

# 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



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# 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
  - Probiotics
  - Fecal Microbiota Transplant

# Defining and diagnosing irritable bowel syndrome



# Irritable Bowel Syndrome: Rome IV Criteria

**Does the patient have recurrent abdominal pain at least 1 d per week (on average) in the last 3 mo associated with two or more of the following?**

- Onset of symptoms related to defecation
- Onset of symptoms associated with a change in frequency of stool
- Onset of symptoms associated with a change in form of stool

Yes

**Were the above criteria fulfilled for the last 3 mo with symptom onset at least 6 mo prior?**

No

No

**Does not meet IBS diagnostic criteria. Consider an alternate diagnosis.**

Yes

**IBS diagnostic criteria met. What is the predominant stool form?**

**Diarrhea**  
(Bristol type 5 or 6)

**Constipation**  
(Bristol type 1 or 2)

**Mixed**  
(Bristol type 1–2 and 5–6)

**IBS-D**

**IBS-C**

**IBS-M**

# 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



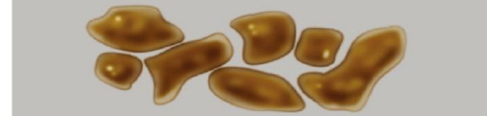
Like a sausage but with cracks on the surface

Type 4



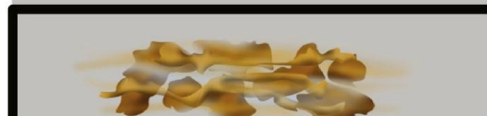
Like a sausage or snake, smooth and soft

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



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

## All IBS Subtypes

CBC

Age-appropriate CRC screening

### IBS-D

- CRP or fecal calprotectin
- IgA TtG ± quantitative IgA
- If colonoscopy performed, obtain random biopsies to rule out microscopic colitis
- Consider SeHCAT, fecal bile acids, or serum C<sub>4</sub> where available

### IBS-M

- CRP or fecal calprotectin
- IgA TtG ± quantitative IgA to rule out celiac disease
- Stool diary
- Consider abdominal plain film to assess for fecal loading

### IBS-C

- If severe or medically refractory, refer to specialist for physiologic testing
- Consider abdominal plain film to assess for fecal loading

