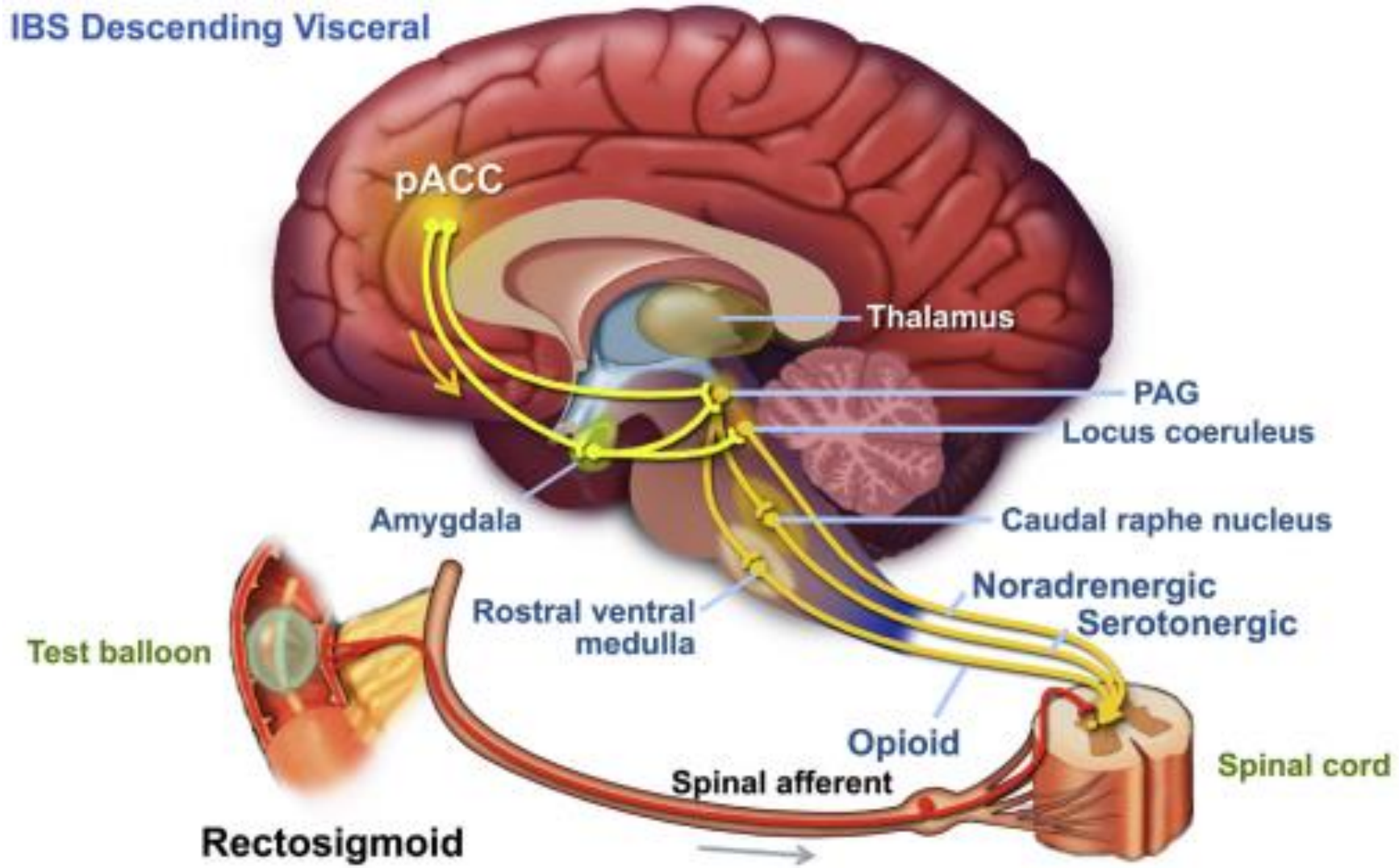
Eijsbouts C, Zheng T *et al. Nat Genet.* 2021 Nov;53(11):1543-1552.

