

**Choosing the Right
Medicines
Treatments for Your
Patient with IBS-
Constipation**

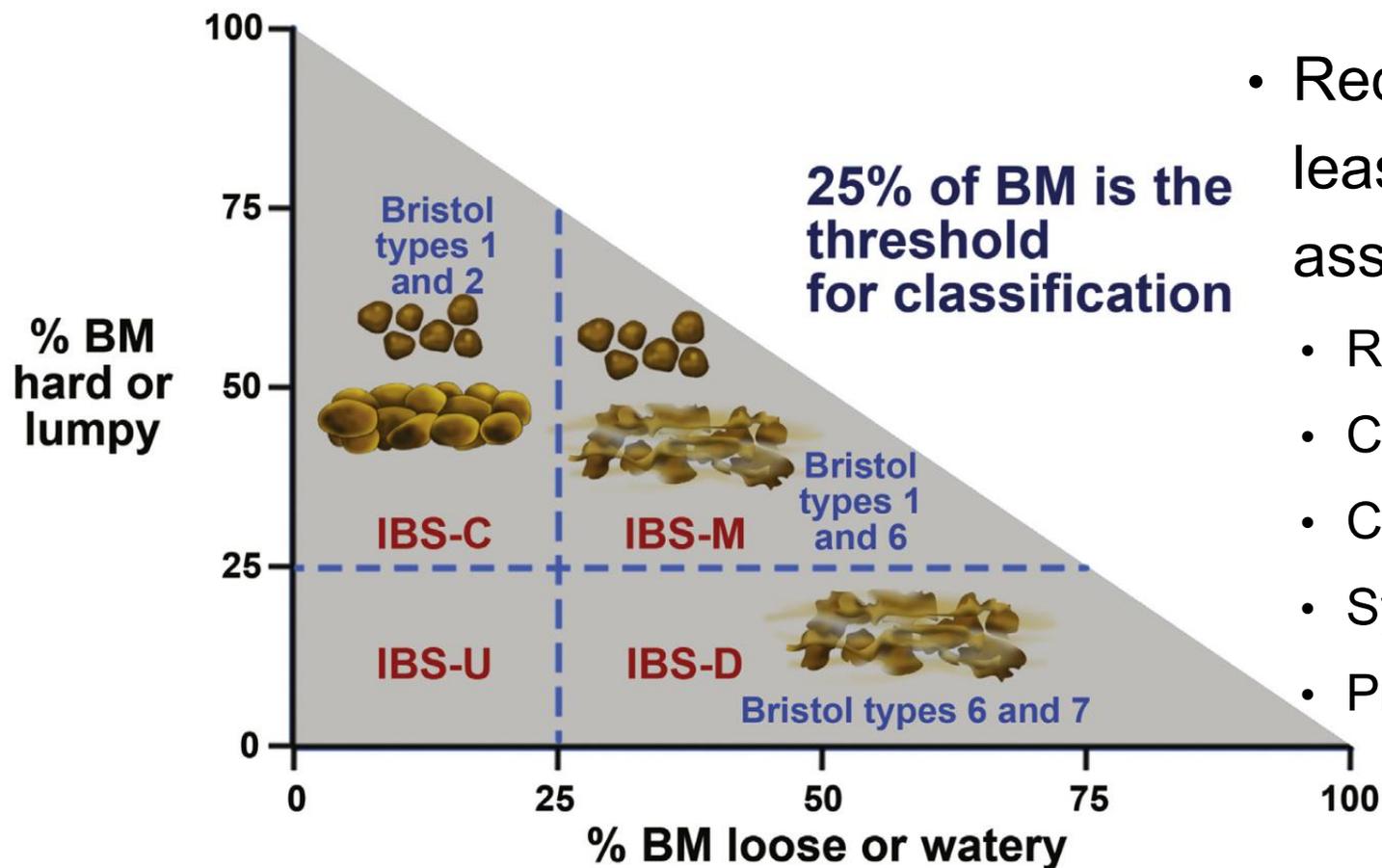
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Objectives

- Define IBS-C and recognize pathophysiology
- Discuss mechanism of action, efficacy, and adverse effects of IBS treatment options
- List clinical pearls for each treatment option
- Review the guideline recommendations for IBS treatments
- Compare options for treatments
- No Disclosures

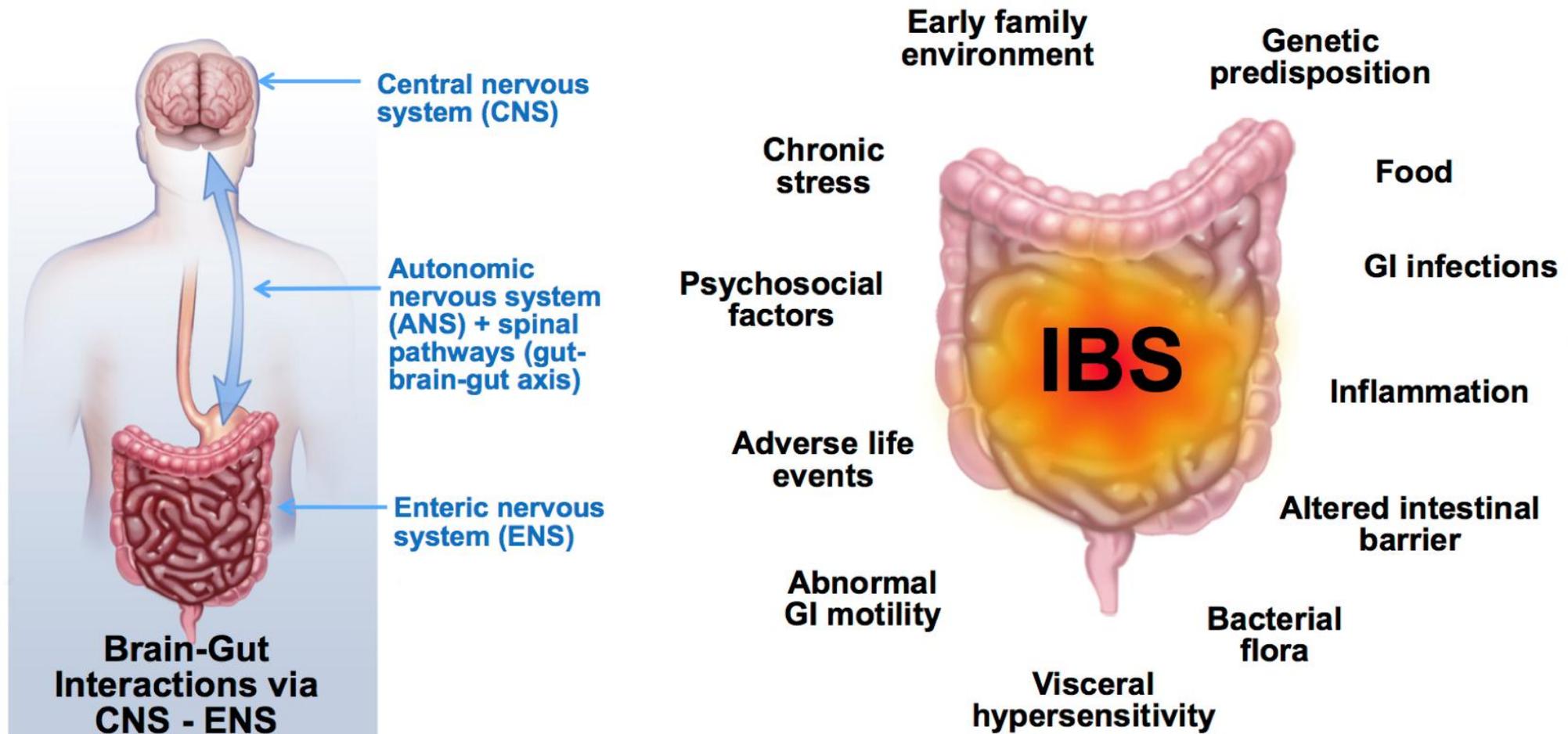


A Positive Diagnostic Strategy: Irritable Bowel Syndrome with Constipation



- Recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with the following:
 - Related to defecation
 - Change in frequency of stool
 - Change in form (appearance) of stool
 - Symptoms must be present for at least 6 months
 - Predominant stools >25% with BSFS 1 or 2

Pathogenesis of IBS is Heterogeneous



Case

33yo F with IBS-C , interstitial cystitis seen for follow-up. Has abdominal pain and constipation with BMs every 3-4 days , BSFS 2 stools. No alarm features. Using squatty potty, eating high fiber diet; Meds are Miralax daily, amitriptyline, oxybutynin.