### \*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.

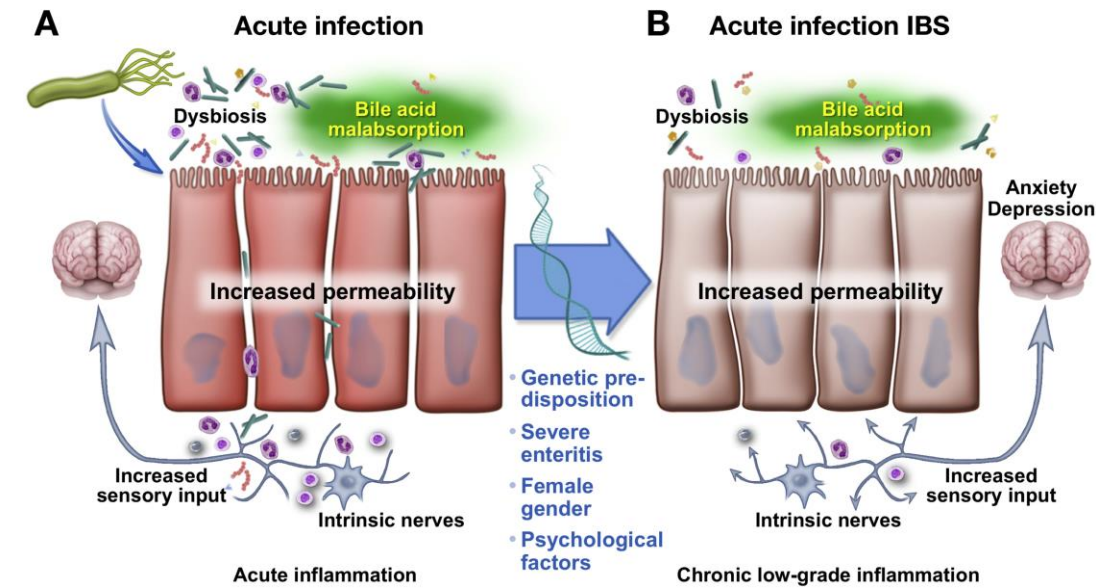


# Conditions potentially associated with IBS

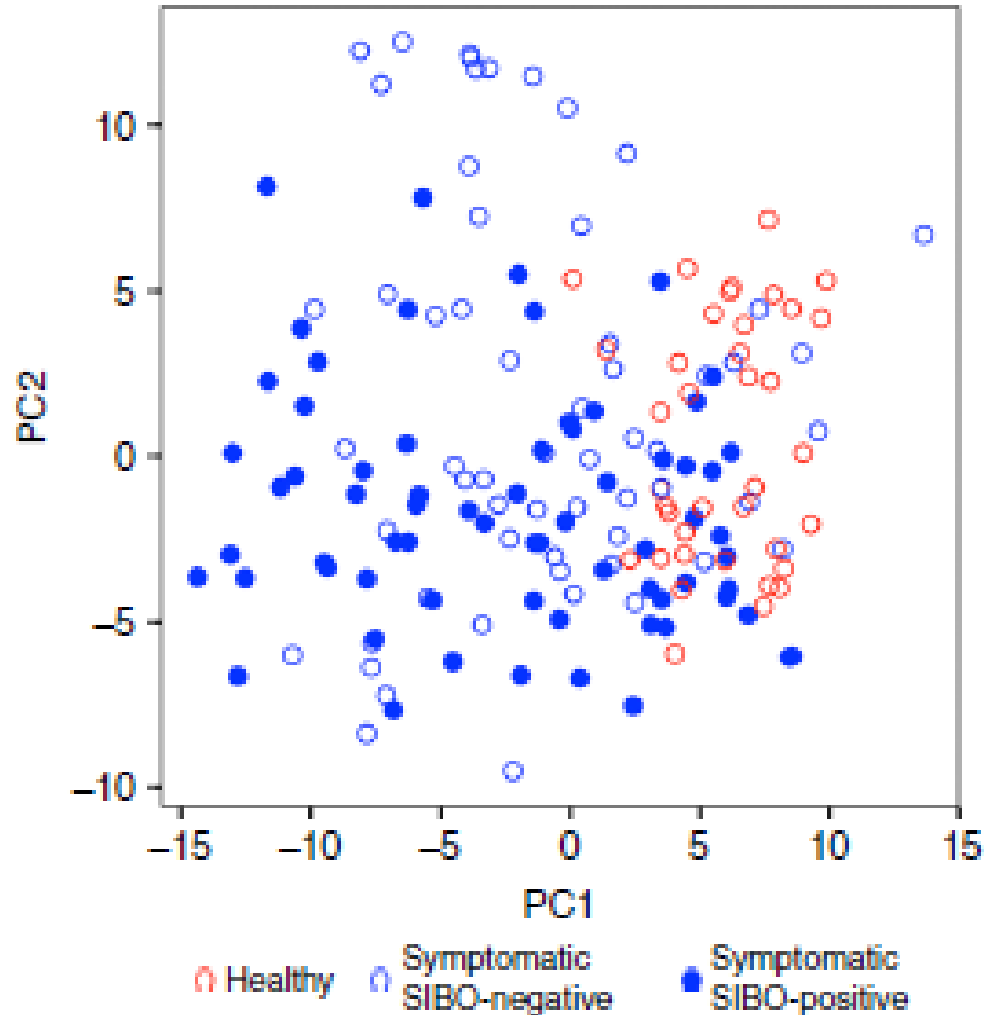


# Post-infection IBS

- 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

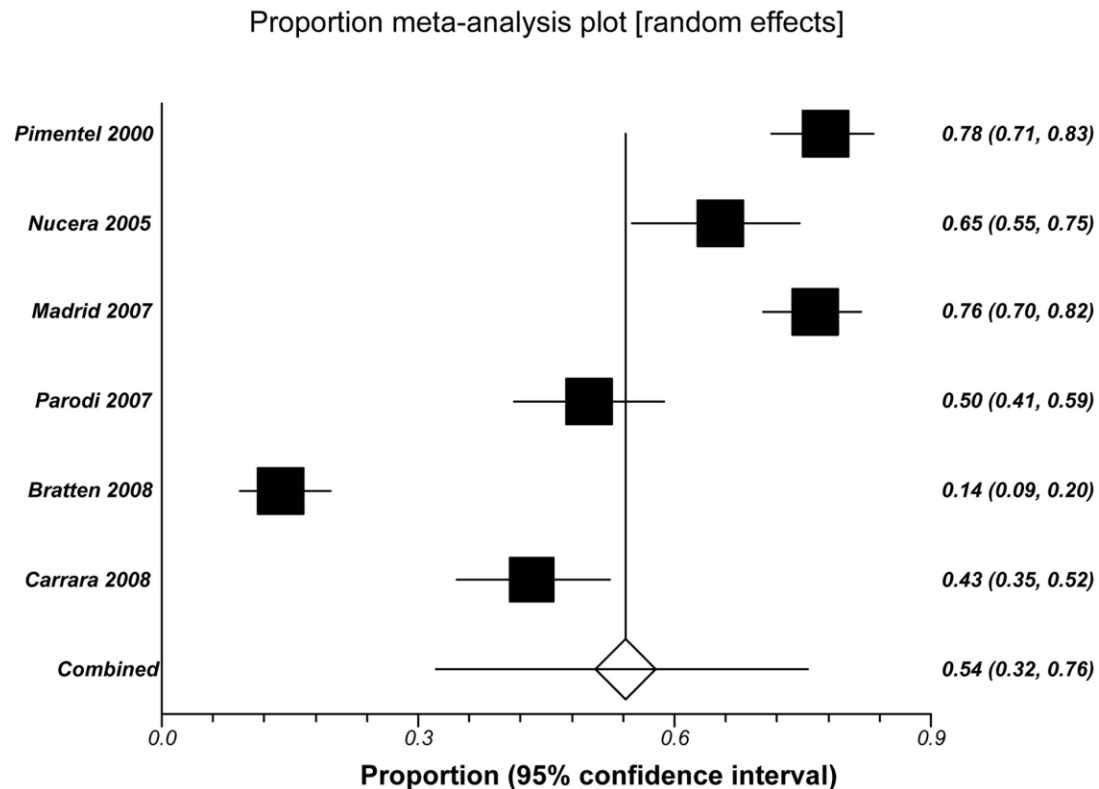


# What about small intestinal bacterial overgrowth (SIBO)?



- 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

# Rates of SIBO in IBS

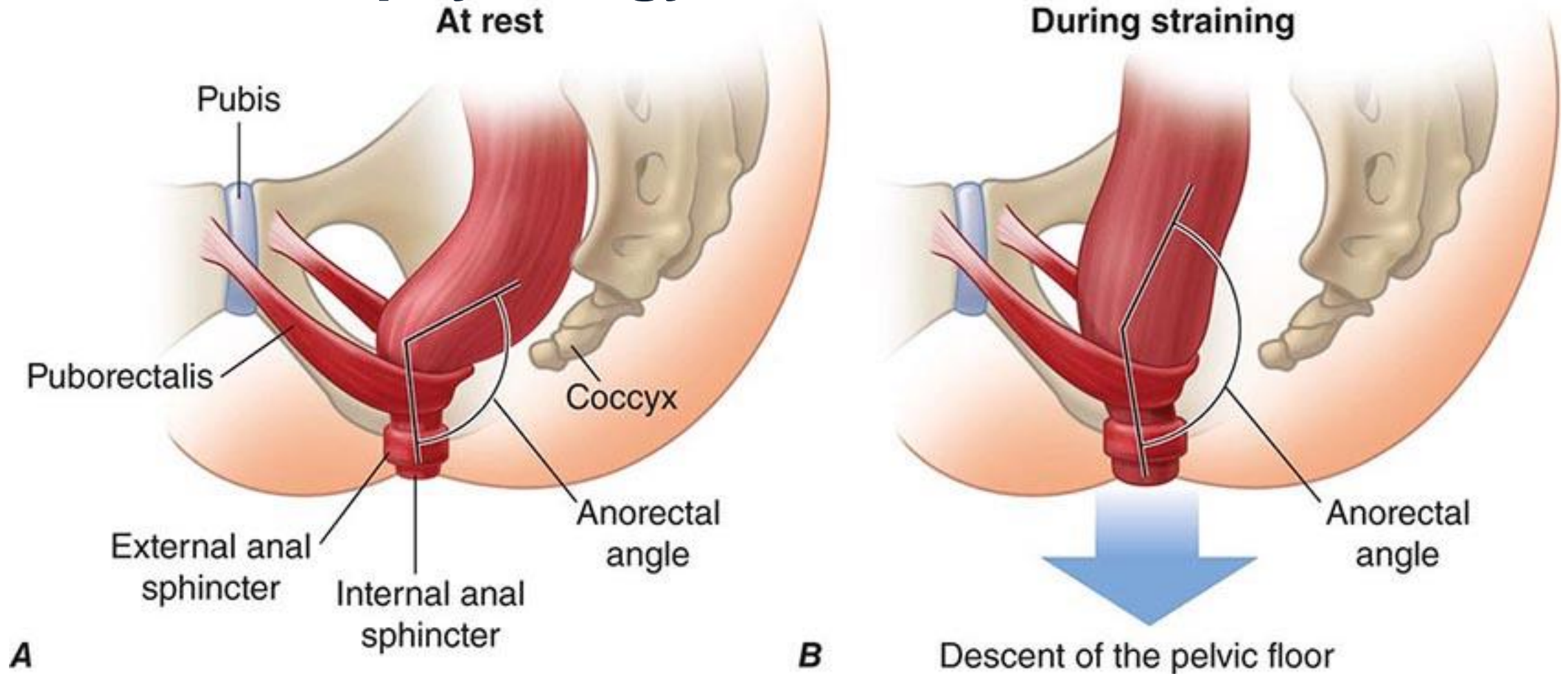


## AGA Clinical Practice Update on Small Intestinal Bacterial Overgrowth: Expert Review

Eamonn M. M. Quigley,<sup>1</sup> Joseph A. Murray,<sup>2</sup> and Mark Pimentel<sup>3</sup>

“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

# **Dietary treatments for irritable bowel syndrome**





# Fiber!



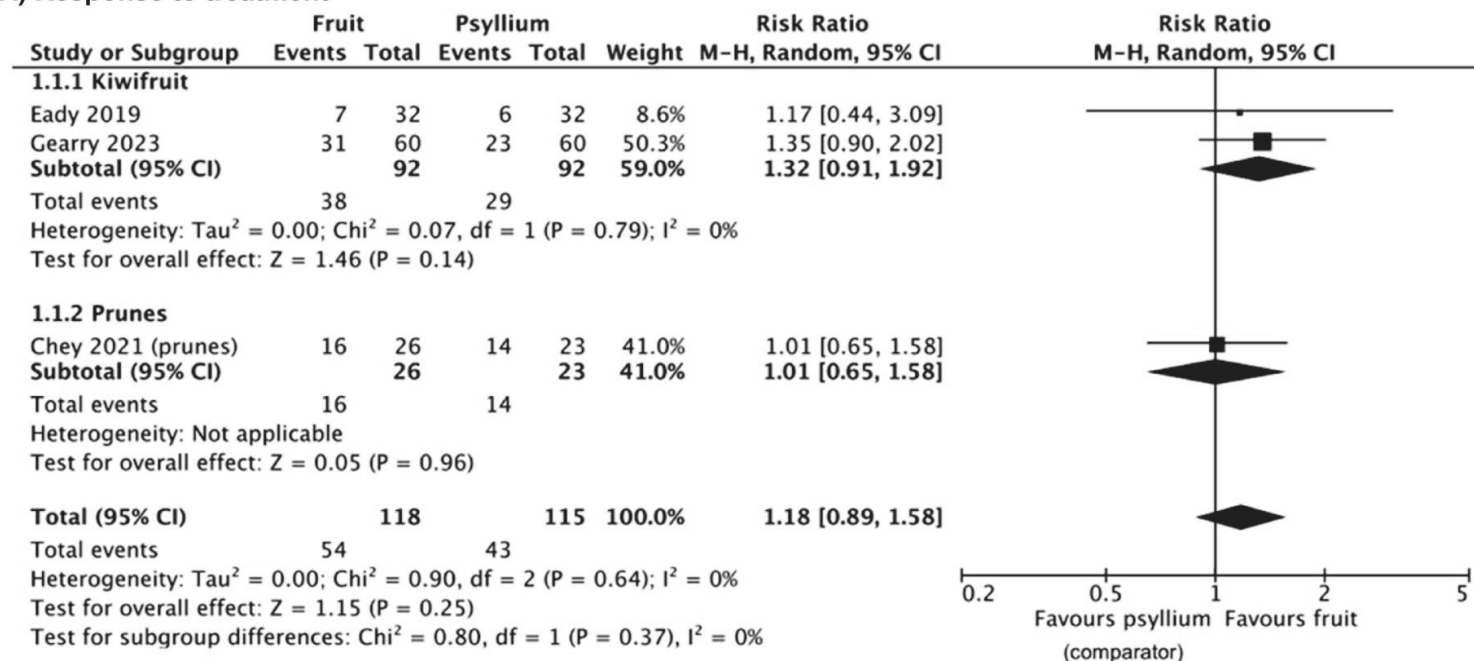
- Why not just eat more fiber?
- Psyllium has the best evidence in IBS for *both* diarrhea and constipation
  - ↑ stool bulk and normalizes colon transit (speeds up or slows down)
  - Slowly fermented
  - Doses: 7.5-22 g/day (1 teaspoon = 5.8g)
- Methylcellulose can be useful in constipation
  - Speeds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



