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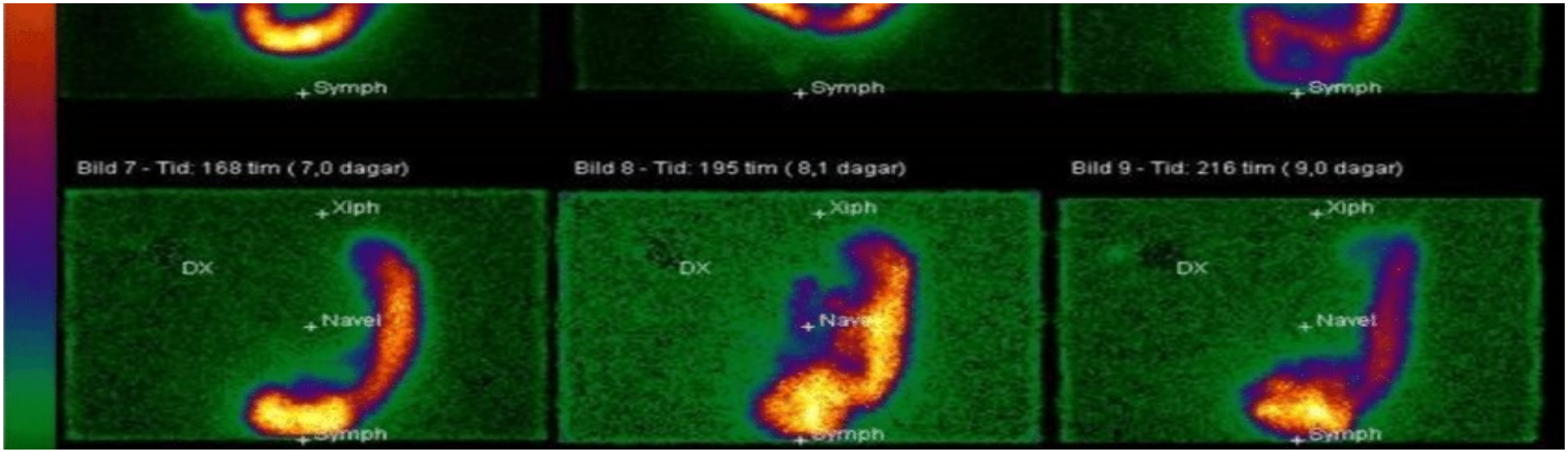
Bauchzentrum BERN

Irritable Bowel Syndrome

Bible Class 2023 / F.Bravo



History

- Galen (*Galēnos*, 129–c. 200 CE): Passions and emotions
- Plato, Aristolte, Hippocrates: Holism (mind and body are integrated and inseparable, and the study of medical disease must take into account the whole person rather than merely the diseased part)

- René Descartes, 1637: «res cogitans» (thinking mind) vs. “res extensa (the machine-like body)
- Thinking takes hold within evolving sociocultural influences

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History

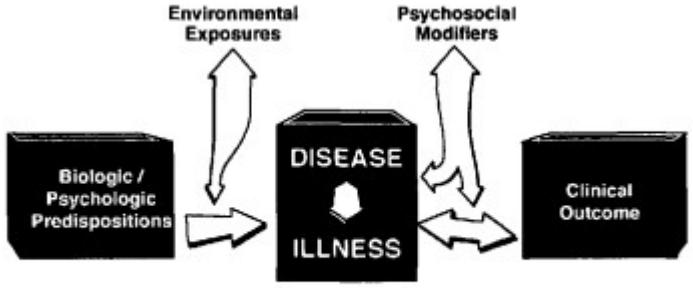
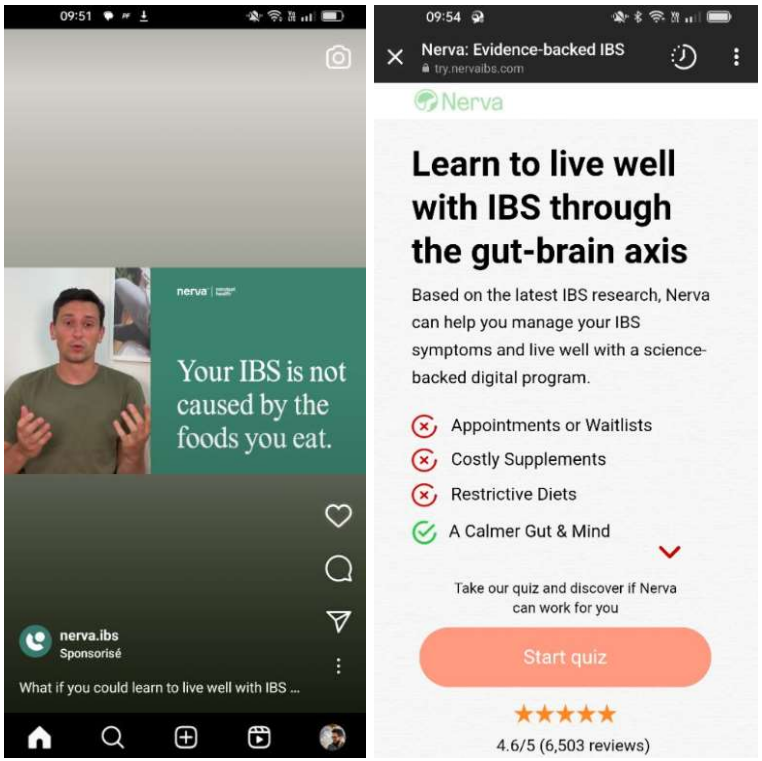


Figure 3. Schematic representation of the Biopsychosocial Model. (See text for details.)