What is the next step in management?

- A. Soluble fiber supplement
- B. Linaclotide
- C. Tenapanor
- D. Anorectal manometry
- E. Prucalopride



Symptom Management

for IBS



Yoga



Studies show practicing yoga provides a variety of health benefits.

Hypnosis

4 to 12 hypnosis sessions may improve symptoms.

Cognitive

Behavioral Therapy

1/3 of people treated with CBT for IBS will improve.

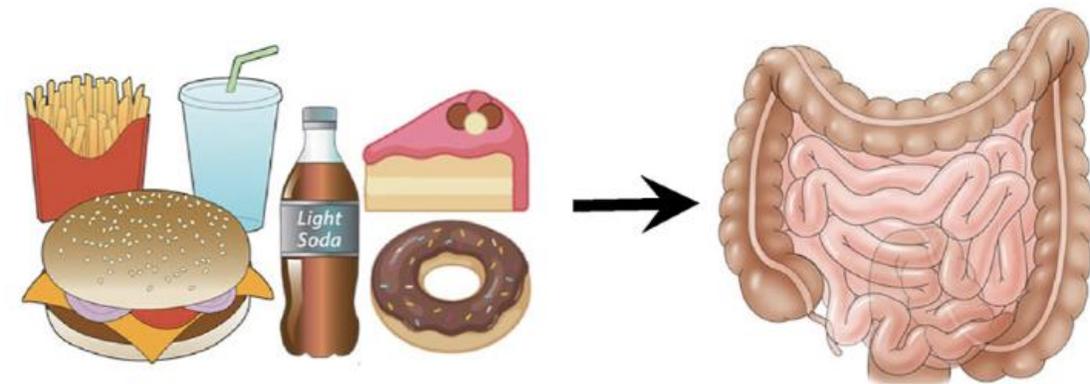


Diet

Changes



65% of IBS patients associate symptoms with food.



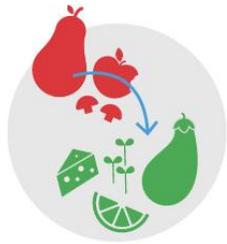
FODMAPs increase SCFA and intestinal secretions leading to bloating, pain, diarrhea.

Low FODMAP diet helps in IBS especially with Bloating

Simplified low FODMAP diet easier, more compliance with equal benefits

Avoid in patients at risk for eating disorders

Low or Gentle FODMAP Diet in IBS



HIGH FODMAP FOODS

Vegetables

Artichoke, asparagus, garlic, green peas, leek, mushrooms, onion, red capsicum (bell pepper)

Fruits

Apples, apple juice, cherries, dried fruit, mango, nectarines, peaches, pears, plums, watermelon

Dairy and alternatives

Cow's milk, custard, evaporated milk, ice cream, soy milk (made from whole soybeans), sweetened condensed milk, yoghurt

Protein sources

Most legumes/pulses, some marinated meats/poultry/seafood, some processed meats

Breads and cereal products

Wheat/rye/barley based breads, breakfast cereals, biscuits and snack products

Sugars/
sweeteners
& confectionery

High fructose corn syrup, honey, sugar free confectionery

Nuts and seeds

Cashews, pistachios



A "Gentle" FODMAP Diet

What does it eliminate?

Wheat & Rye-Based Products



Onion, Garlic, Leek,
Cauliflower, Mushrooms



Apple, Pear, Dried Fruit,
Stone Fruit, Watermelon



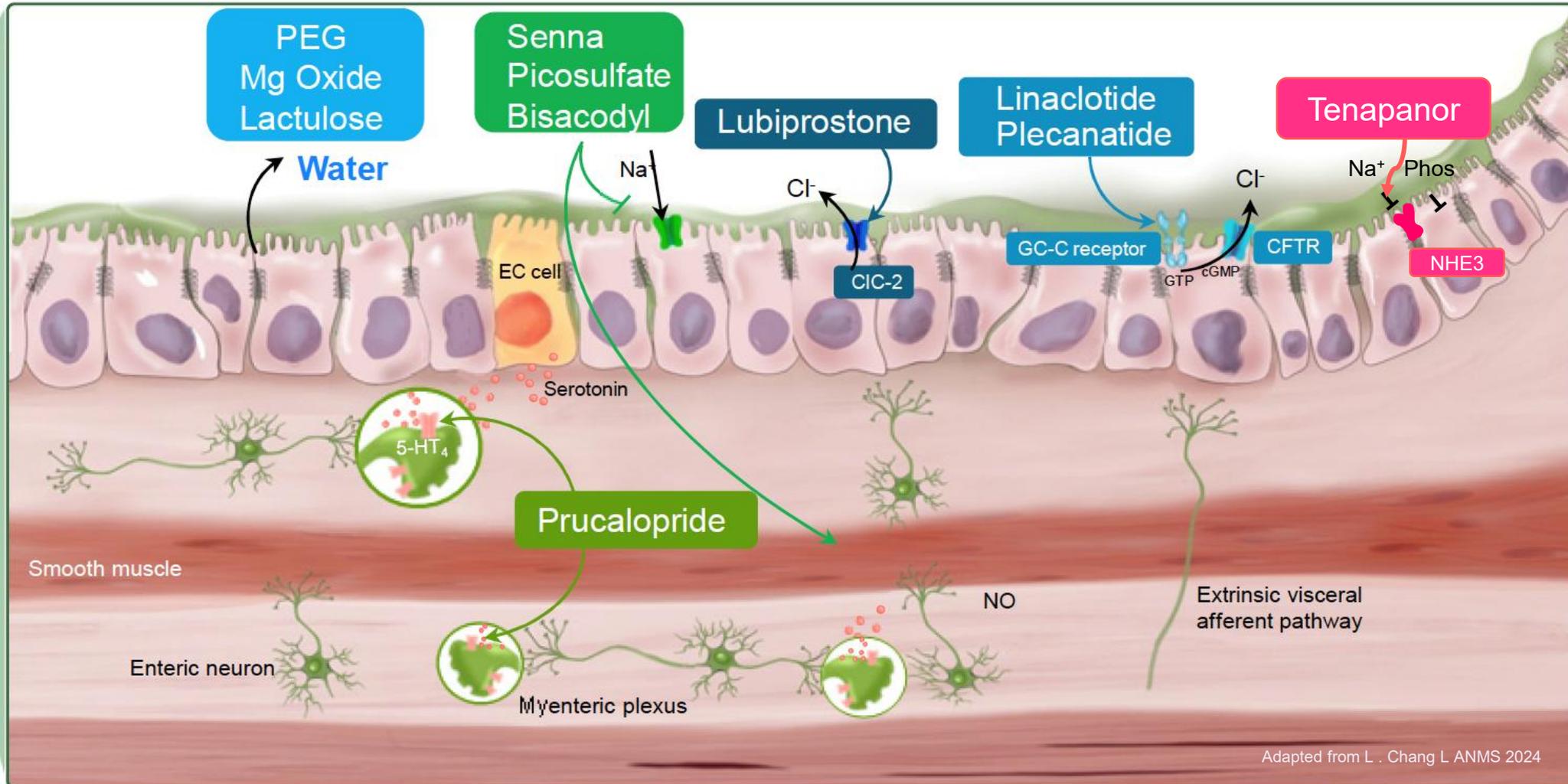
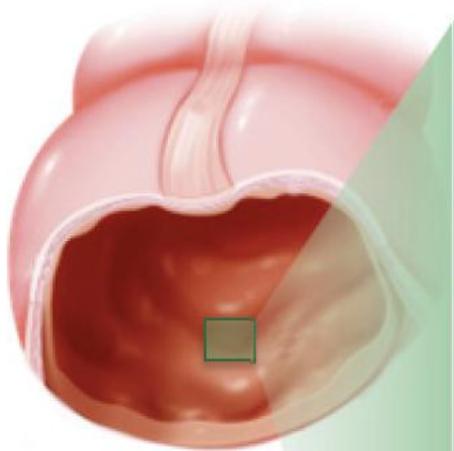
Milk & Yoghurt