How sensory signals from the colon reach consciousness: ascending pathways



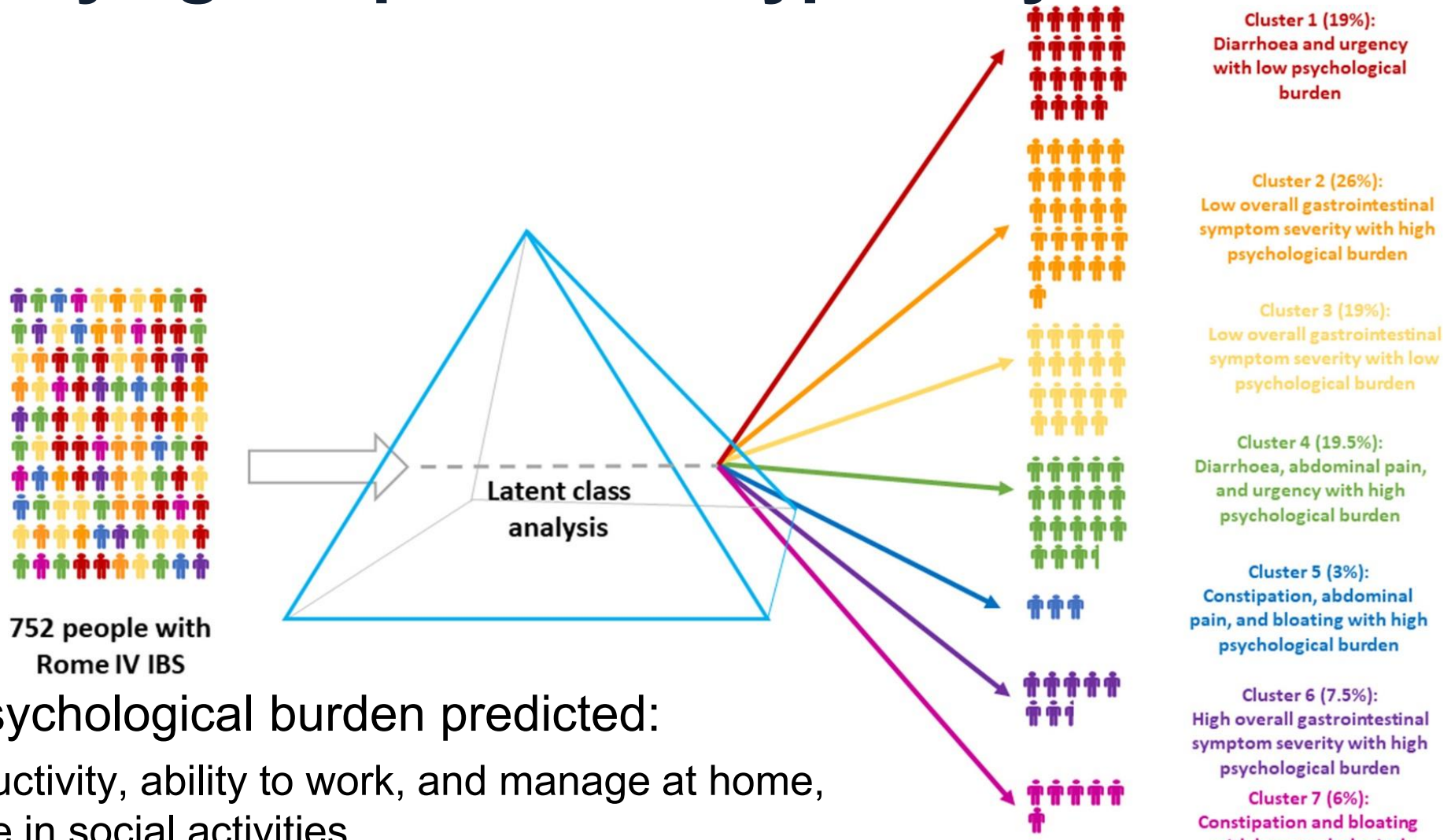
Drossman DA, Tack J, et al. *Gastroenterology.* 2018 Mar;154(4):1140-1171.e1.