Drossmann, Psychosomatic Medicine 1998

19-20th century



2023

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Case presentation

- Frau B.N., 1974
  - H: Low-grade symptoms for years w/ intermittent constipation, exacerbation w/ abdominal pain and bloating after HP Eradication 2019 (SBM every other day, sometimes manual evacuation, so far avoided medications, intermittent diarrhea without association to meals or specific foods
  - PS: Born in Ukraine, Nurse in a OB-GYN ward, married, 1 27yo son who currently is in Ukraine
  - FA: Granfather w/ stomach cancer 40yo, Father with CRC
  - Medications: Flroadela (Lactobacillus reuteri + rhamnosus), ViDe 3

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Case presentation

- Frau B.N., 1974
  - Other Dx:
    - Chronisches Handekzem gemischter Ätiologie mit/bei toxisch irritativer Kontaktdermatitis + Typ IV-Sensibilisierung auf Nickel (Epikutantestung 04/2021)
    - Chronic pelvic pain syndrome, pelvic MRI 2021 without pathological findings
    - Vulvodynia
    - Chronic back pain

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EGD 2018 **Motivo de exame:** Dor abdominal

Mucosa gástrica sem alterações em visão directa ou retroflexão (luz branca). Distensibilidade conservada com insuflação. Faz-se teste de urease

Bulbo e D2 sem lesões

CT 2021 Ausgeprägte, alle Colonsegmente betreffende Koprostase - die Auffälligkeit ist ausgeprägt, dass sie klinisch symptomatisch sein könnte.

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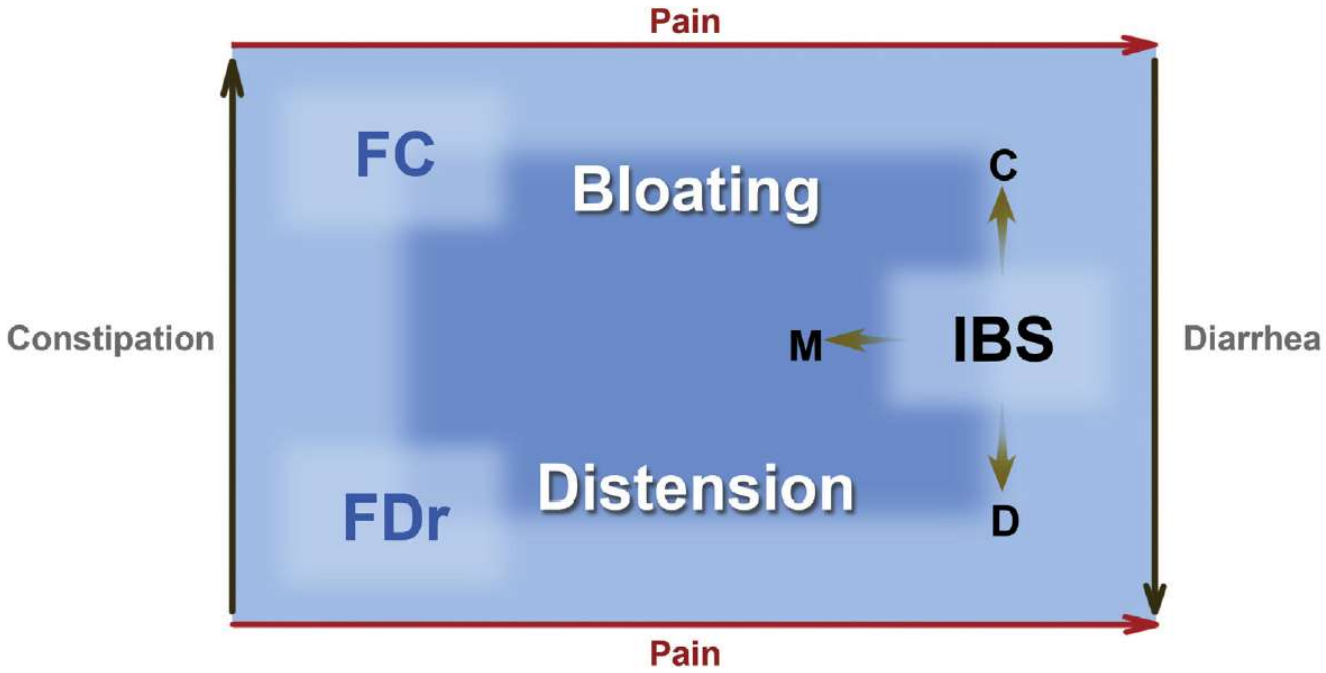
IBS - Definition

BSG 2021: abdominal pain or discomfort, in association with altered bowel habit, for at least 6 months, in the absence of alarm symptoms or signs

	Diagnostic criteria
IBS	Recurrent abdominal pain, on average for at least 1 day per week in the past 3 months, associated with two or more of the following: related to defecation, a change in frequency of stool, a change in stool form; criteria must be fulfilled for the past 3 months, with symptom onset at least 6 months before diagnosis
IBS with constipation	≥25% of bowel movements of Bristol Stool Form types 1 or 2, and <25% of Bristol Stool Form types 6 or 7
IBS with diarrhoea	≥25% of bowel movements of Bristol Stool Form types 6 or 7, and <25% of Bristol Stool Form types 1 or 2
IBS with mixed stool pattern	≥25% of bowel movements of Bristol Stool Form types 1 or 2, and ≥25% of bowel movements of Bristol Stool Form types 6 or 7
IBS unclassified	Patients who meet criteria for IBS, but do not fall into one of the other three subgroups according to Bristol Stool Form type

Adapted from Mearin and colleagues.[5] IBS=irritable bowel syndrome.