Legumes

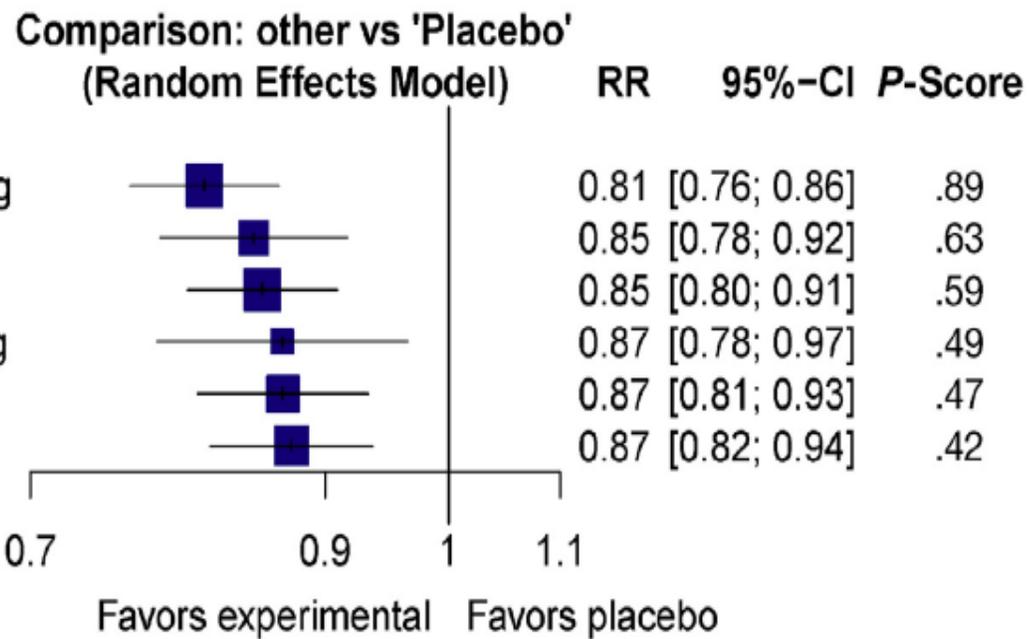
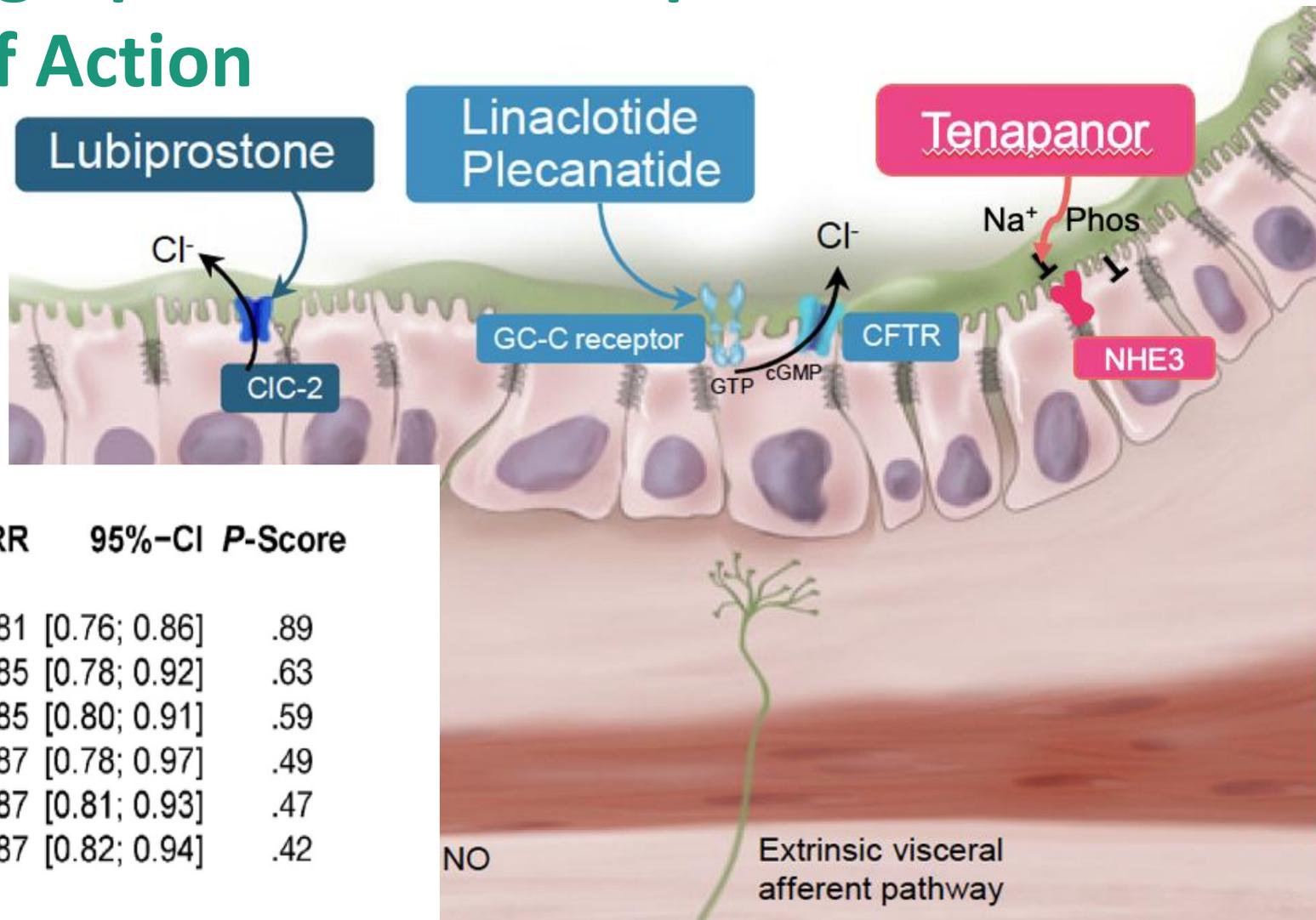