How sensory signals from the colon reach consciousness: descending pathways



Drossman DA, Tack J, et al. *Gastroenterology.* 2018 Mar;154(4):1140-1171.e1.

Identifying IBS patient subtypes beyond stool form

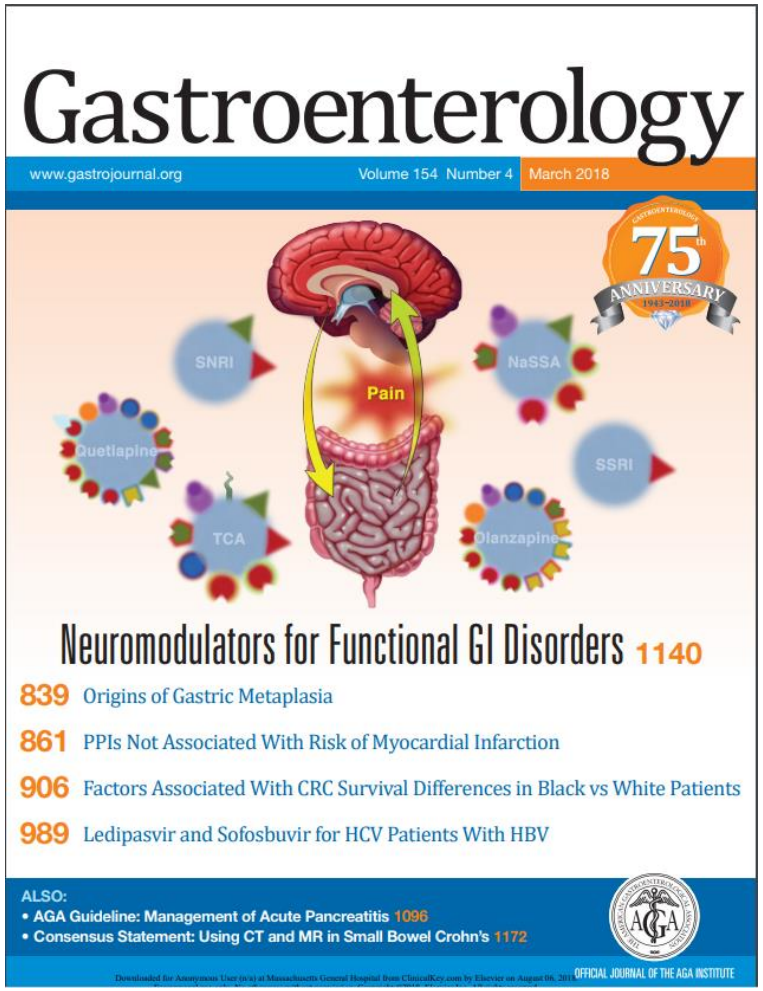


- High psychological burden predicted:
  - ↓ productivity, ability to work, and manage at home, engage in social activities
  - ↑ healthcare costs over previous 12 months

CJ Black, Ng C, *et al*. *Clin Gastroenterol Hepatol.* 2024 Feb;22(2):386-396.e10.

Use of neuromodulators in IBS

- Many patients have improved bowel frequency on laxatives, but bloating/abdominal pain remain
- Neuromodulators reduce global IBS symptoms and pain in IBS patients
- Potential benefits:
  - Reduction in pain/?bloating
  - Treatment of psychological distress and comorbid psychiatric disease
  - Leverage motility effects
  - Long-term treatment may reverse maladaptive brain-gut axis changes



Khasawneh M, Mokhtare M, *et al. Lancet Gastroenterol Hepatol*. 2025 Jun;10(6):537-549.