Table 1: The Rome IV criteria for IBS and its subgroups



Lacy et al., Gastroenterology 2016;150:1393–1407

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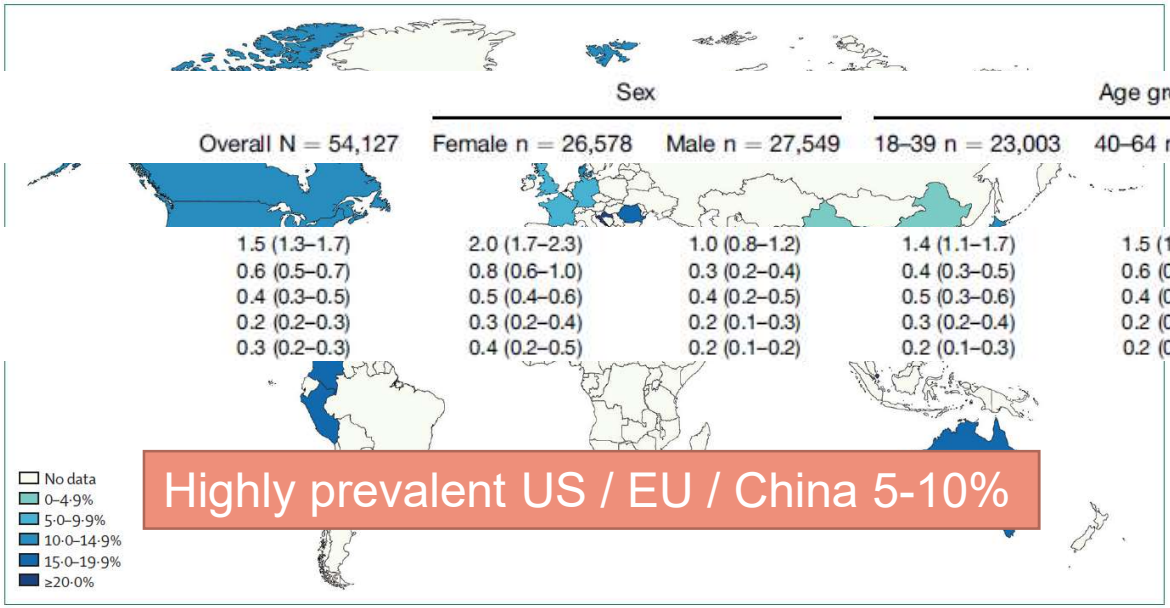
IBS - Epidemiology



FGID	Overall N = 54,127	Sex: Female n = 26,578	Sex: Male n = 27,549	Age group (y): 18–39 n = 23,003	Age group (y): 40–64 n = 22,281	Age group (y): 65+ n = 8843
Rome-IV IBS	1.5 (1.3–1.7)	2.0 (1.7–2.3)	1.0 (0.8–1.2)	1.4 (1.1–1.7)	1.5 (1.2–1.7)	1.9 (1.4–2.4)
IBS-C	0.6 (0.5–0.7)	0.8 (0.6–1.0)	0.3 (0.2–0.4)	0.4 (0.3–0.5)	0.6 (0.4–0.7)	1.0 (0.6–1.3)
IBS-D	0.4 (0.3–0.5)	0.5 (0.4–0.6)	0.4 (0.2–0.5)	0.5 (0.3–0.6)	0.4 (0.3–0.6)	0.3 (0.1–0.4)
IBS-U	0.2 (0.2–0.3)	0.3 (0.2–0.4)	0.2 (0.1–0.3)	0.3 (0.2–0.4)	0.2 (0.1–0.3)	0.2 (0.0–0.3)
IBS-M	0.3 (0.2–0.3)	0.4 (0.2–0.5)	0.2 (0.1–0.2)	0.2 (0.1–0.3)	0.2 (0.1–0.3)	0.5 (0.2–0.7)

Highly prevalent US / EU / China 5-10%

Figure 1: **Global prevalence of IBS according to the Rome III criteria**
Prevalence data taken from studies that used the Rome III criteria for IBS.[4,12,13] IBS=irritable bowel syndrome.