Understanding Options for Constipation Mechanism of Action



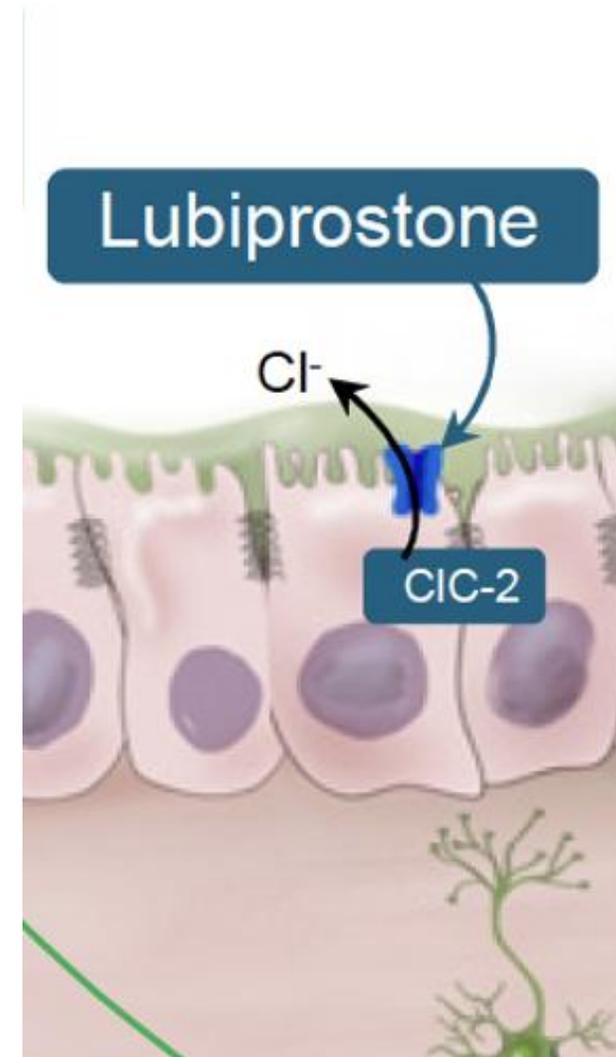
Adapted from L. Chang ANMS 2024

Understanding Options for Constipation Mechanism of Action

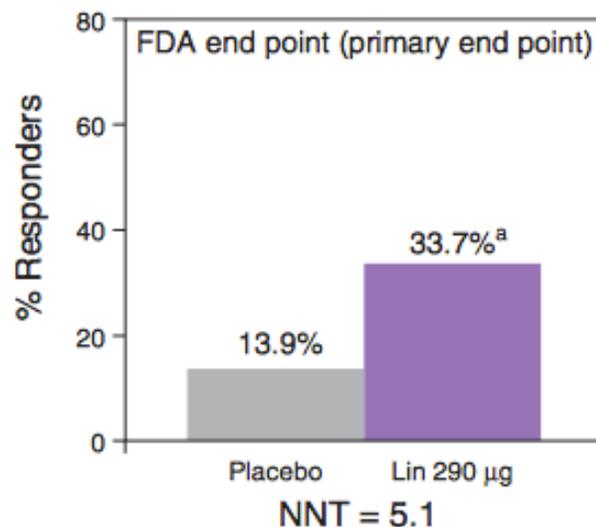
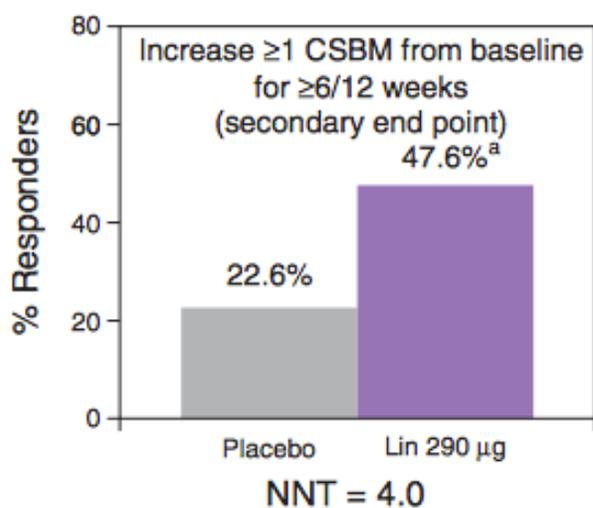
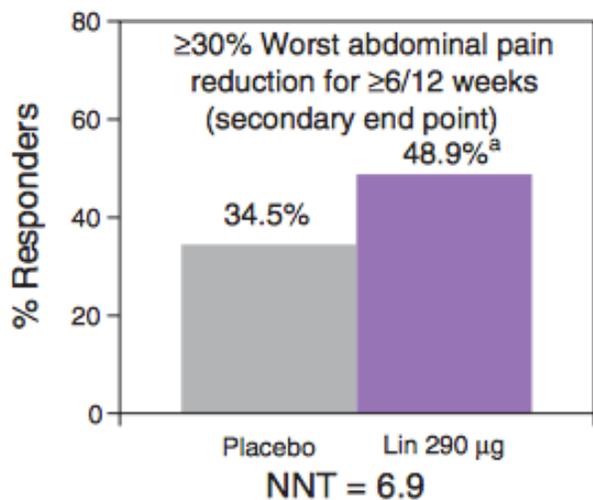


— Lubiprostone for IBS-C

- Type 2 Chloride channel agonist
- 17.9% Response Rate compared to 10% Placebo
- Approved for women with IBS-C
- NNT 12.5
- AE: nausea, diarrhea, distension



Linaclootide is Effective at 290mcg for IBS-C



Binds to GC-C receptors in gut, releases cGMP; Intracellular secretory effect

Stimulates fluid secretion, promotes consistency

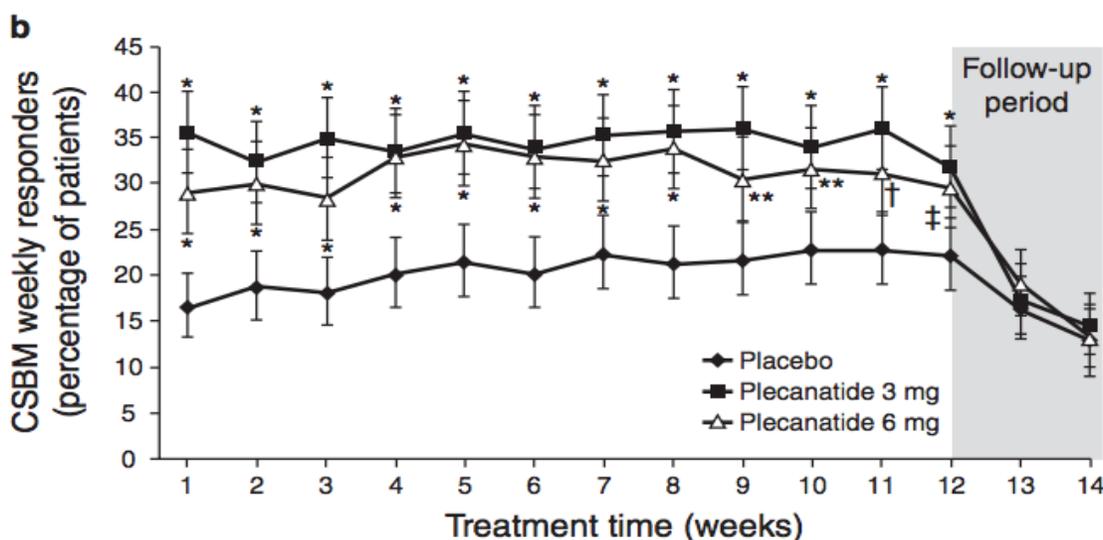
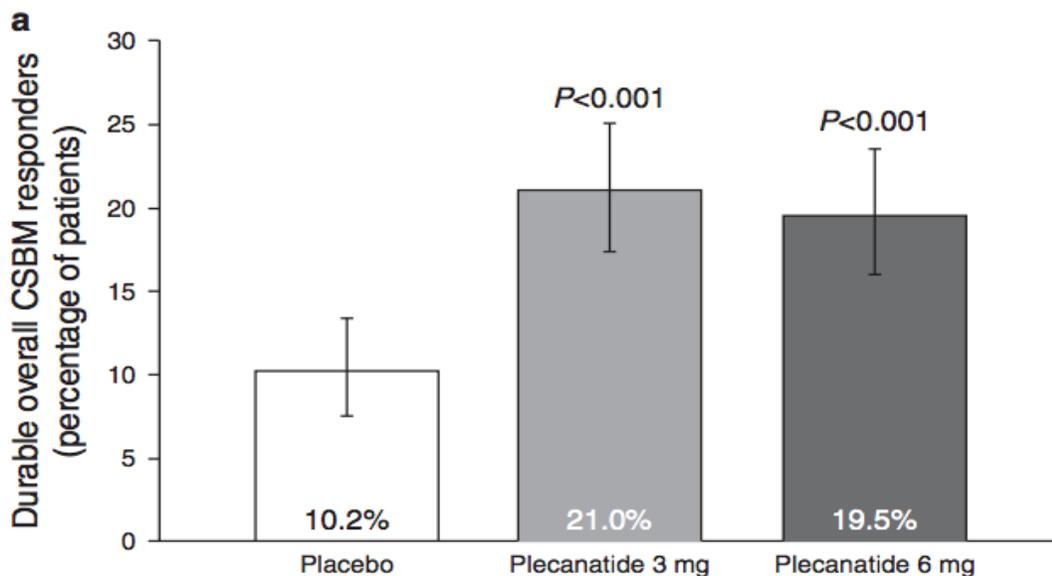
Start low dose to minimize diarrhea

Anti-nociceptive effect takes >3 months

Response rate of 34% vs 14% Placebo

NNT 5-6

Plecanatide for IBS-C



Human GI peptide uroguanylin analog
(guanylate cyclase activator)

Stimulates fluid secretion, promotes
consistency

Improves pain and bloating over months

Response rate 33% vs 19% placebo

Dose: 3mg daily ; anytime

NNT 10

Plecanatide Treatment for IBS-C, by Bloating Severity

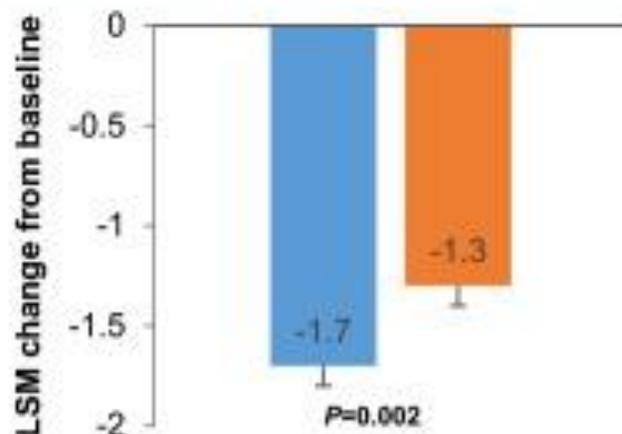
Plecanatide 3 mg or placebo for 12 weeks (two phase 3 RCTs)
Baseline stratification post hoc (11-point scale): moderate-to-severe bloating >5