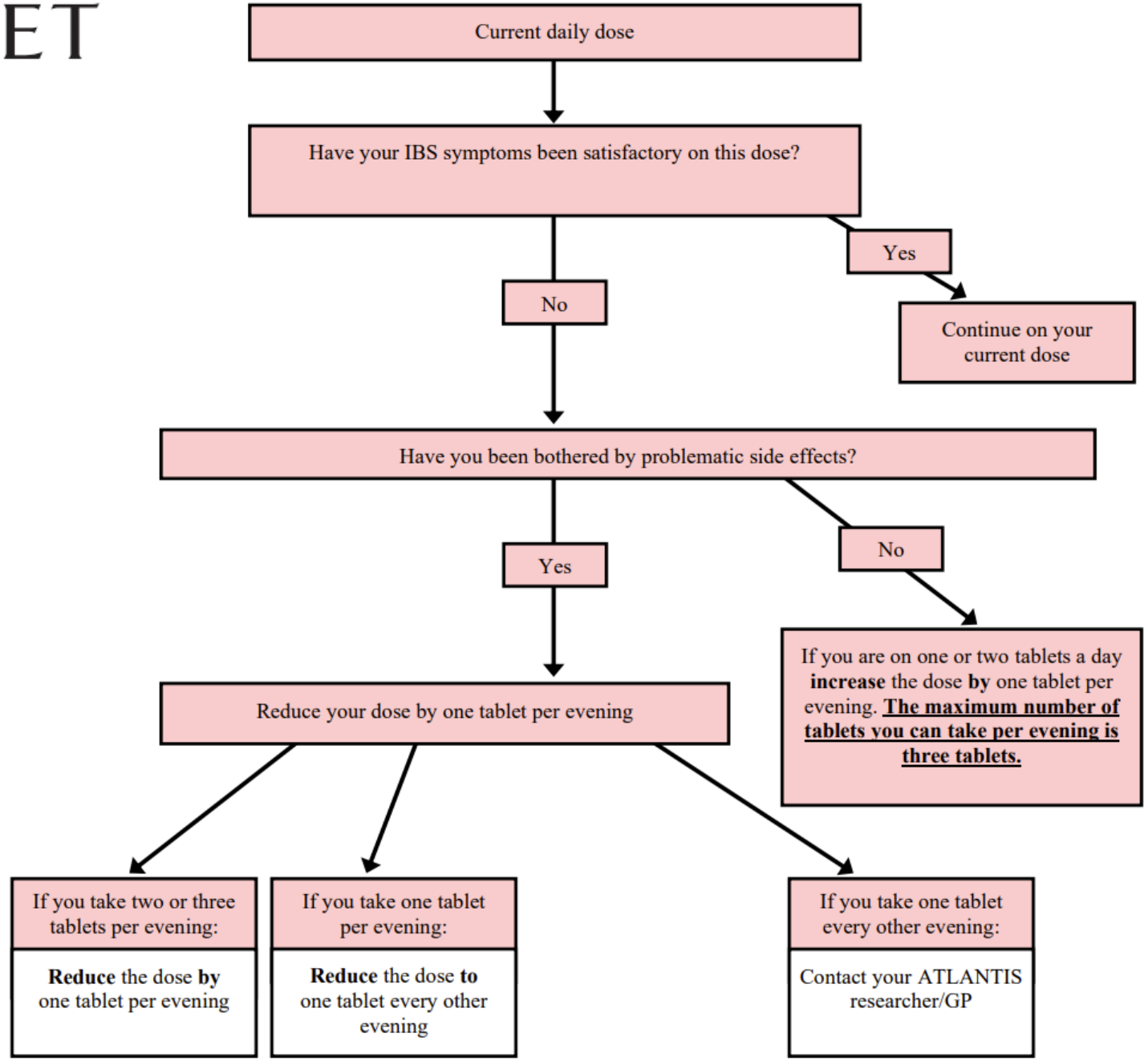
Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in primary care (ATLANTIS): a randomised, double-blind, placebo-controlled, phase 3 trial