# **“Natural” treatments for constipation: fruits**

# Fruit for constipation: overall

## (A) Response to treatment

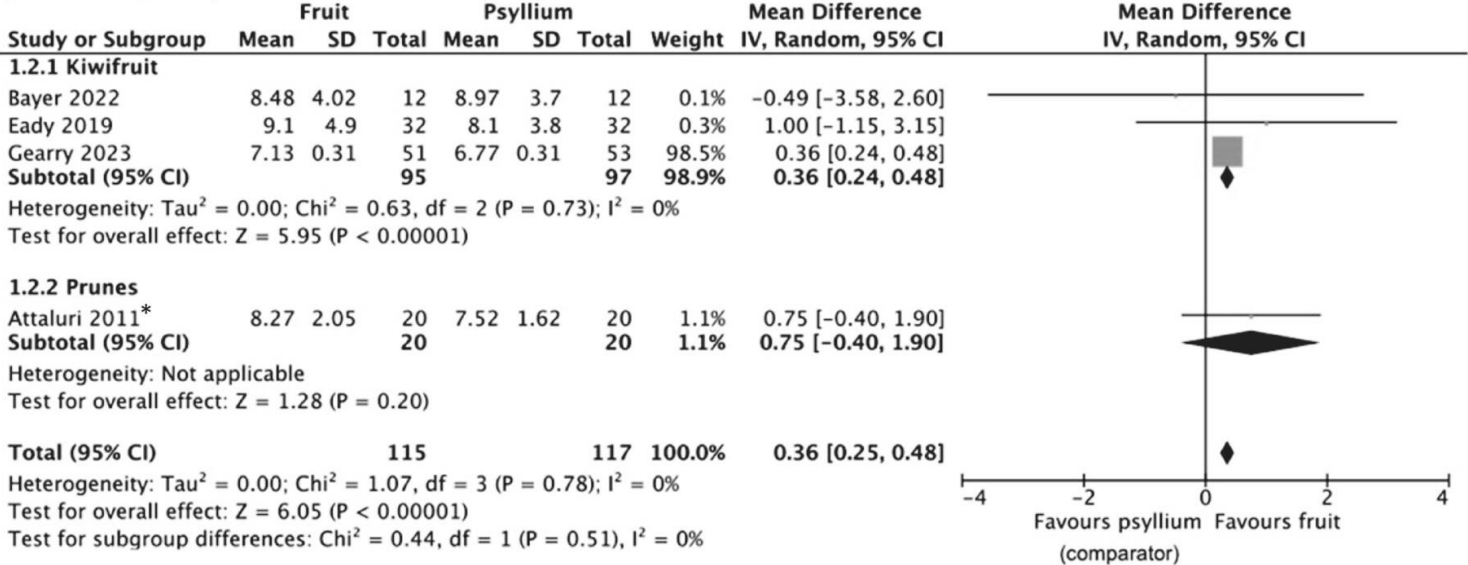


## Response to treatment:

Kiwifruit and prunes equivalent to psyllium

# Fruit for constipation: stool frequency

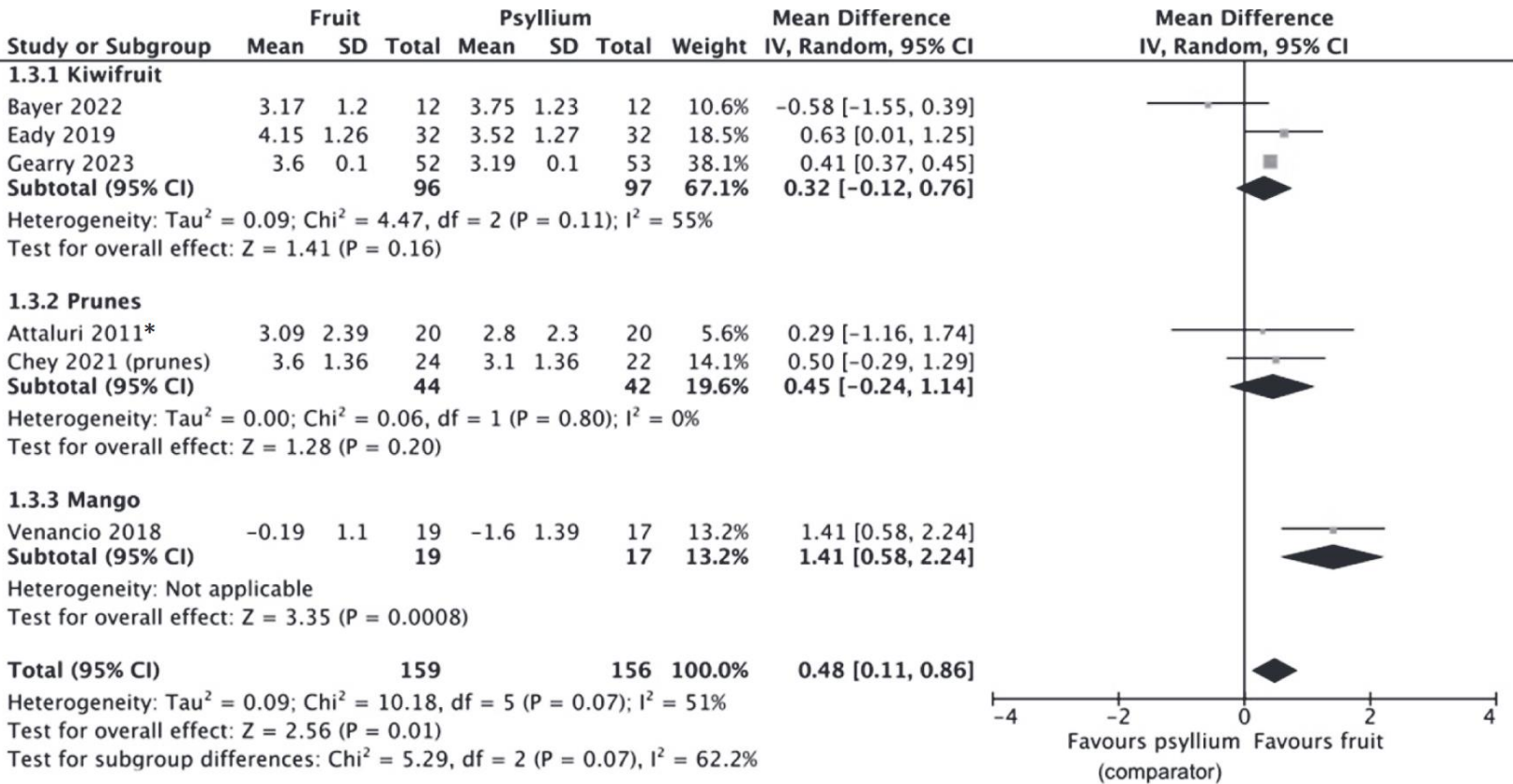
(B) Stool frequency



Stool frequency:  
Kiwifruit and prunes superior to psyllium



# Fruit for constipation: stool consistency



Stool consistency:

Only mango superior to psyllium

# 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)
- Mangoes (based on one trial)
  - High in fiber and polyphenols (↓ inflammation?)
  - Dose: 1 large mango per/day

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

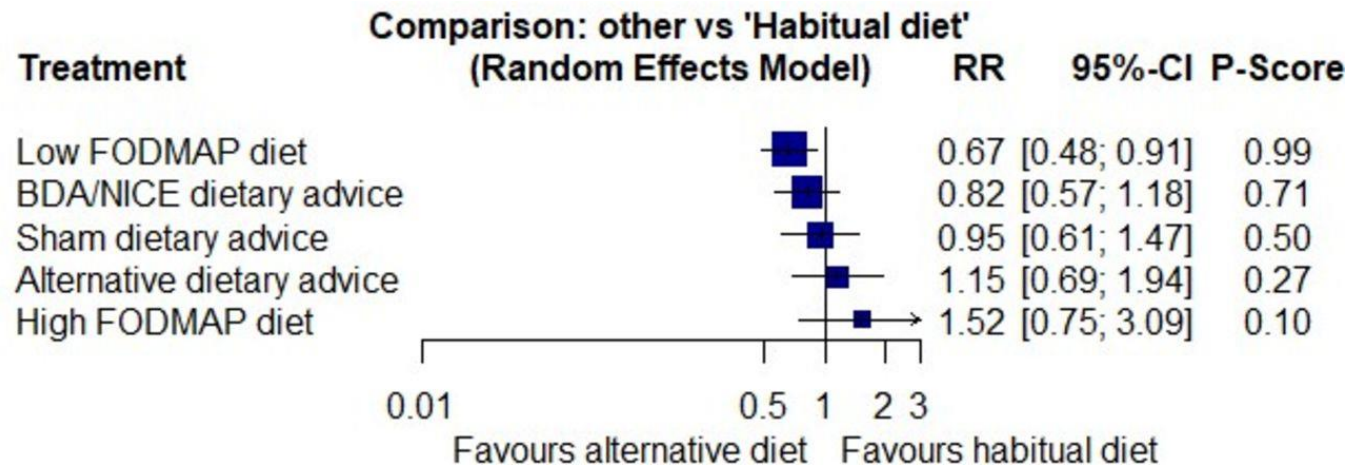
- More than 70% of IBS patients believe that food plays a role in their symptoms
- Self-reported food intolerance in IBS is associated with more severe symptom severity
- Like it or not, your patients will look to you for dietary guidance
- Evolution of concept of non-celiac gluten (wheat) sensitivity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





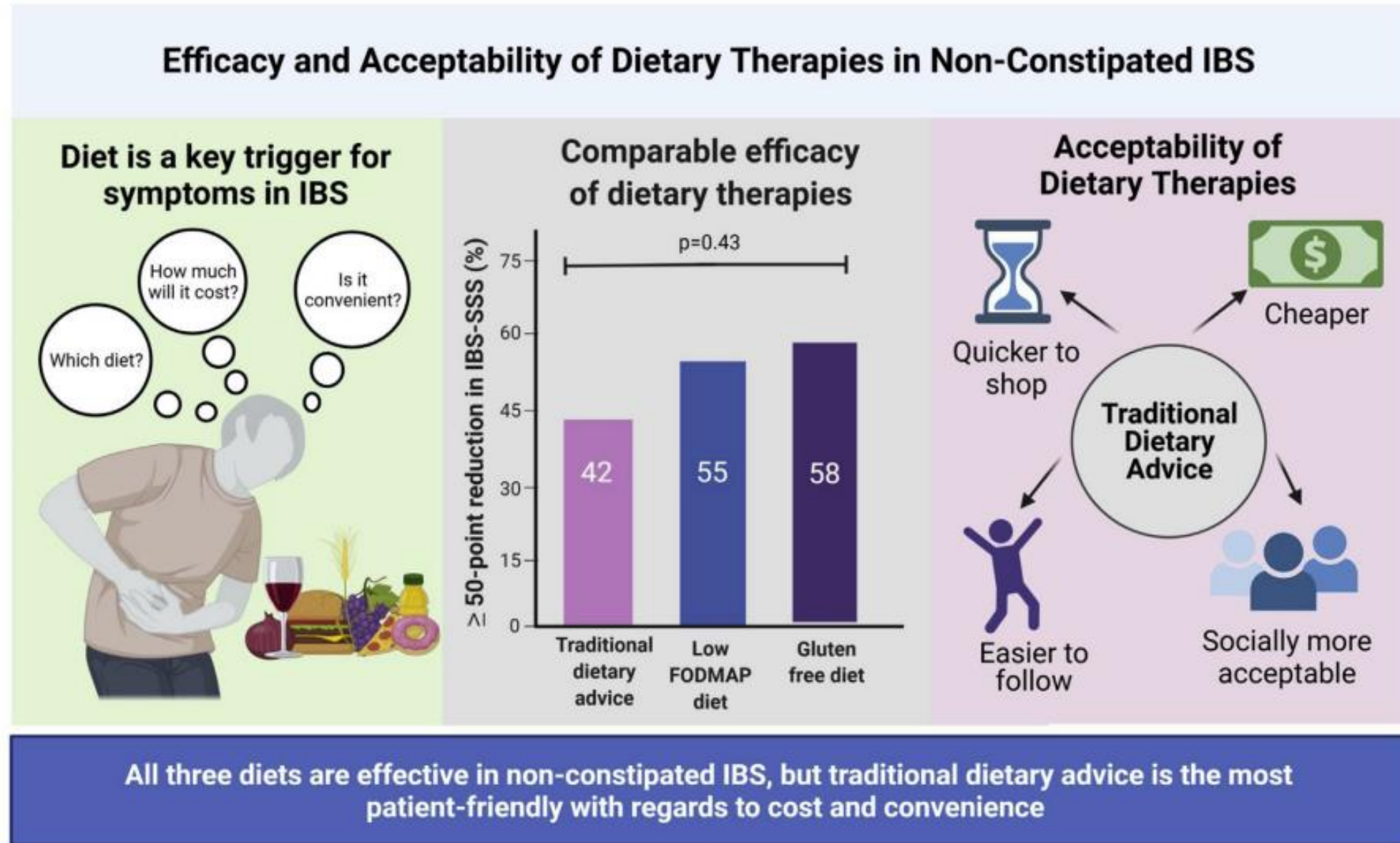
# Dietary approaches to the treatment of IBS

- The most robust data is for the low-FODMAP diet
- Short-chain carbohydrates that are slowly absorbed or poorly digested by the small intestine and can cause distension of the intestinal lumen
- Network meta-analysis ranked low-FODMAP diet 1<sup>st</sup> compared with habitual diet for global symptoms
- Fructans and mannitol most common triggers





# Maybe any diet will do (for IBS-D)?



# 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
  - Future: apps may fill the gap
- Caution in patients w/ disordered eating
  - Can reinforce harmful cognitions/ behaviors
  - Look out for “orthorexia nervosa”
    - Obsessive focus on food choice
    - Food for 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  $\geq 1$  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

# 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
<b>Primary outcome</b>				
30% reduction in API	70 (59.6%)	44 (42.1%)	17.5% (2.6, 32.5)	0.02
<b>Secondary outcomes</b>				
IBS-API <sup>a</sup>	−1.3 (0.24)	−0.9 (0.23)	−0.4 (0.24) (−0.9, 0.0)	NA
Bloating <sup>a</sup>	−1.2 (0.25)	−0.8 (0.25)	−0.5 (0.26) (−1.0, 0.1)	NA
IBS-SSS <sup>a</sup>	−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 <sup>a</sup>	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.