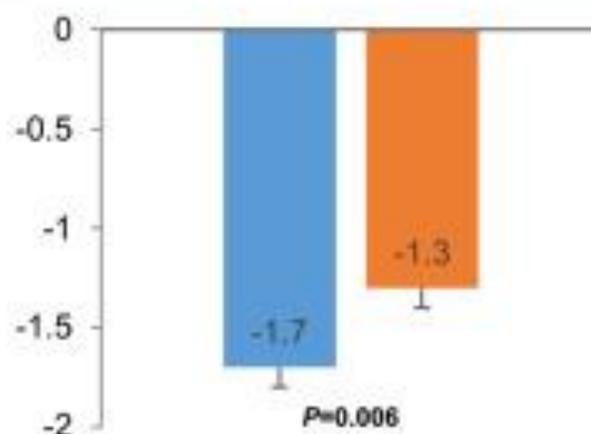
76.9% of 1436 adults had moderate-to-severe bloating at baseline

Improvements in bowel and abdominal symptoms across the 12-week treatment period

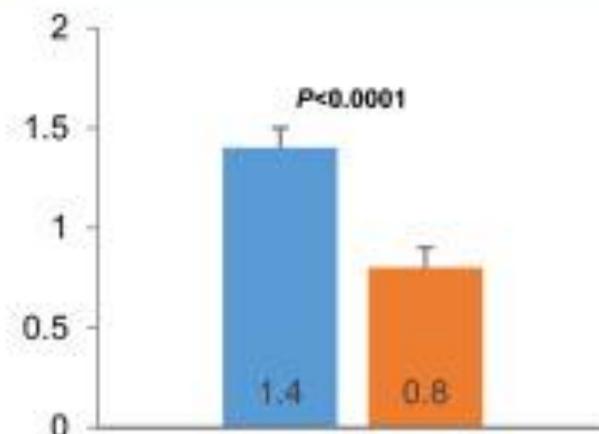
Bloating severity*



Abdominal pain severity*



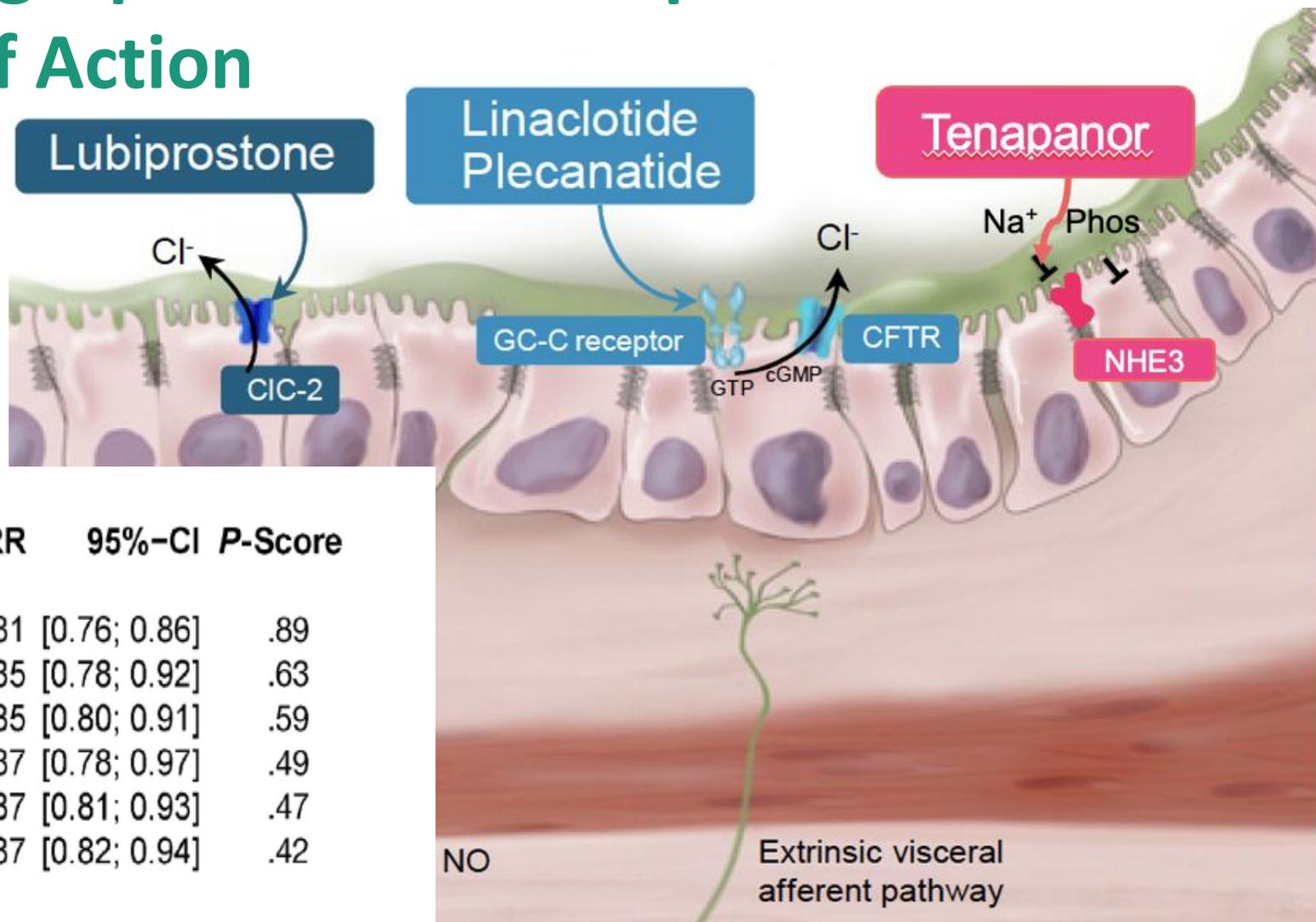
CSBMs/week



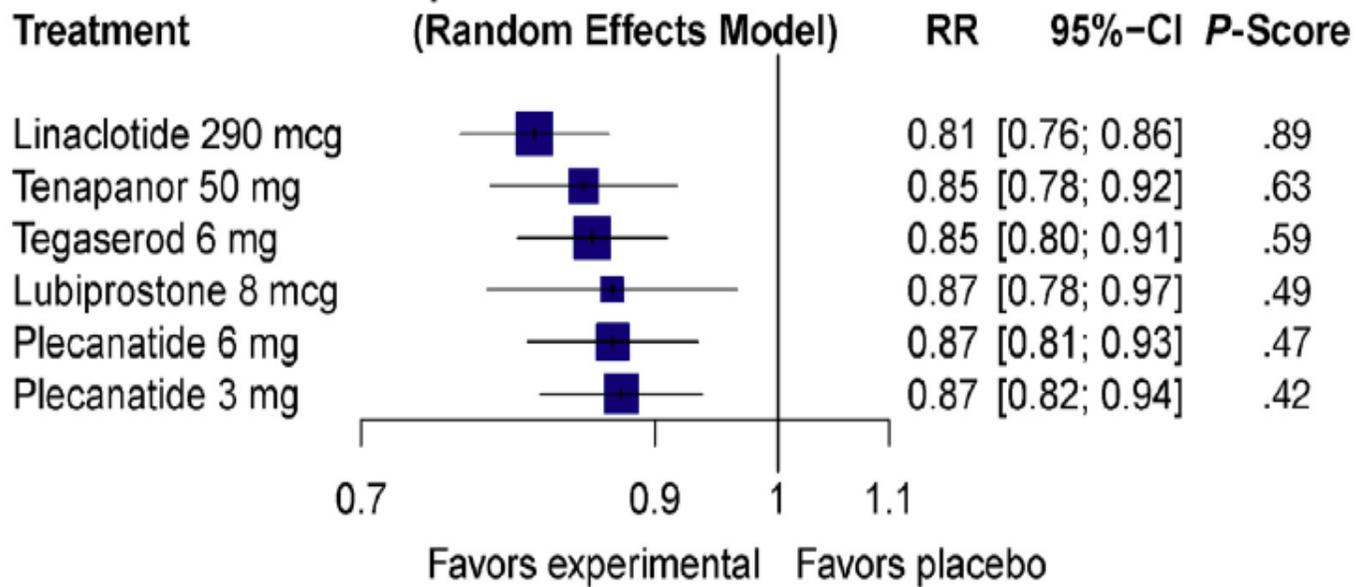
■ Plecanatide ■ Placebo

*Rated using an 11-point scale (range, 0 [“none”] to 10 [“worst possible”]). Negative change from baseline indicates improvement.
CSBM complete spontaneous bowel movement; IBS-C irritable bowel syndrome with constipation; LSM least-squares mean; RCT randomized controlled trial.