THE LANCET

- Amitriptyline, self-titrated between doses of 10-30 mg at bedtime vs placebo
- Inclusion criteria:
  - Active IBS of any subtype followed in primary care
  - Normal labs (Hemoglobin, platelets, CRP, celiac serology)
  - Tried first-line treatments without success:
    - Dietary changes and lifestyle advice
    - Soluble fiber
    - Antispasmodics
    - Laxatives
    - Antidiarrheals

Ford AC, Wright-Hughes A, et al. *Lancet*. 2023 Oct 16:S0140-6736(23)01523-4.

THE LANCET



Ford AC, Wright-Hughes A, et al. *Lancet*. 2023 Oct 16:S0140-6736(23)01523-4.

THE LANCET

Amitriptyline at Low-Dose and Titrated for Irritable Bowel Syndrome as Second-Line Treatment in primary care (ATLANTIS): a randomised, double-blind, placebo-controlled, phase 3 trial

Outcomes	Mean scores		Between-group difference (95% CI) at 6 mo	
	Amitriptyline	Placebo		
IBS-SSS†	170.4	200.1	-27.0 (-46.9 to -7.1)	
	Event rates		RBI (CI)‡	NNT (CI)‡
Relief of IBS symptoms§	61%	45%	32% (10 to 52)	7 (5 to 24)
Amitriptyline increased treatment-emergent adverse events (mean ASEC‖ scores) at 3 mo (9.9 vs. 8.4, $P = 0.013$) but not at 6 mo (9.3 vs. 8.7, $P = 0.68$).				

ASEC = Antidepressant Side Effect Checklist; IBS = irritable bowel syndrome; IBS-SSS = Irritable Bowel Syndrome Severity Scoring System; other abbreviations defined in Glossary. Primary outcome indicated by boldface.
†Score range, 0 to 500 (more severe symptoms). Negative between-group difference favors amitriptyline.
‡RBI, NNT, and CI calculated from placebo event rate and odds ratio in article.
§Self-report of symptoms being at least somewhat relieved on the subjective global assessment.
‖Score range, 0 to 63 (worst).

Bottom line:
In primary care patients with IBS, second-line therapy with amitriptyline vs. placebo reduced symptoms at 6 months.

- Amitriptyline increased treatment-emergent AEs at:
  - 3 months (9.9 vs 8.4, *P*=0.013)
  - But not 6 months (9.3 vs. 8.7, *P*=0.68)
- AEs mostly anticholinergic
- Most aside effects mild and these pts still completed 6 months of treatment

Ford AC, Wright-Hughes A, et al. *Lancet*. 2023 Oct 16:S0140-6736(23)01523-4.
Gupta T, Cash BD. *Ann Intern Med*. 2024 Feb;177(2):JC15. doi: 10.7326/J23-0122.

Prescribing neuromodulators smartly

- Overall efficacy
  - TCAs most effective for global IBS symptoms
  - SSRIs should be a second-line agent or a first-line agent in pts w/ comorbid anxiety, depression, social anxiety
  - SNRIs extensively studied for fibromyalgia and diabetic neuropathy but can be useful in IBS-C or in those who failed TCA trial
- Start with low dose and titrate slowly
- Secondary amines (nortriptyline, desipramine) better tolerated than tertiary amines (amitriptyline, imipramine)