Ford et al. Lancet 2020; 396: 1675–88
Sperber AD et al. Gastroenterology 2020

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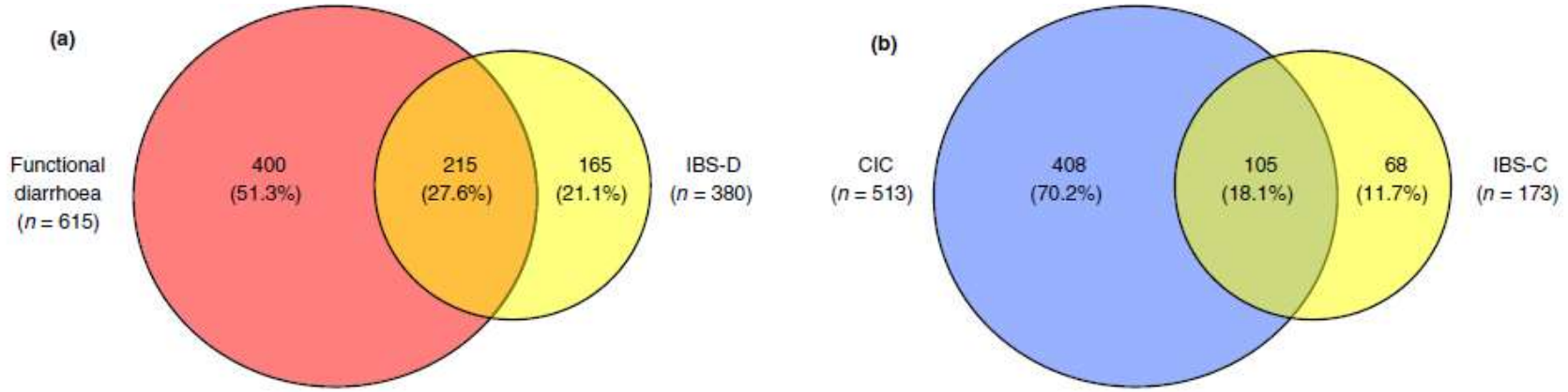
IBS - Epidemiology



Significant overlap between FGID diagnostic clusters

Ford et al. Aliment Pharmacol Ther 2014

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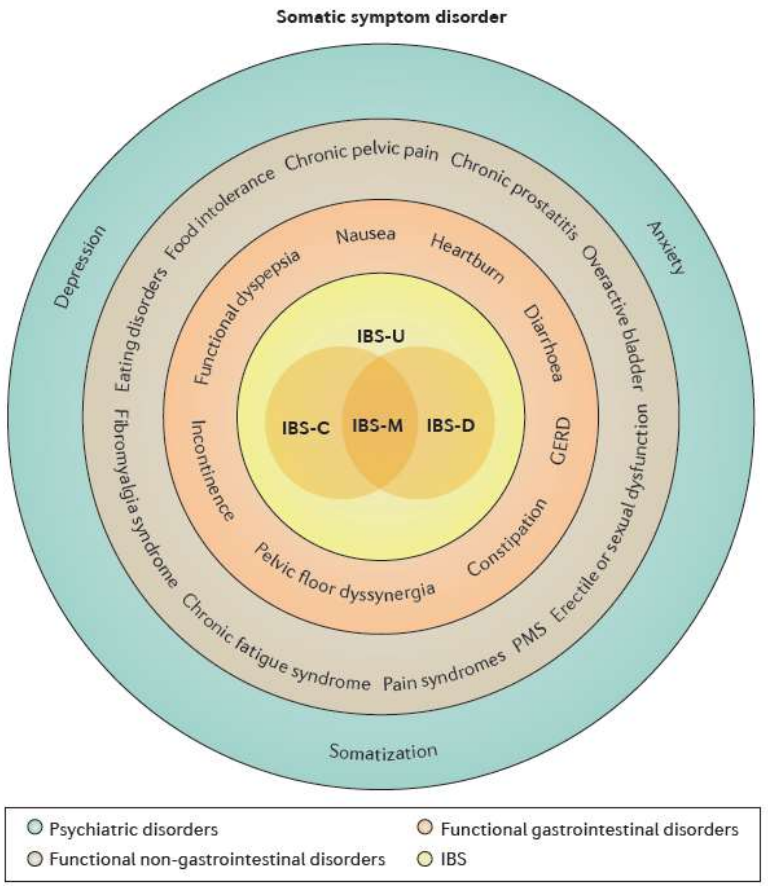
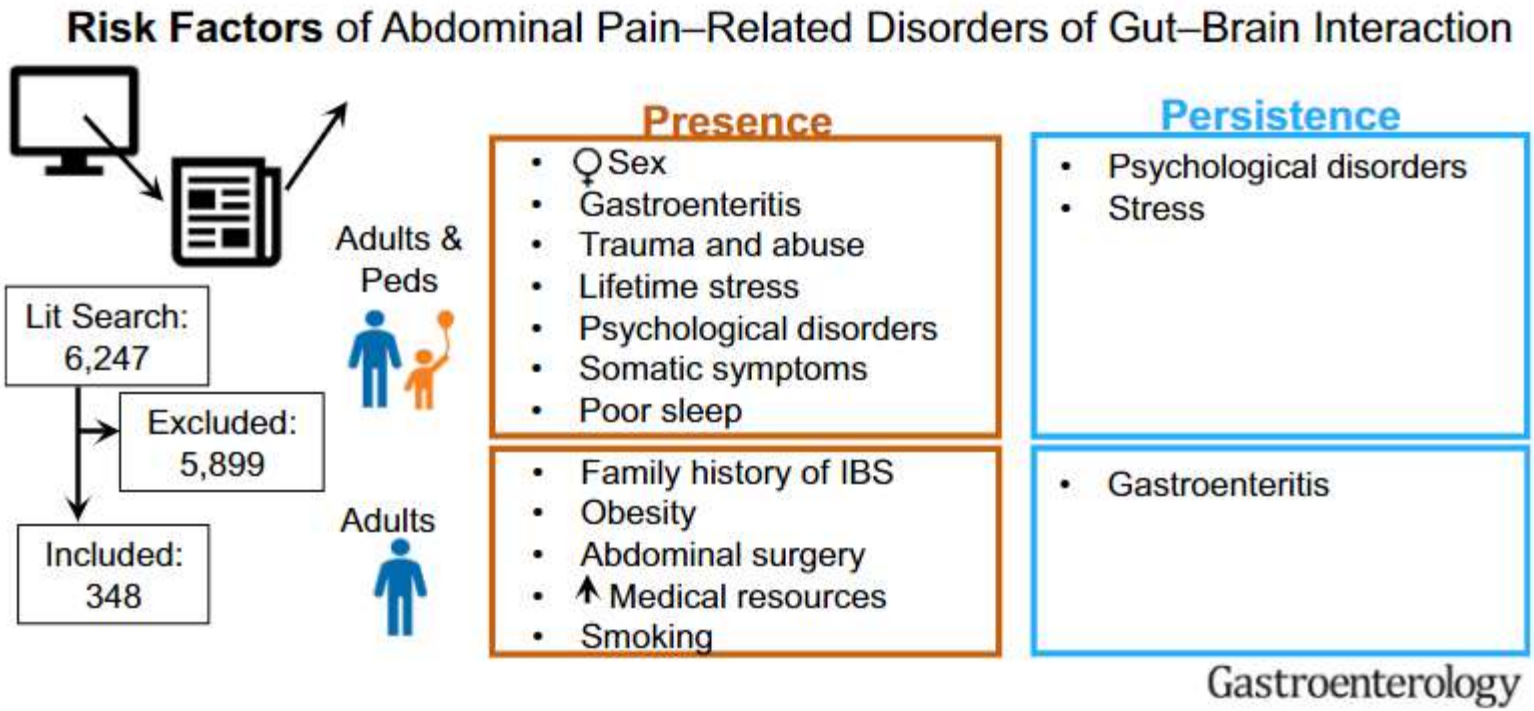
IBS - Epidemiology