# Questions about probiotics are a reality of taking care of patients with IBS

- Probiotics likely provide some benefit to patients with IBS
- On the whole, products containing *Bifidobacterium* (either alone or in a cocktail) are effective in IBS
- ↑ quality of evidence is associated with ↓ treatment effect
- Any advice to patients limited by poor quality of existing data



# Questions about probiotics are a reality of taking care of patients with IBS

- Probiotics likely provide some benefit to patients with IBS

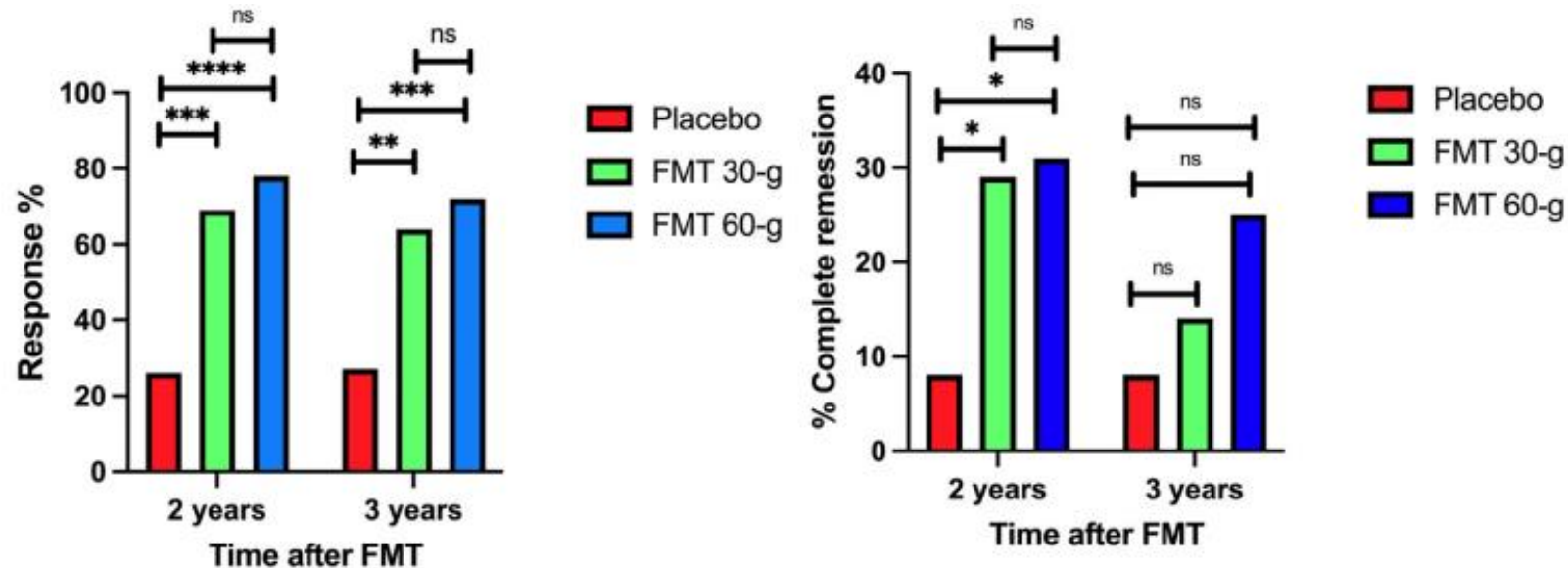


In symptomatic children and adults with irritable bowel syndrome, we recommend the use of probiotics only in the context of a clinical trial. *No recommendations, knowledge gap.*

- Any advice to patients limited by poor quality of existing data

# Fecal microbiota transplant for IBS

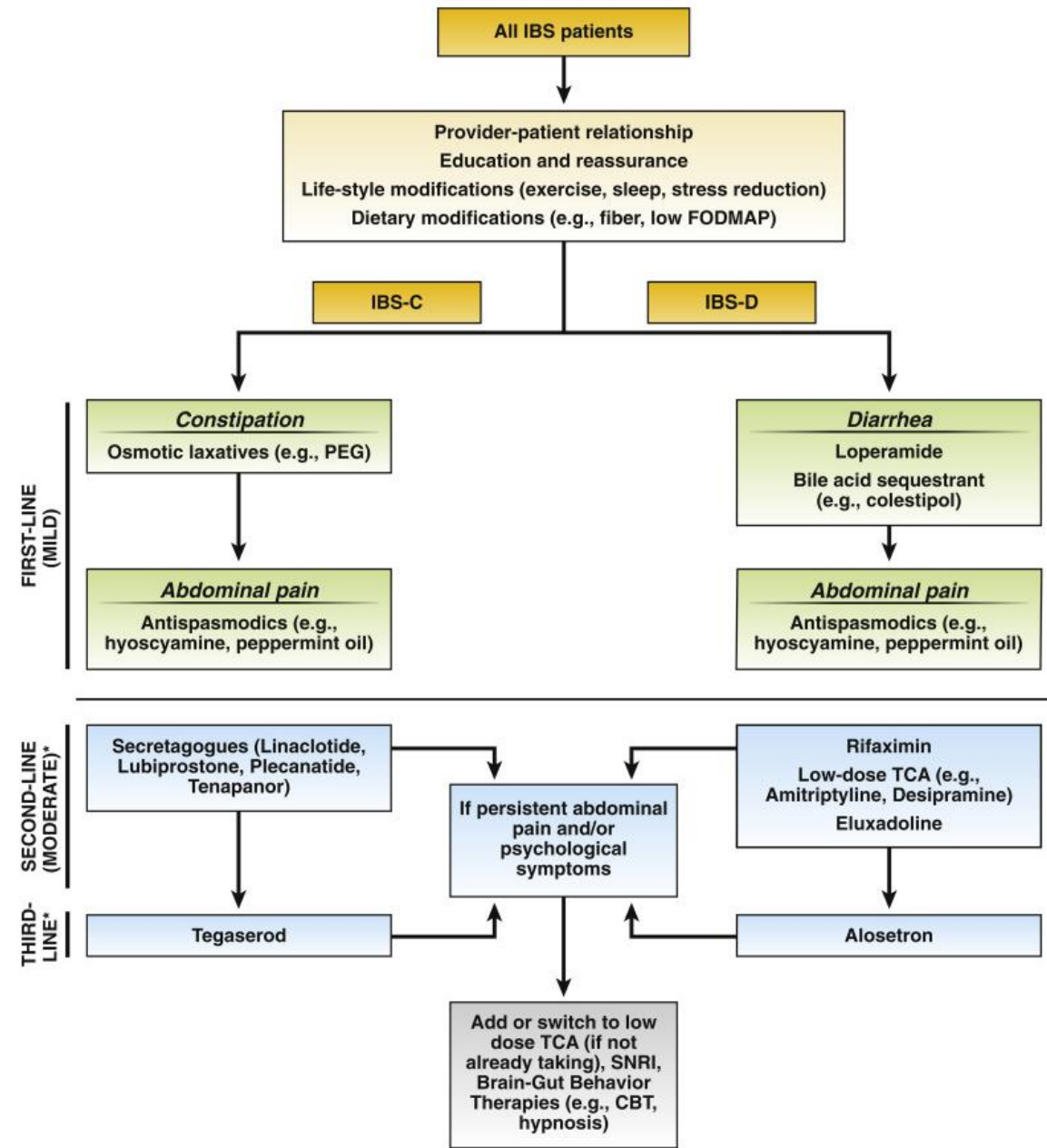
- FMT trials for IBS have been mixed
- Recent long-term trial results:
  - Patients with IBS receiving FMT continued to have fewer abdominal symptoms and fatigue and a better QOL than before procedure
  - 3 years after FMT: the response rate was 64.9% in 30g group, 71.8% in 60g group, vs. 27% in the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





# Thinking about pharmacologic treatments for IBS

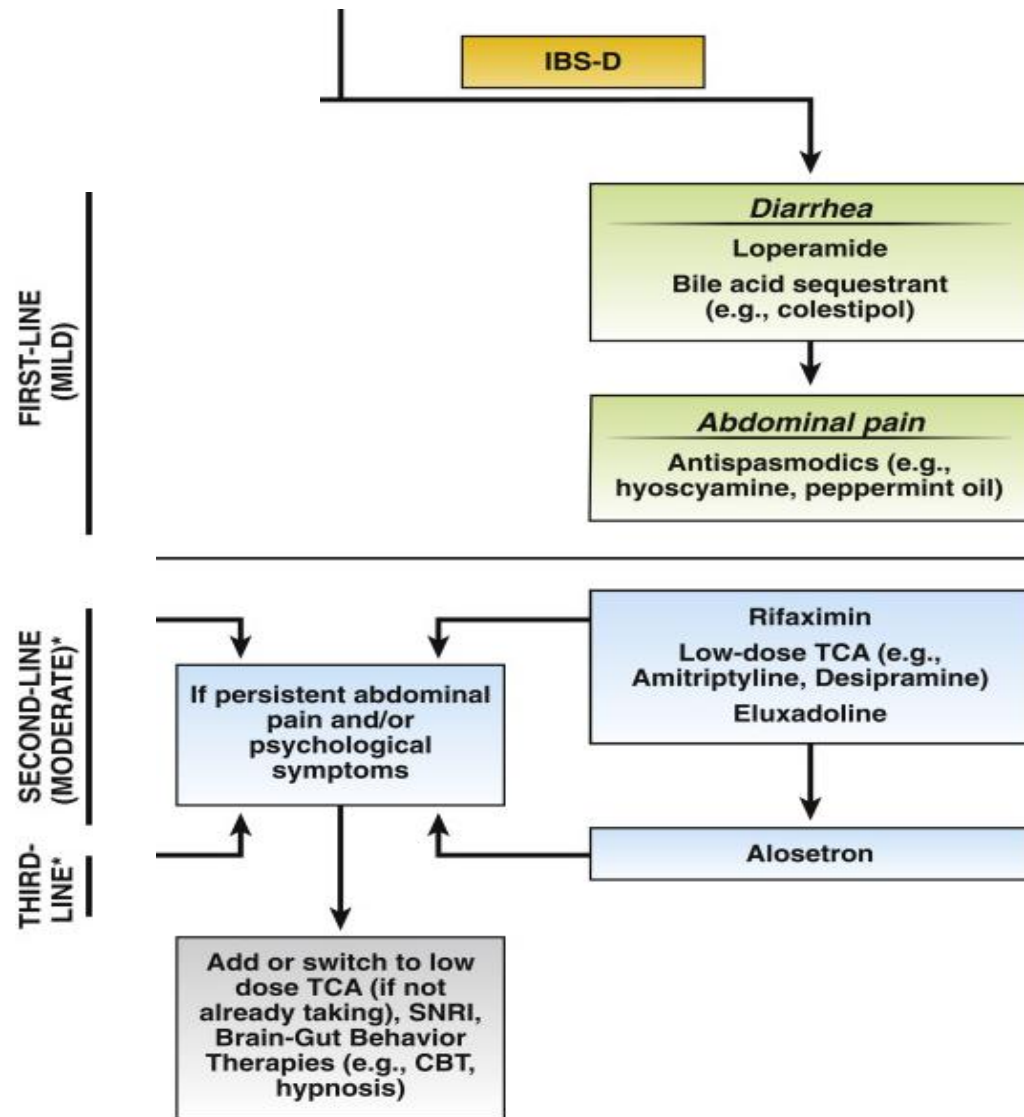




\*Selection of the medication should be based on the clinical features and needs of the patient.  
TCA, tricyclic antidepressant; SNRI, serotonin-norepinephrine reuptake inhibitor; PEG, polyethylene glycol; CBT, cognitive behavioral therapy