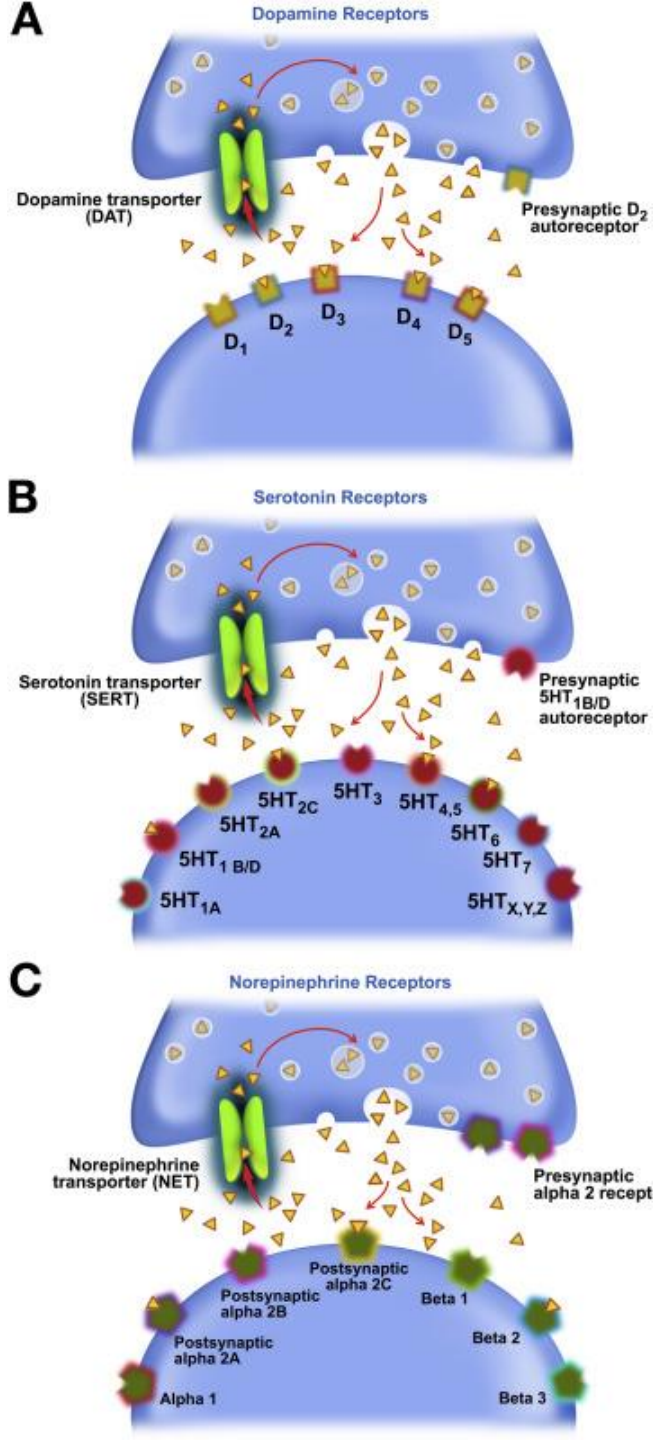
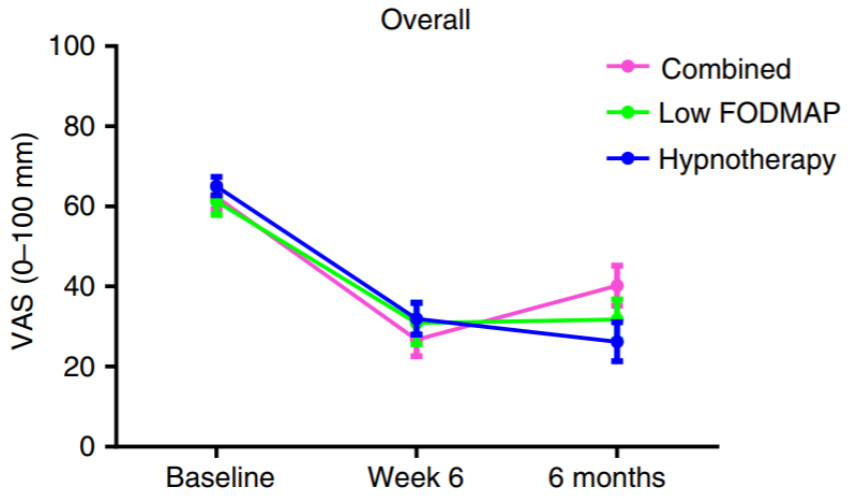