Overlap often beyond the expected prevalence rates for individual diseases



Ford et al. Lancet 2020; 396: 1675–88
Sperber AD et al. Gastroenterology 2020

IBS - Risk factors



Zia et al., Gastroenterology Vol. 163, No. 4, 2022

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Post infectious IBS

- Pooled odds ratio is 7.3 (95% CI: 4.7–11.1) for the development of IBS after infectious gastroenteritis
- Median prevalence of ~10%

Thabane, M et al. Systematic review and meta-analysis: the incidence and prognosis of post-infectious irritable bowel syndrome. Aliment. Pharmacol. Ther. 26, 535–544 (2007).

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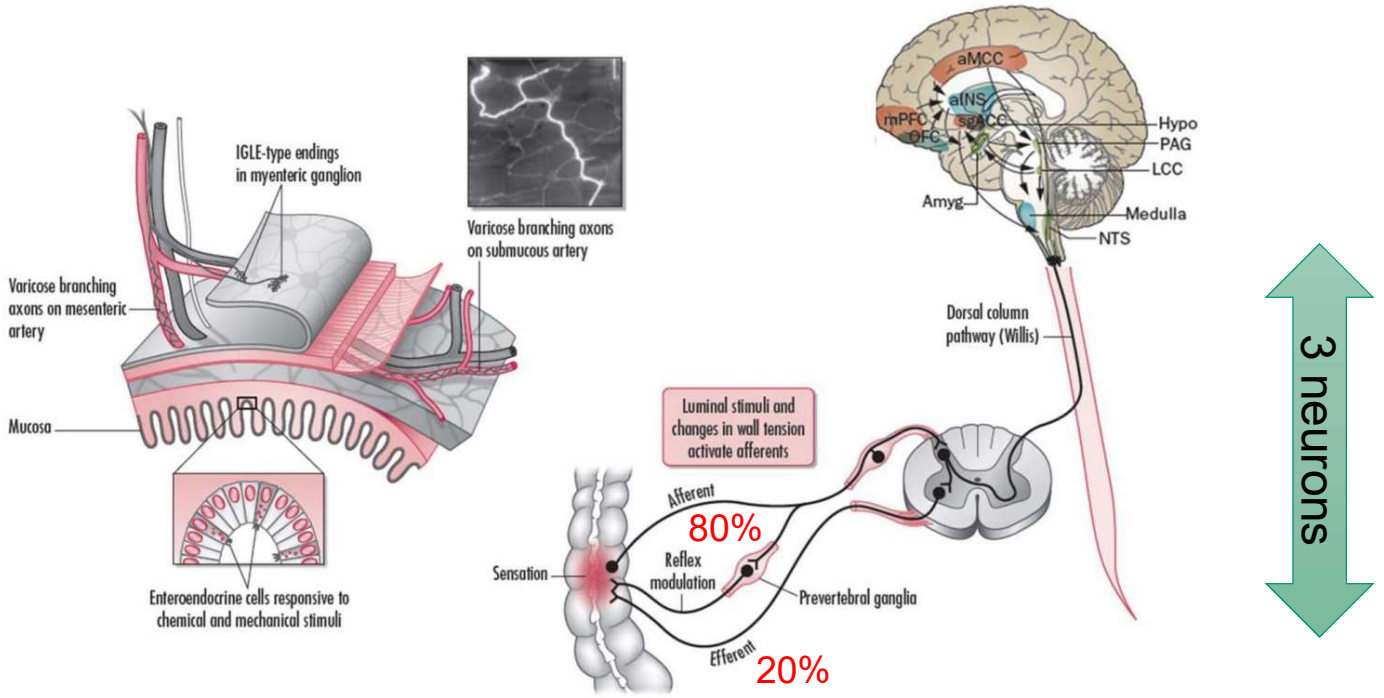
Physiopathology