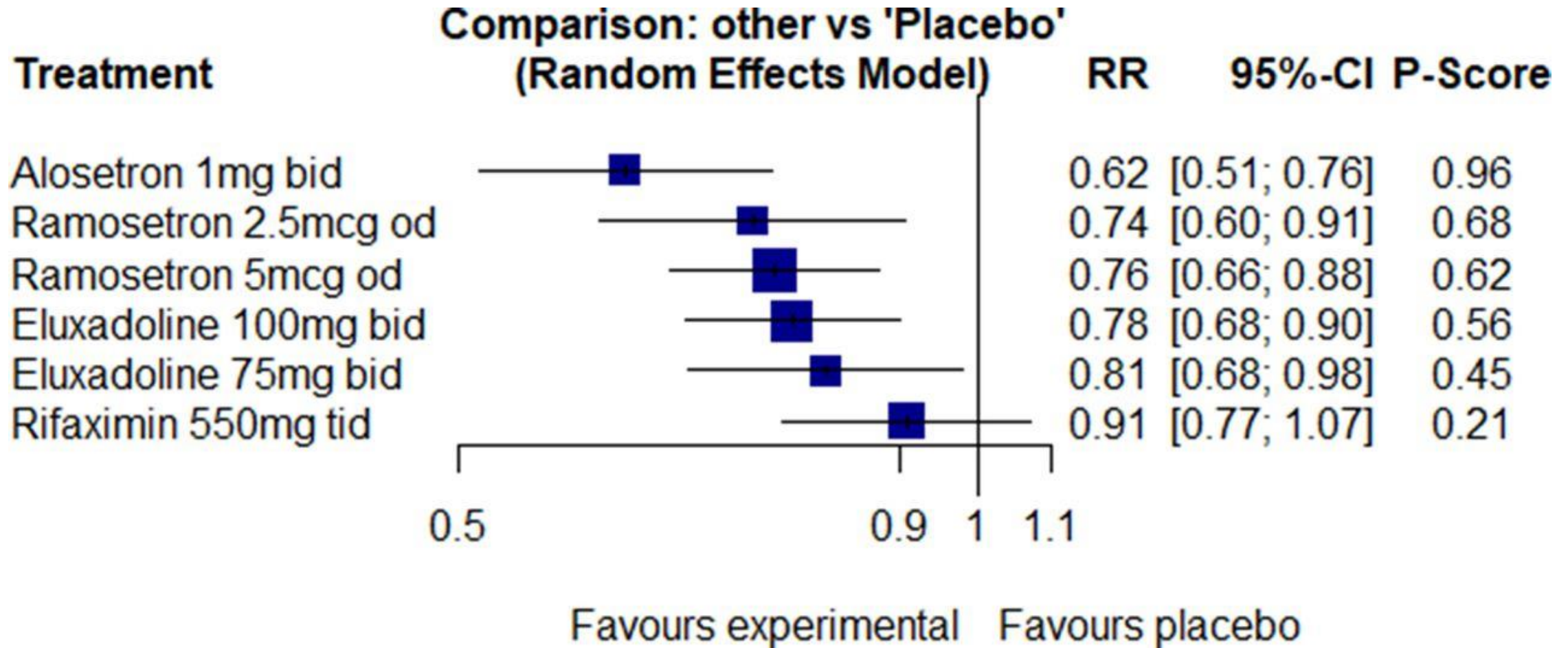
# Latest US guidelines for the pharmacologic treatment of IBS-D



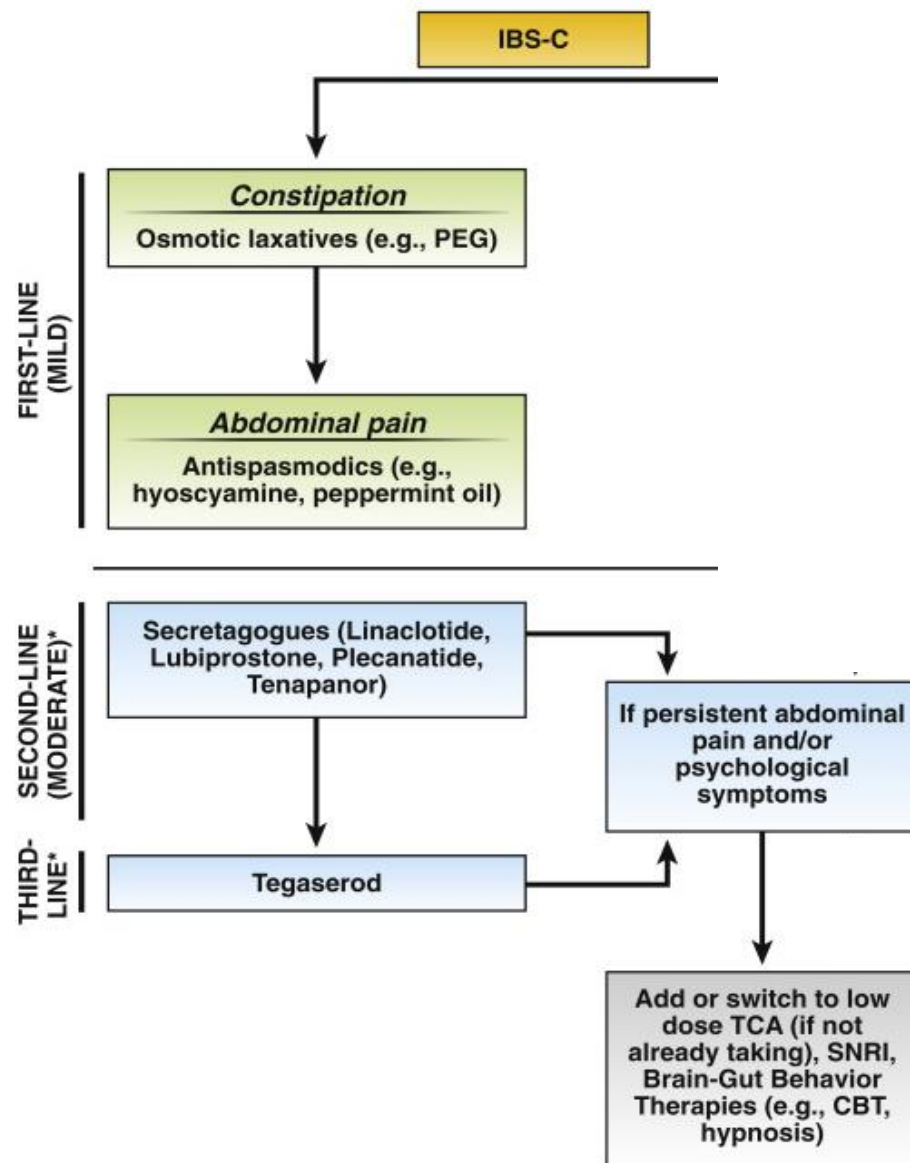
\*Selection of the medication should be based on the clinical features and needs of the patient.

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

# Comparative evidence of approved IBS-D therapies



# Latest US guidelines for the pharmacologic treatment of IBS-C

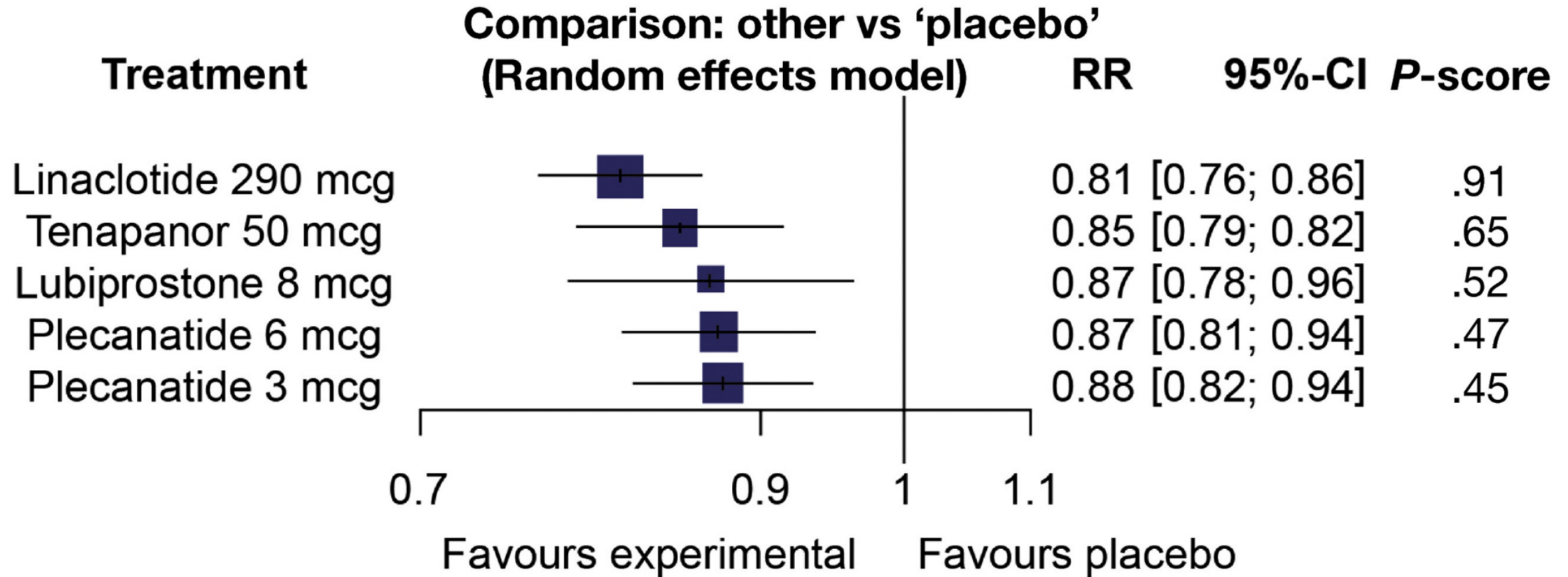


\*Selection of the medication should be based on the clinical features and needs of the patient.