Image from: Mearin F, Lacy BE. *Gastroenterology.* 2016; Feb 15; 150:1393-1407.
Sobin WH, Heinrich TW, et al. Am J Gastroenterol. 2017 May;112(5):693-702.

Psychological therapies improve IBS symptoms

- Psychosocial therapies have been shown to be effective in improving IBS symptoms
- Cognitive behavioral therapy (CBT)
  - Multiple studies suggesting efficacy
- Gut hypnotherapy:
  - Positive data from a multicenter RCT with 6 sessions of group or individual treatments
  - Benefits up to 12 months
- Use limited by lack of skilled therapists in managing IBS
  - Digital apps may fill the gap, but market evolving



Flik CE, Laan W, *et al. Lancet Gastroenterol Hepatol.* 2019 Jan;4(1):20-31.
Peters SL, Yao CK, *et al. Aliment Pharmacol Ther.* 2016 Sep;44(5):447-59.

What type of IBS patient am I seeing today?

Clinical feature	Mild (40%)	Moderate (35%)	Severe (25%)
Physiological factors	Primarily bowel dysfunction	Bowel dysfunction and CNS pain dysregulation	Primarily CNS pain dysregulation
Psychosocial	None or mild psychosocial distress	Moderate psychosocial distress	Severe–high psychosocial distress, catastrophizing, abuse history
Sex	Men = women	Women > men	Women >>> men
Age	Older > younger	Older = younger	Younger > older
Abdominal pain	Mild/intermittent	Moderate, frequent	Severe/very frequent or constant
Number of other symptoms	Low (1–3)	Medium (4–6)	High (≥7)
Health-related quality of life	Good	Fair	Poor
Health care use	0–1/y	2–4/y	≥5/y
Activity restriction	Occasional (0–15 days)	More often (15–50 days)	Frequent/constant (>50 days)
Work disability	<5%	6%–10%	≥11%

Adapted from Drossman DA. *Gastroenterology.* 2016; 150(6): 1262-1279.

How I explain IBS

- Visceral hypersensitivity
  - Normal gut sensations improperly amplified in PNS and CNS
  - Abnormal sensory response to normal physiologic processes
- Treatment is a “3-legged stool”
  1. Motility agents (laxatives, anti-diarrheals)
  2. Dietary changes, fiber
  3. Leverage the brain-gut connection

  Neuromodulators Cognitive behavioral therapy
  Gut hypnotherapy
- Investing time up front can pay dividends later on