- Genetics
- Visceral sensation
- CNS/autonomic modulation
- Luminal factors: bile acids, SCFA
- Motility
- Microbiota
- Foods and intolerance
- Mucosal permeability
- Immune activation

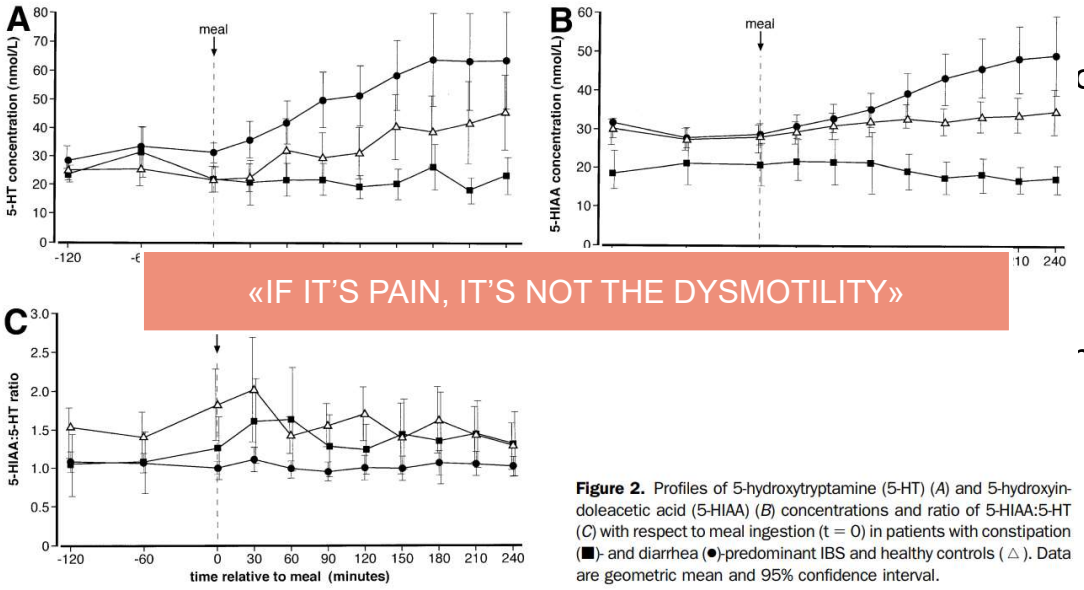
CNS/autonomic modulation/visceral sensation



Camilleri M, Boeckxstaens G. Gut 2017;66:966–974.

Colonic motility

- Abnormal in … of patients with IBS-D
- symptoms of … all, with colonic trans…
- abdominal di… sensation of bloating) cor… stool consistency
- Changes ma…

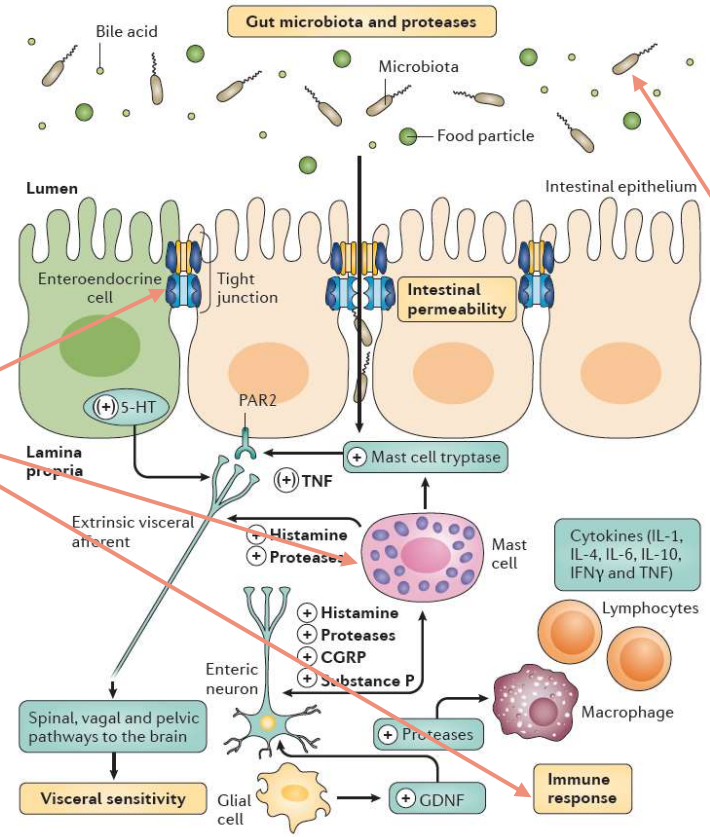


«IF IT'S PAIN, IT'S NOT THE DYSMOTILITY»

Figure 2. Profiles of 5-hydroxytryptamine (5-HT) (*A*) and 5-hydroxyindoleacetic acid (5-HIAA) (*B*) concentrations and ratio of 5-HIAA:5-HT (*C*) with respect to meal ingestion (t = 0) in patients with constipation (■)- and diarrhea (●)-predominant IBS and healthy controls (△). Data are geometric mean and 95% confidence interval.