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



# Comparative evidence of approved IBS-C therapies



# Rationale and use of neuromodulators

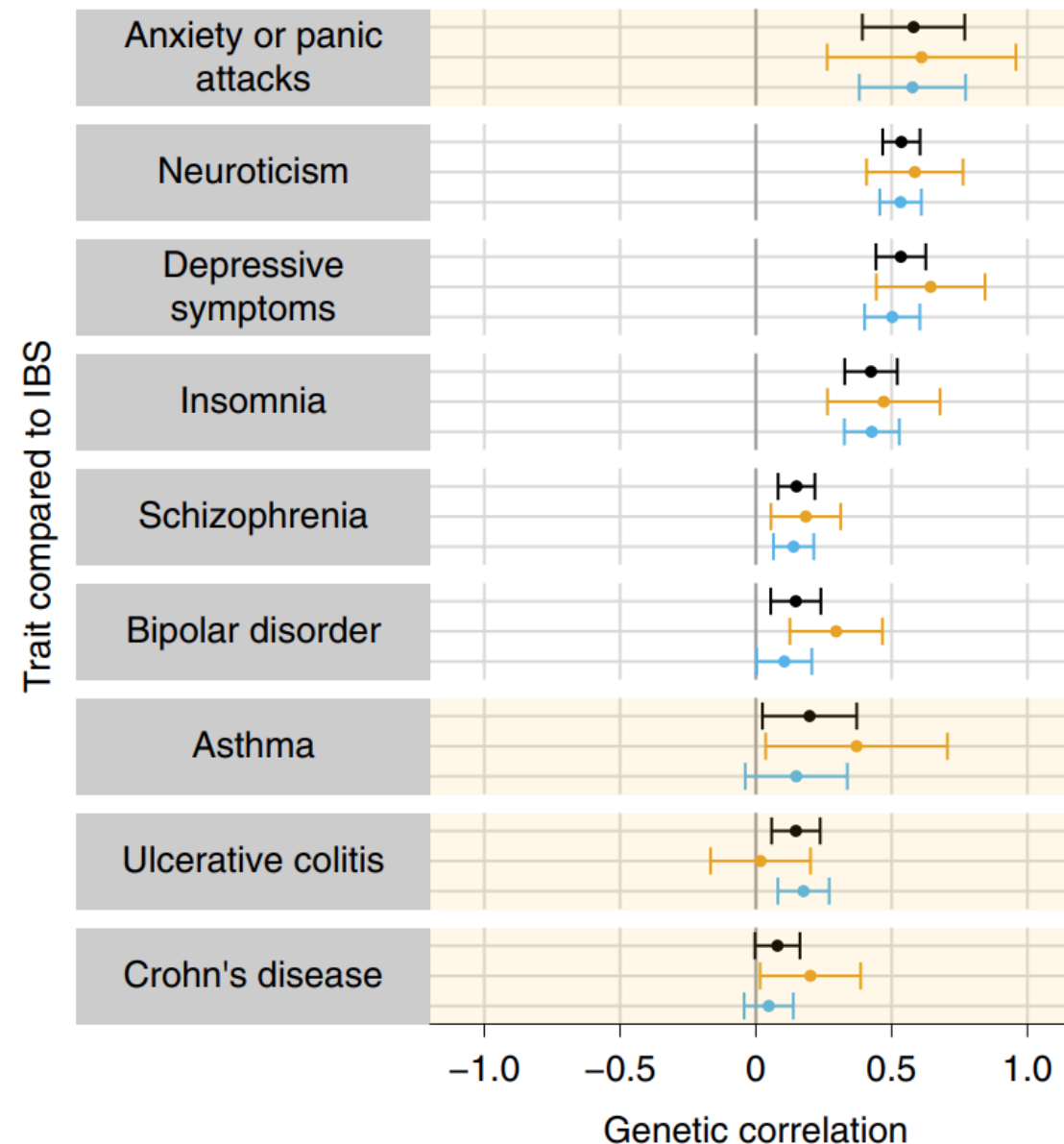


# IBS and psychological disease: chicken or egg?

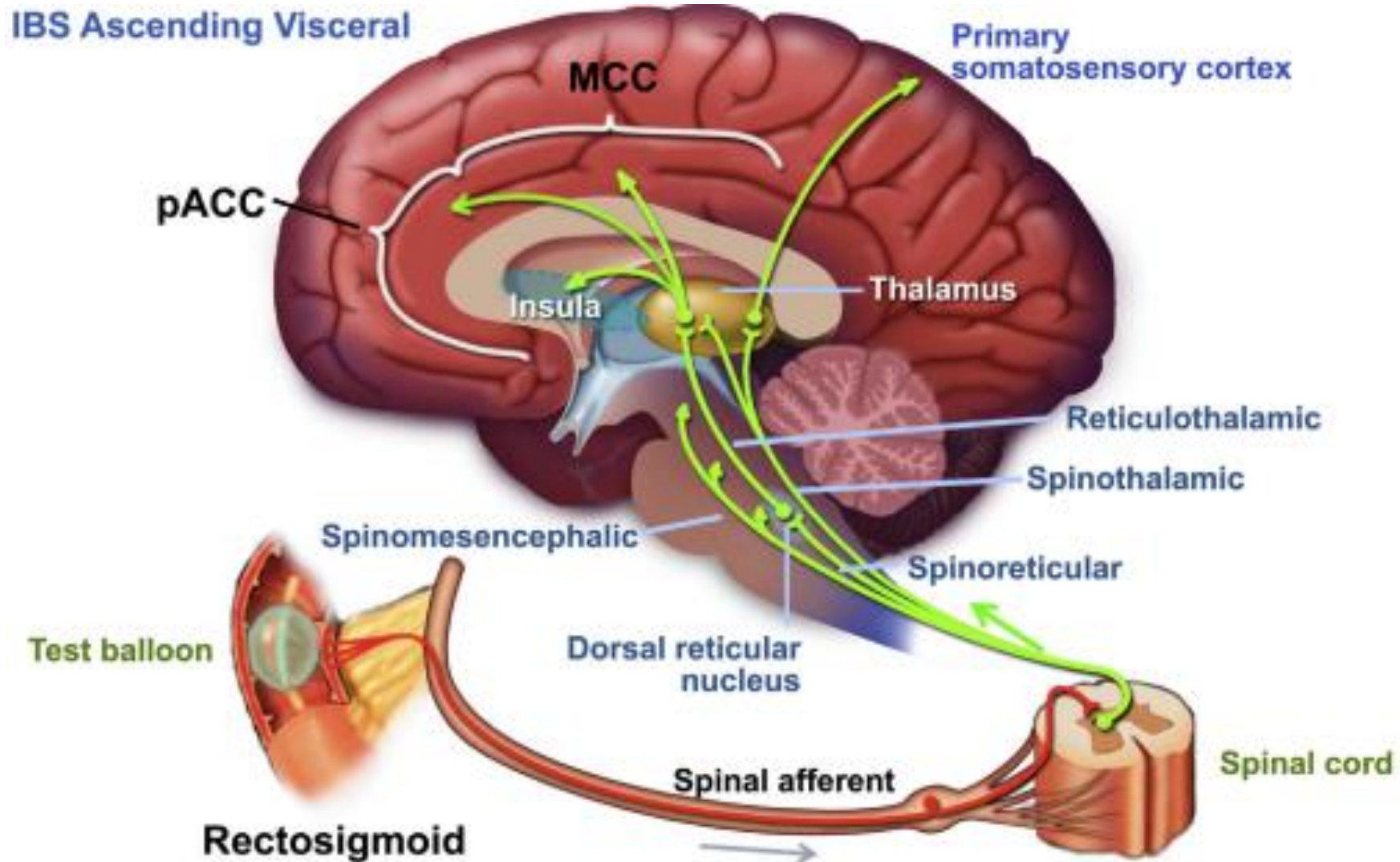
## Genetic correlation between IBS and anxiety