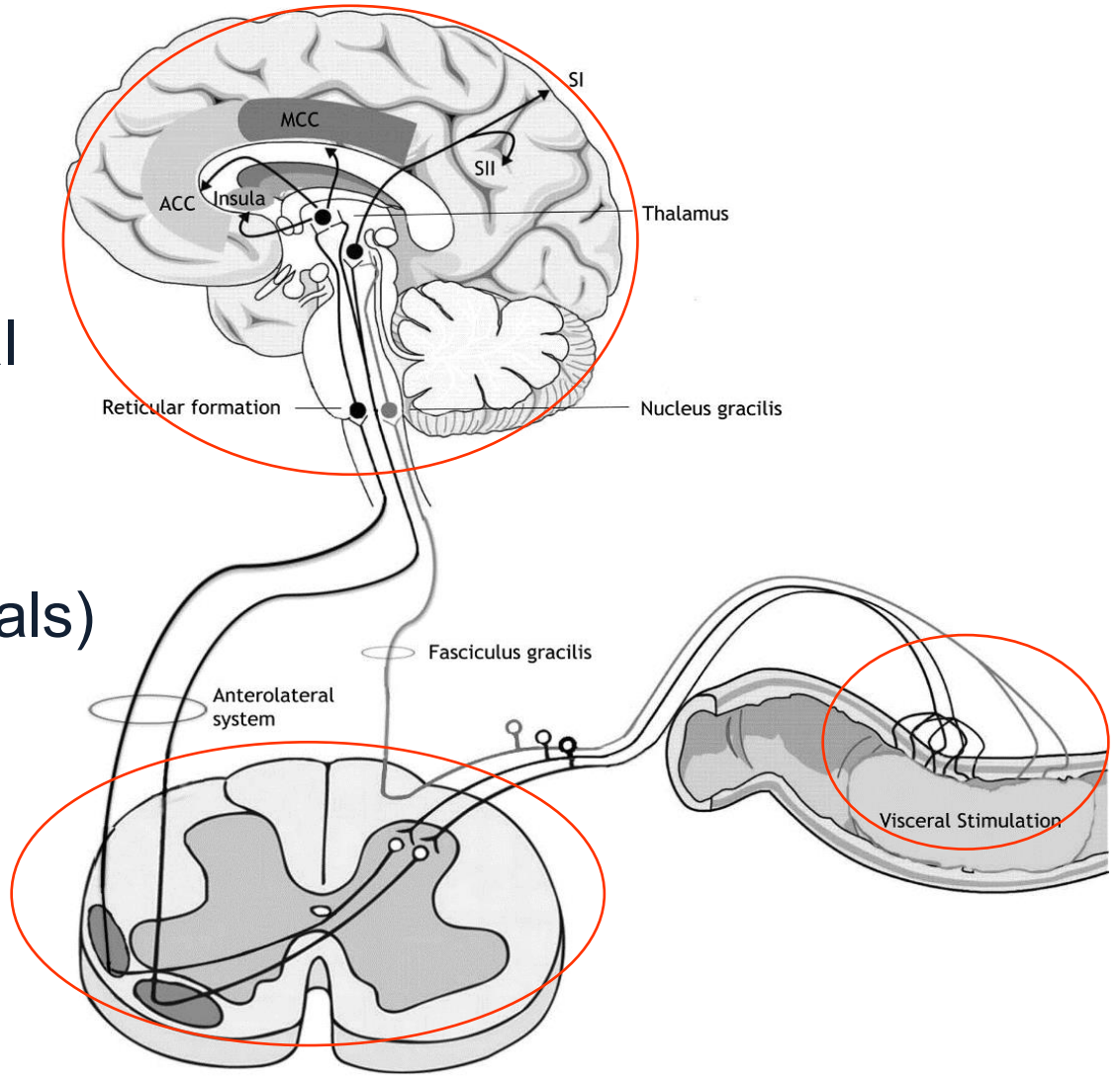


Figure adapted from Keszthelyi D, Troost FJ, *et al. Am J Physiol Gastrointest Liver Physiol.* 2012 Jul 15;303(2):G141-54.

Summary

1. IBS has a specific definition: use it
2. Most IBS does not need a colonoscopy, but know the IBS mimickers
3. The low-FODMAP diet is powerful, but other diets may be easier and less harmful in the long run
4. Evidence for FMT is still limited
5. IBS is fundamentally a disorder of brain-gut interaction; neuromodulators can and should be used early
6. Brain-gut behavioral therapies are now available digitally

- IBS overview: Camilleri M. *JAMA*. 2021 Mar 2;325(9):865-877.
- IBS and mental health management: Staudacher HM, Black CJ, *et al*. *Nat Rev Gastroenterol Hepatol*. 2023 Sep;20(9):582-596.
- Using neuromodulators: Sobin WH, Heinrich TW, Drossman DA. *Am J Gastroenterol*. 2017;112(5):693-702.

Thank you