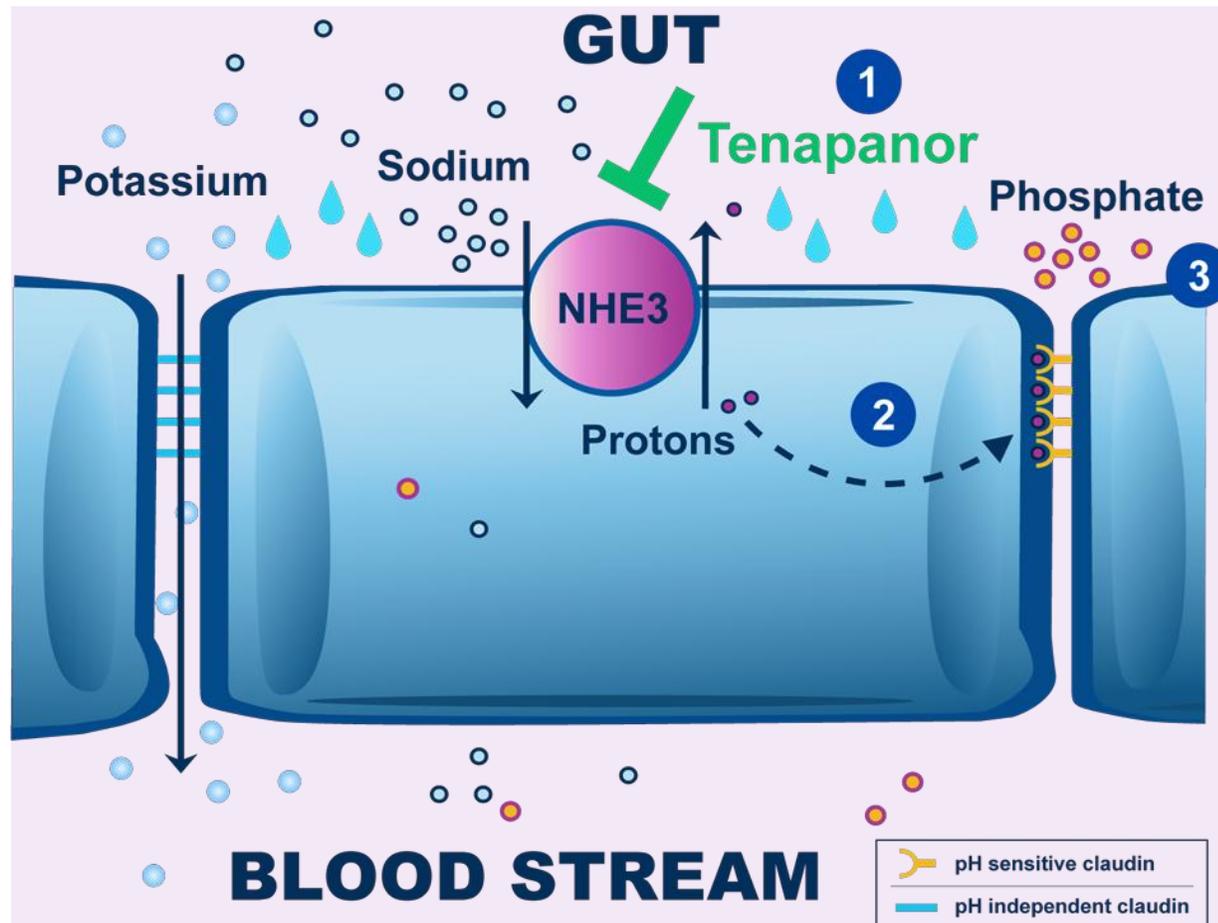
Understanding Options for Constipation Mechanism of Action



Comparison: other vs 'Placebo'
(Random Effects Model)



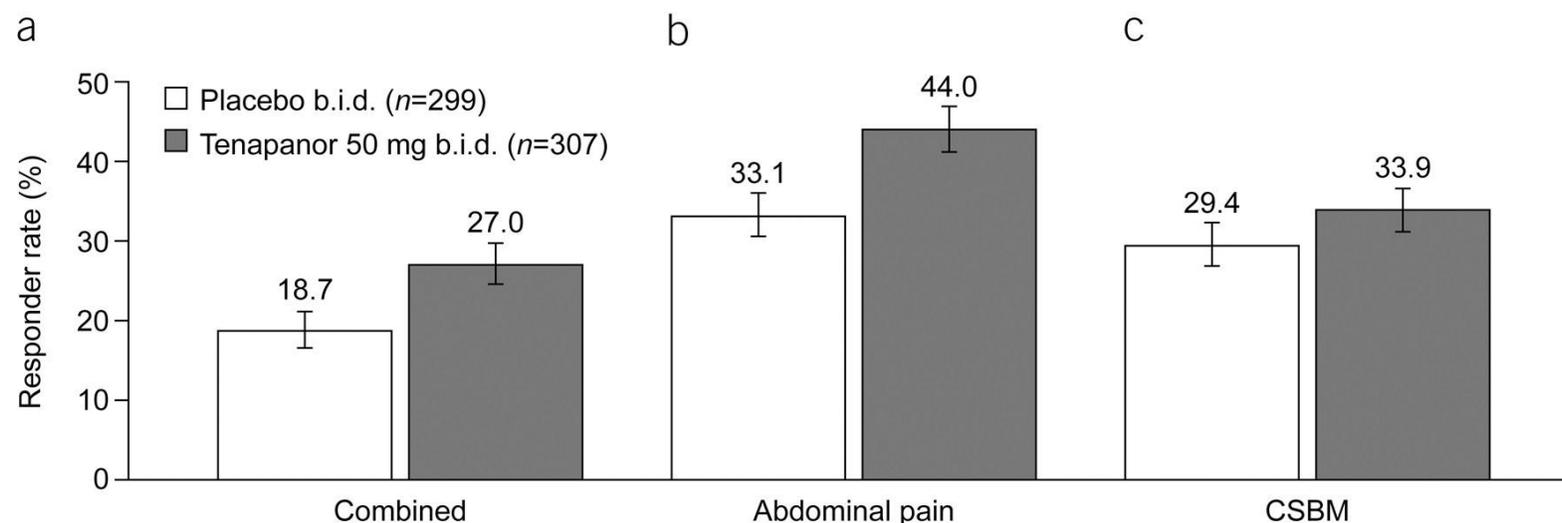
Tenapanor for IBS-C



- minimally absorbed, inhibitor of the gastrointestinal sodium/hydrogen exchanger isoform 3 (NHE3)
- Inhibits luminal sodium absorption and phosphate absorption

Tenapanor for IBS-C

- Dose: 50mg BID ; AE Diarrhea, 1 cardiac event
- NNT 7.8



Responder rate, n (%)	56 (18.7)	83 (27.0)	99 (33.1)	135 (44.0)	88 (29.4)	104 (33.9)
Risk difference vs. placebo, %	—	8.3	—	10.9	—	4.4
95% CI	—	(1.7, 15.0)	—	(3.2, 18.6)	—	(-3.0, 11.8)
Adjusted RR ^a	—	1.42	—	1.32	—	1.14
95% CI	—	(1.05, 1.92)	—	(1.07, 1.62)	—	(0.90, 1.45)
CMH <i>P</i> value ^b	—	0.020	—	0.008	—	0.270

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**ACG and AGA Recommend
the Use of
Tricyclic Antidepressants
to treat Global
IBS Symptoms**