Association remained even after removing those with overlap

Suggests shared etiology rather than one condition causing the other

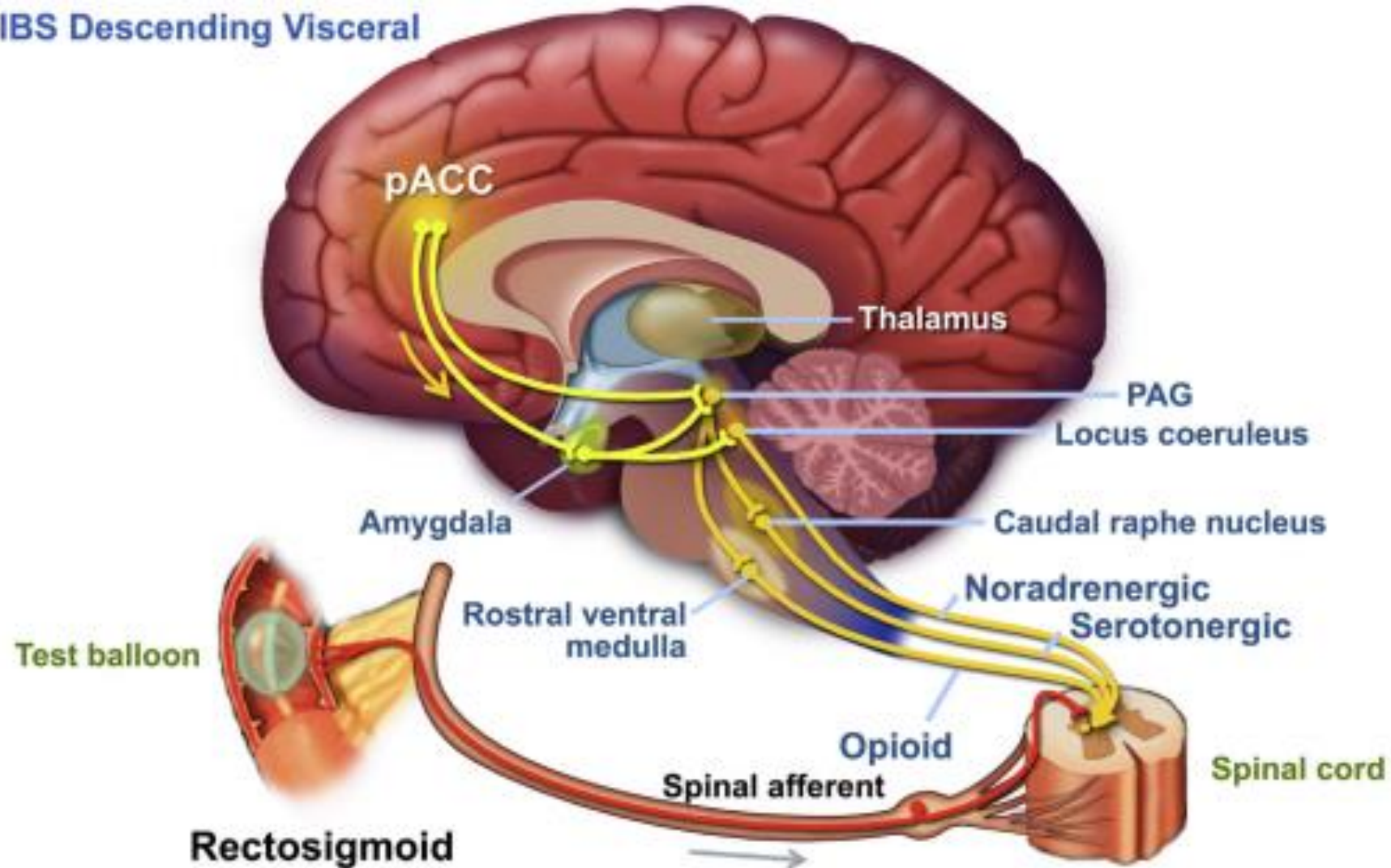


# How sensory signals from the colon reach consciousness: ascending pathways



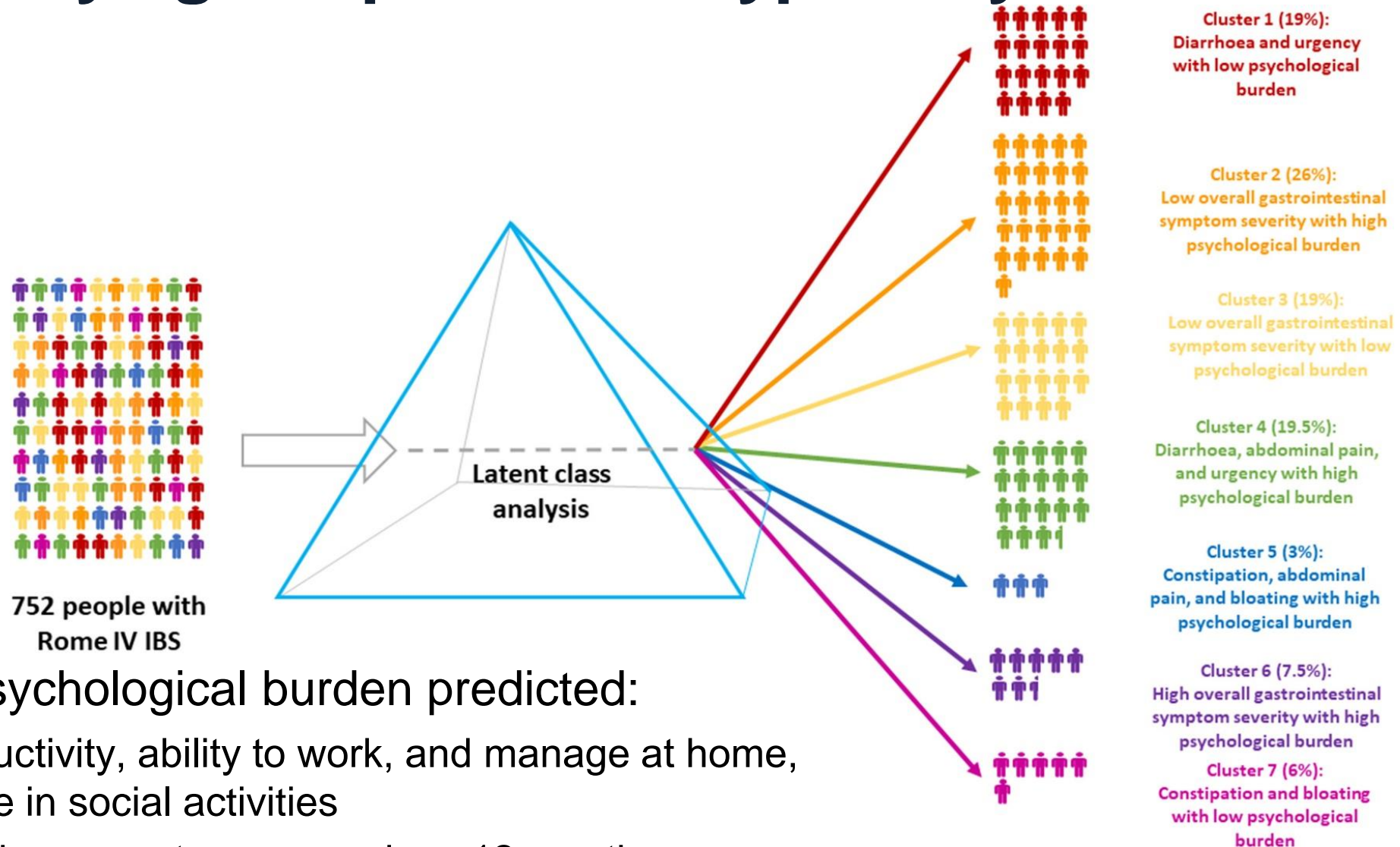
# How sensory signals from the colon reach consciousness: descending pathways

IBS Descending Visceral





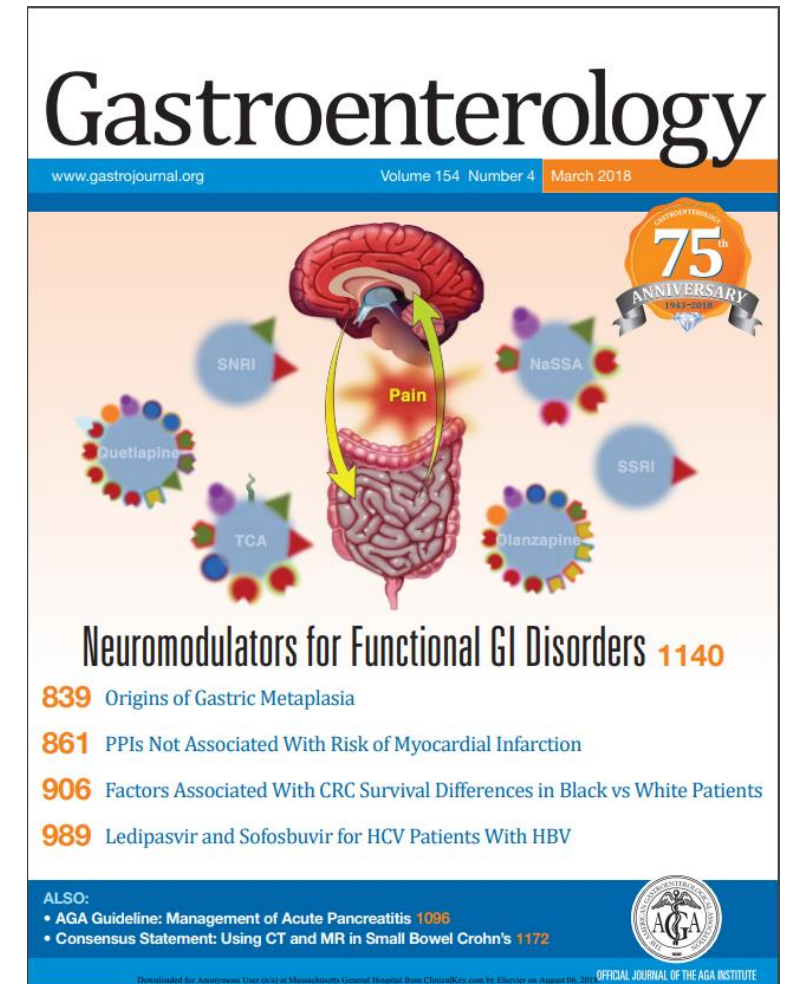
# Identifying IBS patient subtypes beyond stool form



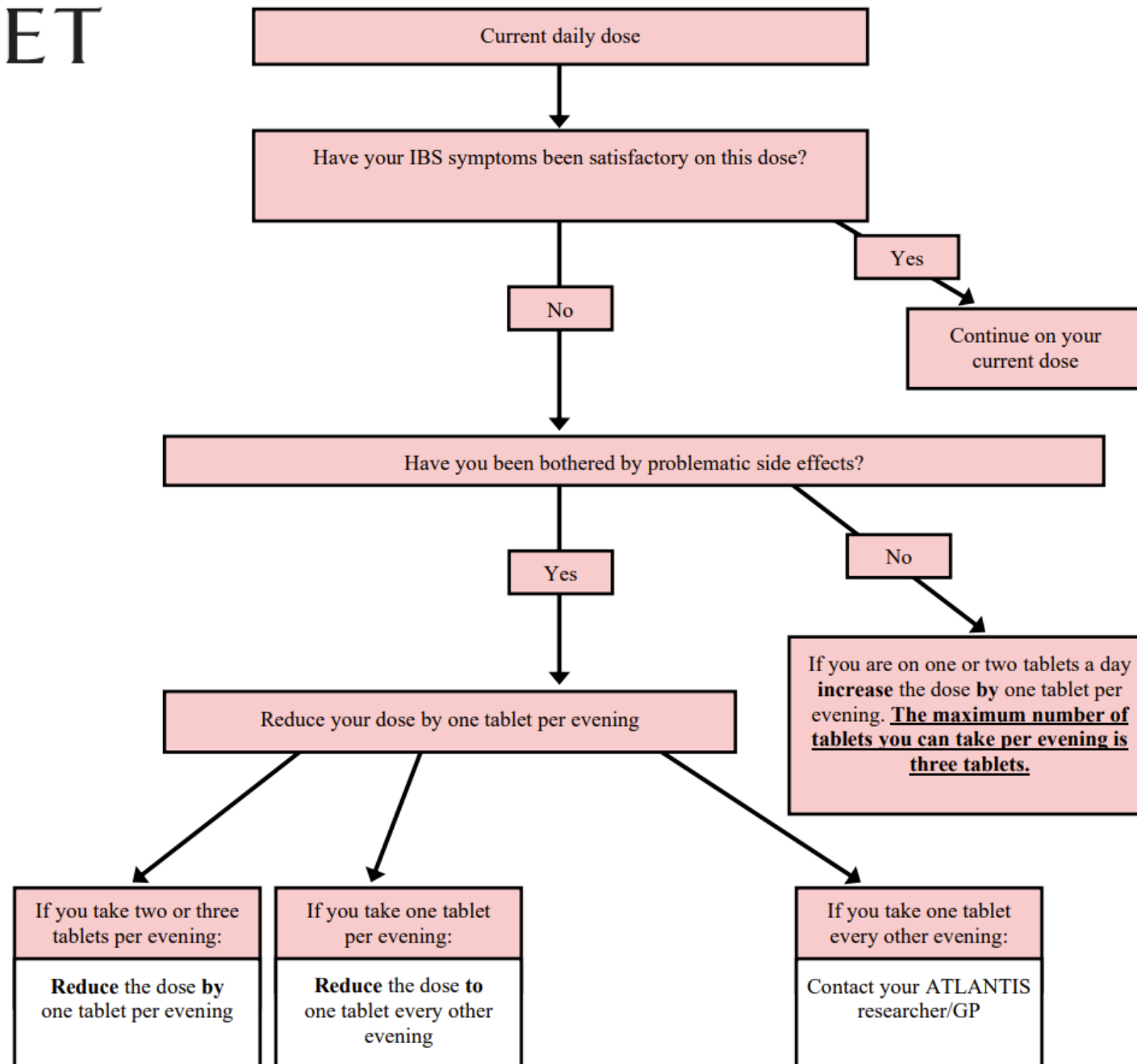
- High psychological burden predicted:
  - ↓ productivity, ability to work, and manage at home, engage in social activities
  - ↑ healthcare costs over previous 12 months

# 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



- 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



# 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

## Bottom line:

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

Outcomes	Mean scores		Between-group difference (95% CI) at 6 mo	
	Amitriptyline	Placebo		
<b>IBS-SSS†</b>	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).