Atkinson et al., Gastroenterology 2006;130:34 –43

Immune regulation, inflammation and permeability



Box 4 | **Dysbiosis in IBS**

Microbiota species increased in IBS

- Enterobacteriaceae
- *Veillonella*
- *Streptococcus**
- *Dorea*
- *Blautia*
- *Roseburia*
- *Ruminococcus*
- *Methanobrevibacter*‡

Microbiota species decreased in IBS

- *Bifidobacterium*
- *Collinsella*
- *Streptococcus*‡
- *Faecalibacterium*
- Christensenellaceae
- Clostridiales
- Uncultured
- *Methanobrevibacter*§

IBS, irritable bowel syndrome. *IBS with diarrhoea. ‡IBS with constipation. §Mixed-type IBS.

Enck et al., Irritable Bowel Syndrome, Nat Rev Dis Primers 2016

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Genetics

Genetic Risk Factors for Post-Infectious Irritable Bowel Syndrome Following a Waterborne Outbreak of Gastroenteritis

ALEXANDRA–CHLOÉ VILLANI,[*,‡] MATHIEU LEMIRE,[§] MARROON THABANE,[‖] ALEXANDRE BELISLE,[‡] GENEVIÈVE GENEAU,[‡] AMIT X. GARG,[¶] WILLIAM F. CLARK,[¶] PAUL MOAYYEDI,[‖] STEPHEN M. COLLINS,[‖] DENIS FRANCHIMONT[*,#] and JOHN K. MARSHALL[‖]

[*]Division of Gastroenterology, Department of Medicine, McGill University, Montréal, Québec, Canada; [‡]McGill University and Génome Québec Innovation Centre, Montréal, Québec, Canada; [§]Ontario Institute for Cancer Research, Toronto, Ontario, Canada; [‖]Farncombe Family Digestive Health Research Institute and Division of Gastroenterology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [¶]Division of Nephrology, Department of Medicine, University of Western Ontario, London, Ontario, Canada; and [#]Department of Gastroenterology, Erasme Hospital, Free University of Brussels, Brussels, Belgium

Specific variants in inflammation susceptibility genes TLR9, IL6, and CDH1 are Independent PI-IBS Risk Factors

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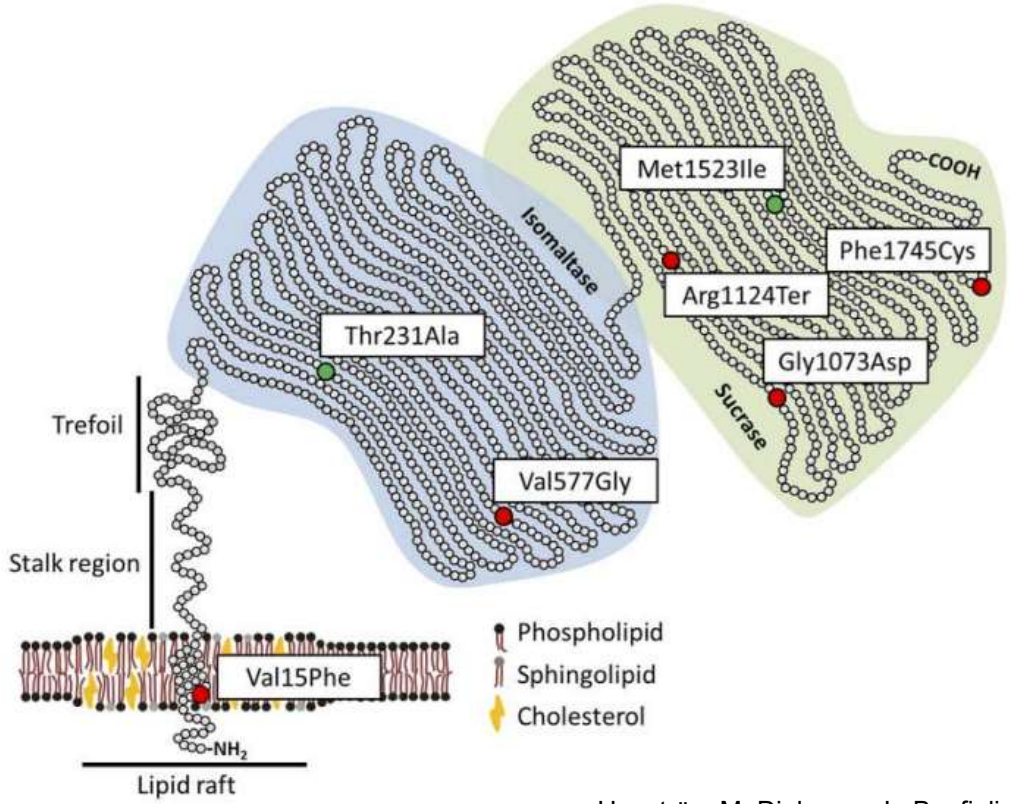
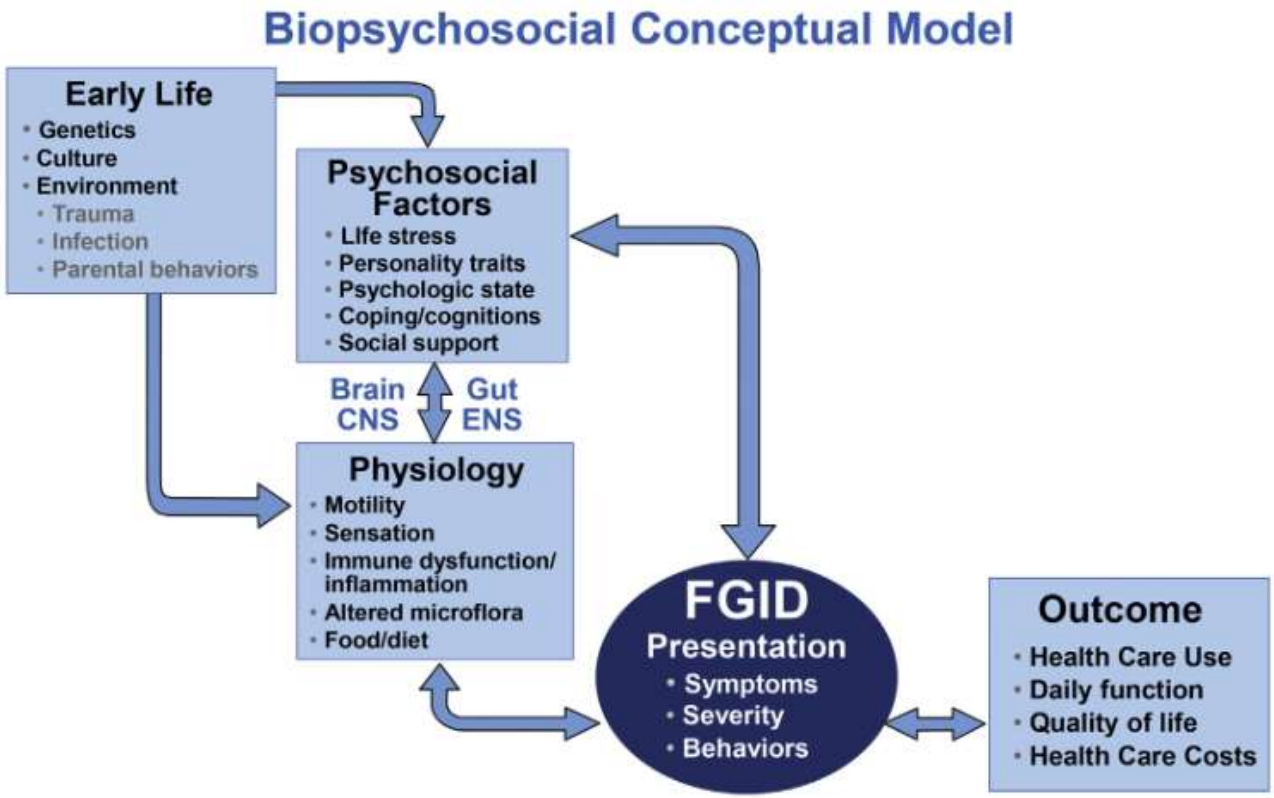
Genetics