Recommendation

ACG: Strong

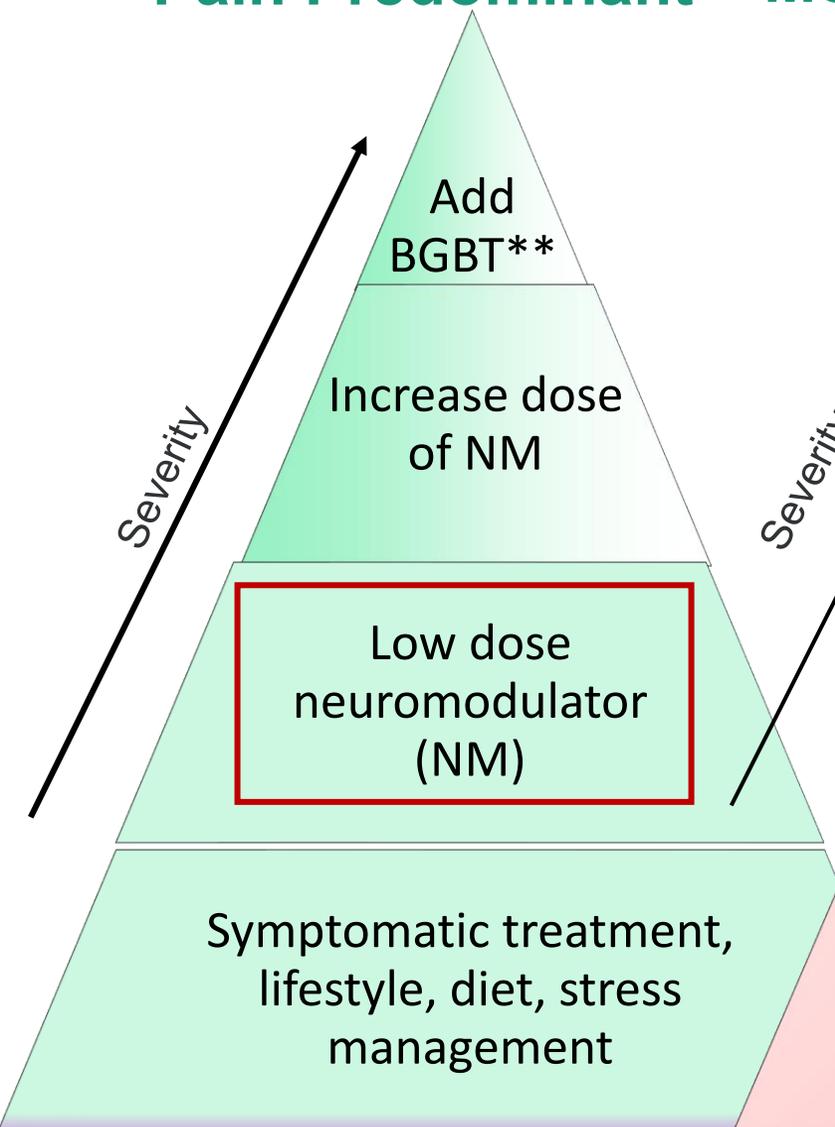
AGA: Conditional

NNT 4.5

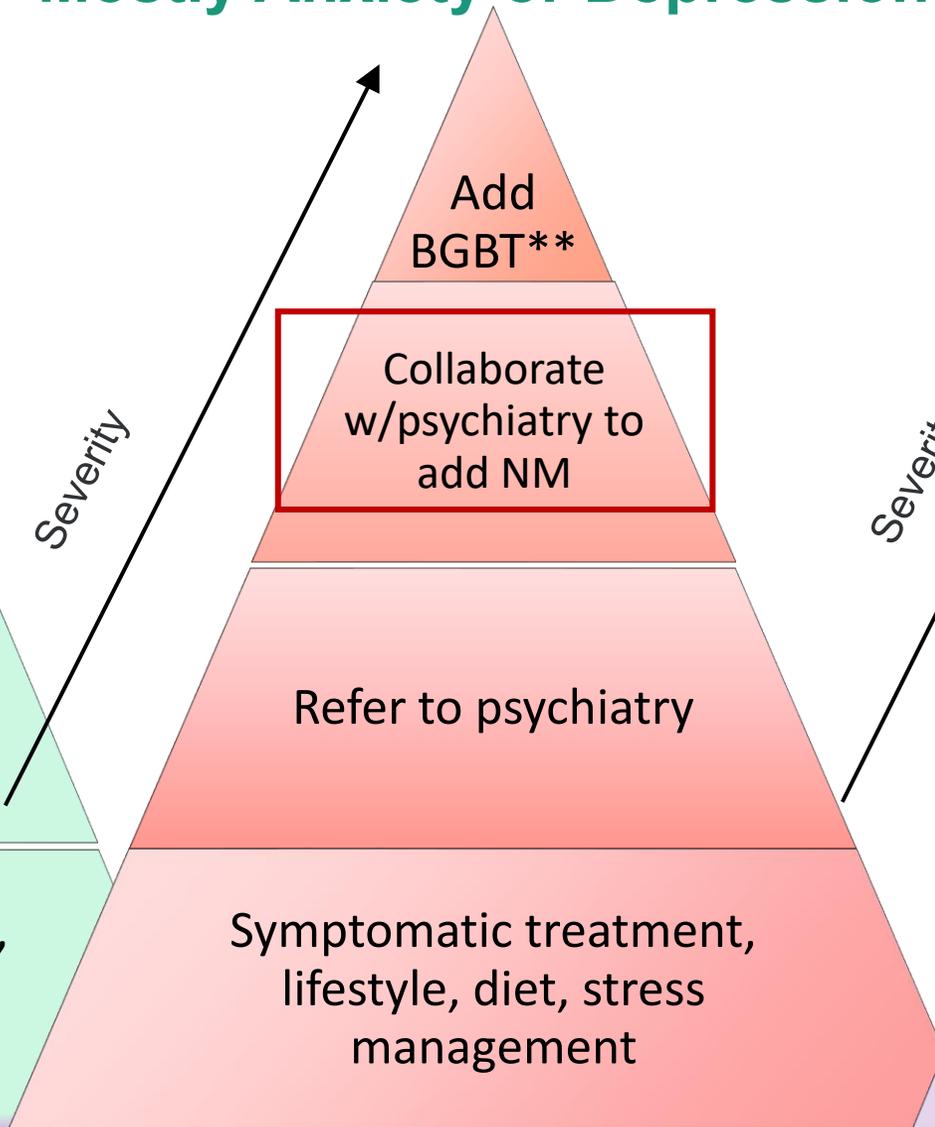
AE: drowsiness, dry mouth

**Start at 10mg daily qHS,
increase gradually to 25mg-
75mg**

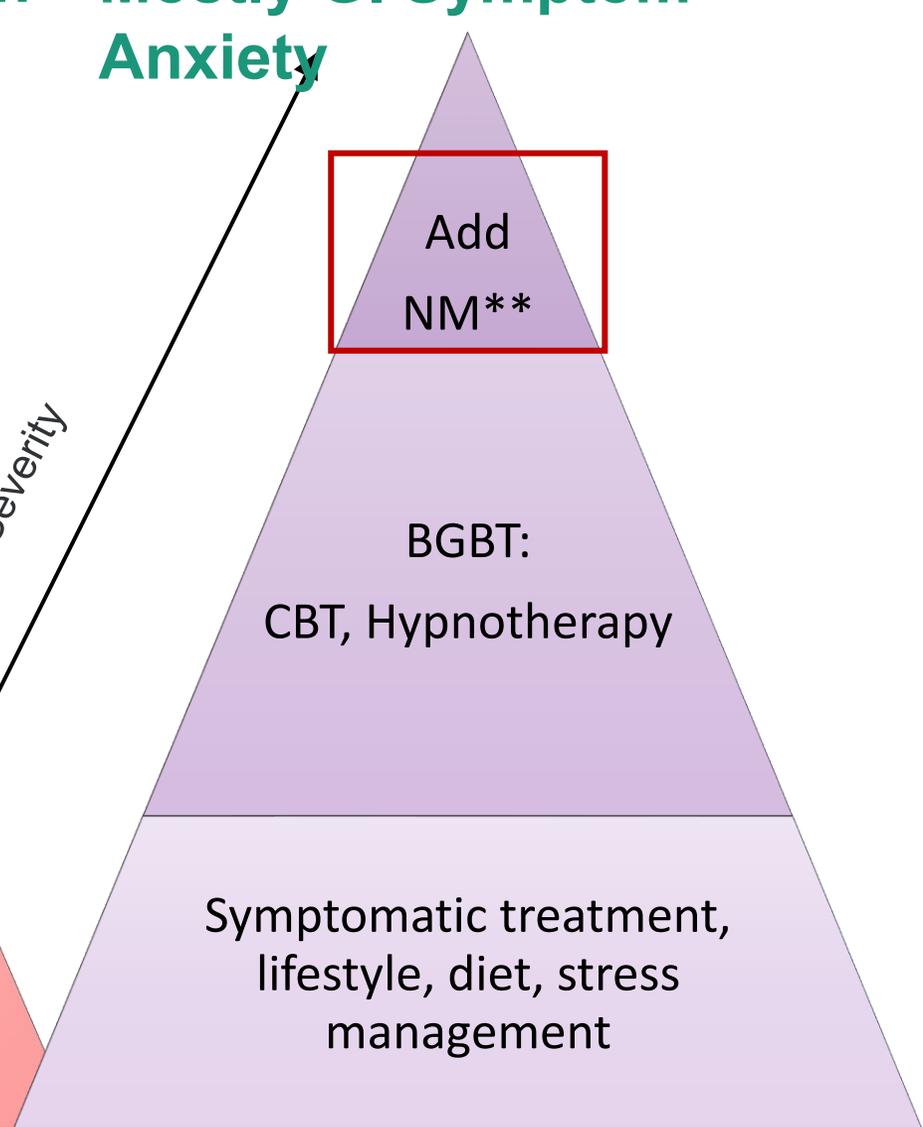
Pain Predominant



Mostly Anxiety or Depression



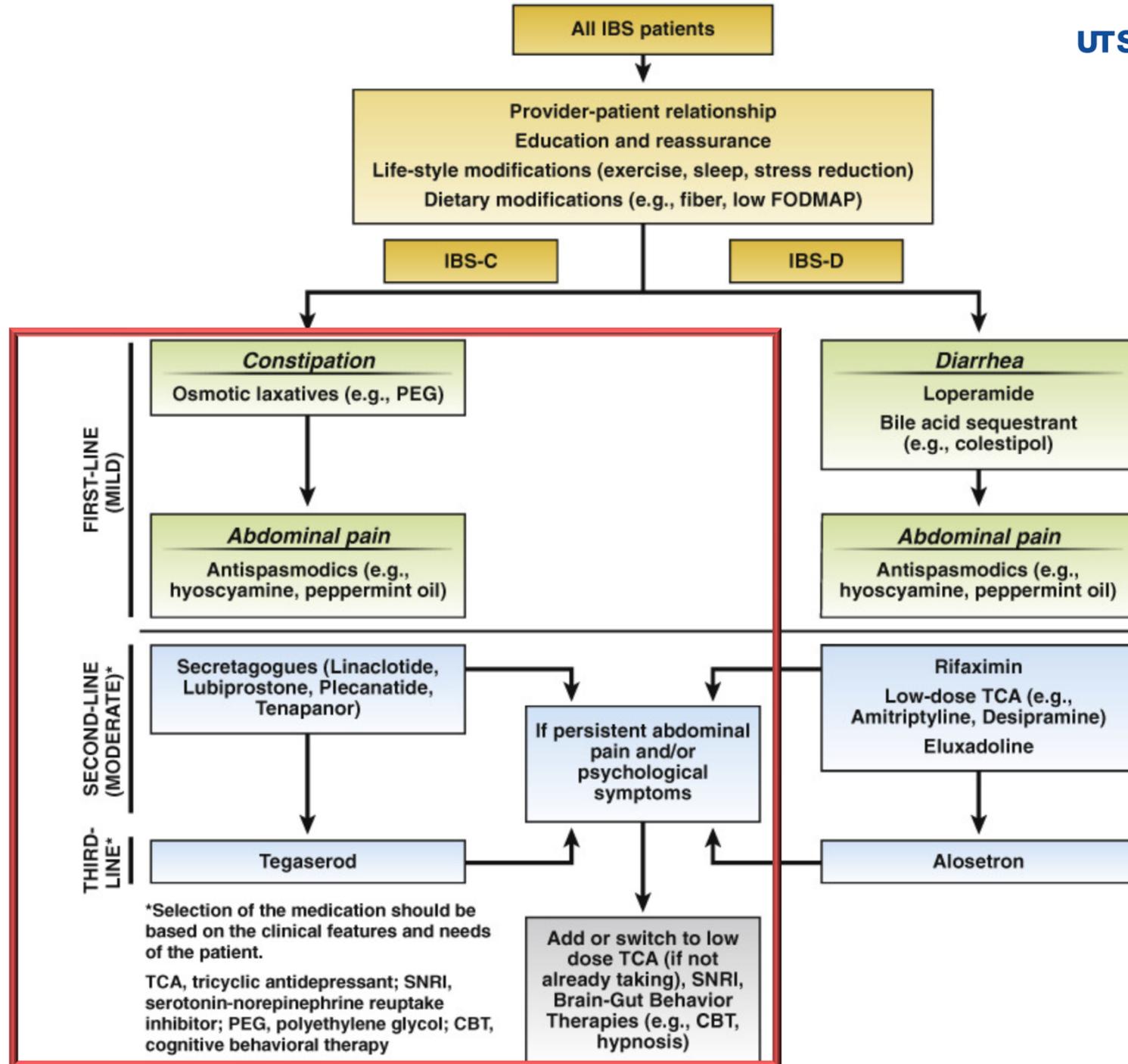
Mostly GI Symptom Anxiety



Integrating NMs with Behavioral Therapy in IBS

Medication:	Mechanism	Dosing	Cost/mo	Adverse effects	Comments
Polyethylene Glycol (Miralax)	Osmotic laxative	17g (1 capful) daily; can use BID	<\$40	Bloating	Improves stools consistency; Not effective for pain, low evidence
Linacotide (Linzess)	Guanylate-cyclase C receptor activator	72mcg-290mcg daily at breakfast	\$523	Diarrhea Significantly with 290mcg dose	AGA/ACG: Strong Rec 290mcg for IBS-C, improves pain
Plecanatide (Trulance)	Guanylate-cyclase C receptor activator	3mg daily anytime	\$528	Diarrhea Less frequent	Pain and bloating improvement
Lubiprostone (Amitiza)	Type 2 Cl channel activator	8mcg-24mcg BID	\$374	Diarrhea, Nausea	Approved in Women, IBS-C dosing is 8mcg BID
Tenapanor (IBSrela)	Intestinal Na-H exchanger 3 inhibitor	50mg BID	\$1680	Diarrhea	Dose reduction in renal failure
TCAs (Amitriptyline, Desipramine)	Serotonin and NE inhibitor, cholinergic, H1 antagonists	10mg-75mg at bedtime	\$9-\$300	Cholinergic effects, elongates QT, constipation	Start low dose and increase quickly over 2-3 weeks to goal 50-75mg
Antispasmodics Hyoscyamine, dicyclomine	Muscarinic , Ca Channel blocker, smooth m relaxation	1-2 tablets 3-4 times daily or PRN	\$10-\$50	Dry mouth, reflux, urinary retention, dizziness	Low evidence, ACG does NOT recommend

AGA Clinical Practice Guidelines



Take Home Points

Diagnose IBS-C with positive strategy; Bristol stool form scale as an objective measure

Use symptom-based treatments with realistic expectations (Diet, fiber, exercise, PEG laxatives, antispasmodics)

Low FODMAP Diet: reintroduce foods and personalize diet after 4 weeks, avoid in eating disorders

Secretagogues (guanylate cyclase activators) Linaclotide and Plecanatide are strongly advised

TCAs especially for abdominal pain at 10mg daily at bedtime and increase gradually to 25-75mg dose

Incorporate brain-gut behavioral therapy for those who are motivated and have insight into symptoms and triggers

Patient-centered, team-based approach with APPs, nursing, dieticians, psychologists, & psychiatrists = Success

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What is the next step in management?

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- B. Linaclotide**
- C. Tenapanor
- D. Anorectal manometry
- E. Prucalopride

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Constipation is a sign that
your body is holding a
grudge...