- 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 side 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.

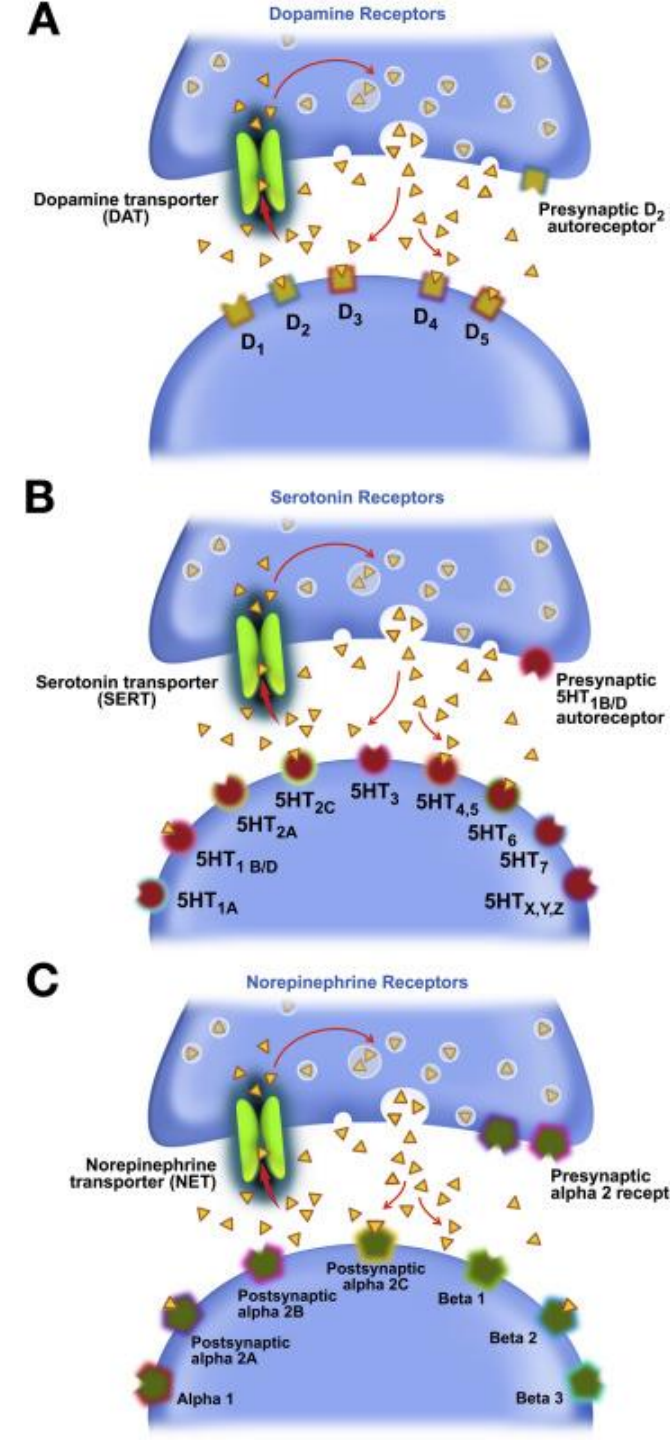
Gupta T, Cash BD. *Ann Intern Med*. 2024 Feb;177(2):JC15. doi: 10.7326/J23-0122.





# Prescribing neuromodulators smartly

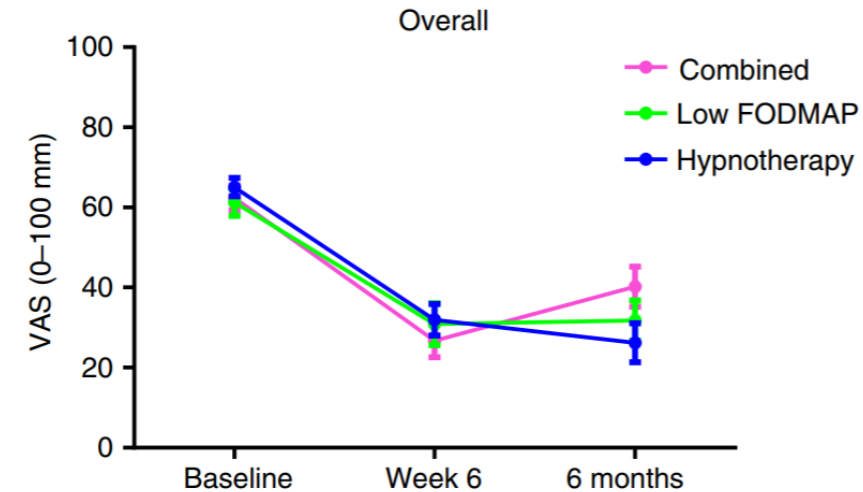
- Overall efficacy
  - TCAs more effective than SSRIs for pain
  - SSRIs should be a second-line agent or a first-line agent in pts w/ comorbid anxiety, depression, social anxiety
  - SNRIs extensively studied for fibromyalgia and diabetic neuropathy but can be useful in IBS-C or in those who failed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





# 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

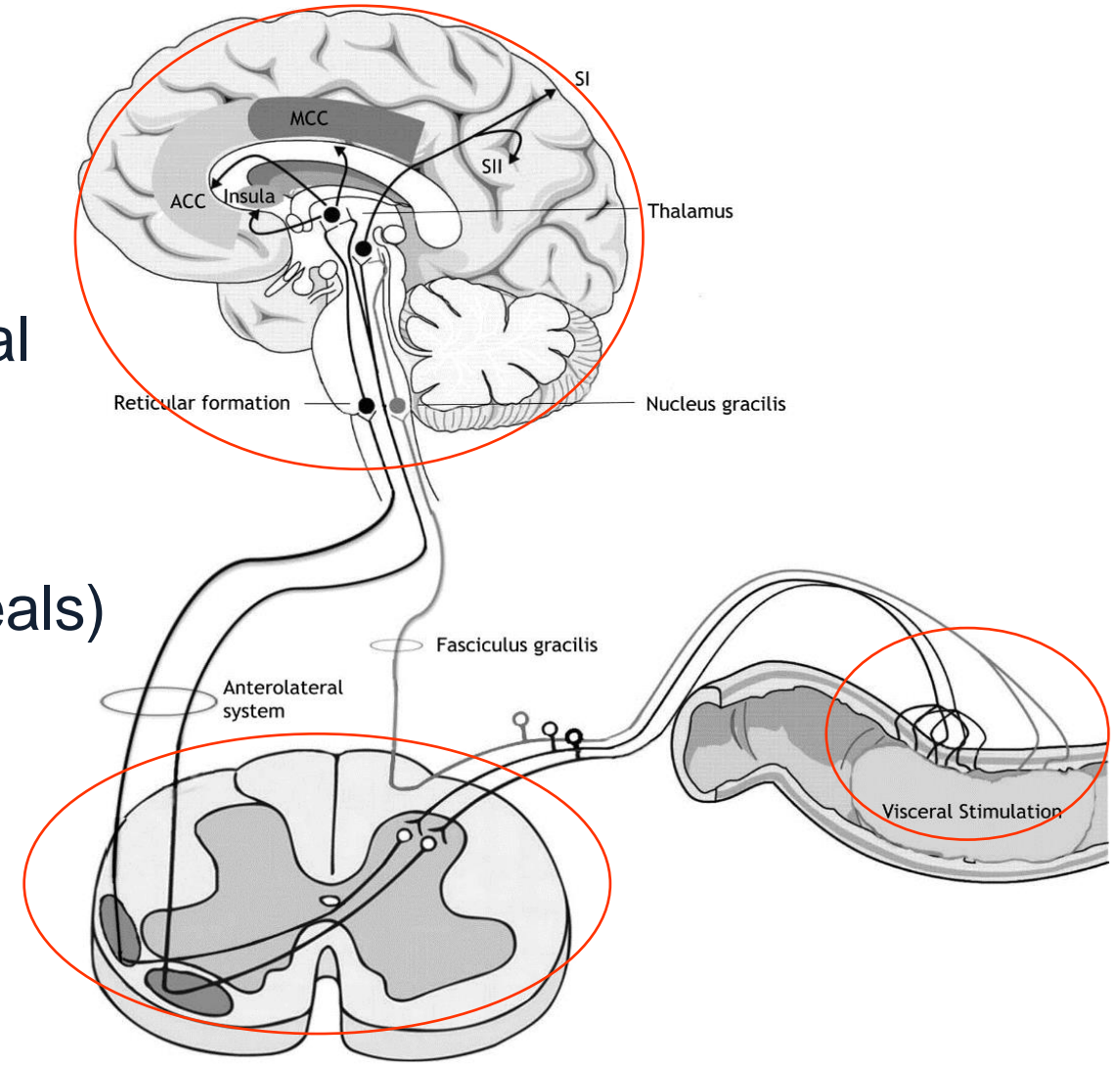


# What type of IBS patient am I seeing today?

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%

# 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
  3. Leverage the brain-gut connection
    - Neuromodulators
    - Gut hypnotherapy
    - Cognitive behavioral therapy
- Investing time up front can pay dividends later on



# 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 a powerful, patient-centered tool but has limitations
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