Henström M, Diekmann L, Bonfiglio F, et al. Gut 2018;67:263–270


Biopsychosocial Conceptual Model
Early Life
• Genetics
• Culture
• Environment
• Trauma
• Infection
• Parental behaviors
Psychosocial Factors
• LIfe stress
• Personality traits
• Psychologic state
• Coping/cognitions
• Social support
Brain CNS
Gut ENS
Physiology
• Motility
• Sensation
• Immune dysfunction/ inflammation
• Altered microflora
• Food/diet
FGID Presentation
• Symptoms
• Severity
• Behaviors
Outcome
• Health Care Use
• Daily function
• Quality of life
• Health Care Costs

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Diagnosis and treatment

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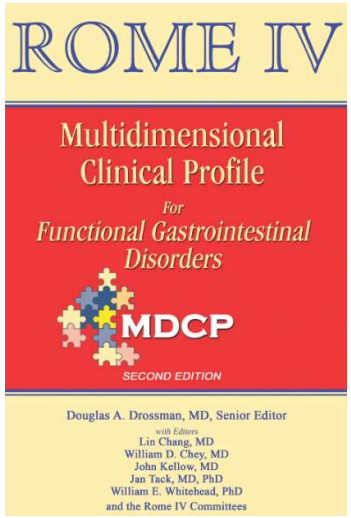
MDCP - Rome Foundation

- A. The categorical Rome diagnosis - symptom-based, may include physiological criteria
- B. Clinical modifier - additional information that subclassifies the diagnosis leading to more specific treatments, e.g., IBS-D, C, M, FODMAP sensitivity, post infectious
- C. The personal impact of the disorder on the patient - mild, moderate, severe
- D. Psychosocial influences - diagnosis, abuse history
- E. Physiological abnormalities or biomarkers - type and severity (delayed emptying, slow transit, inflammation)



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Ms. B.

- Goes to her GP. At first presentation, what investigations should be offered?

- Full blood count
- C reactive protein or erythrocyte sedimentation rate
- Coeliac serology
- In patients <45 years of age with diarrhea, calprotectin
- ! Exam: local guidelines for CRC/ovarian cancer

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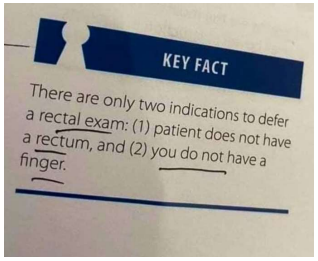
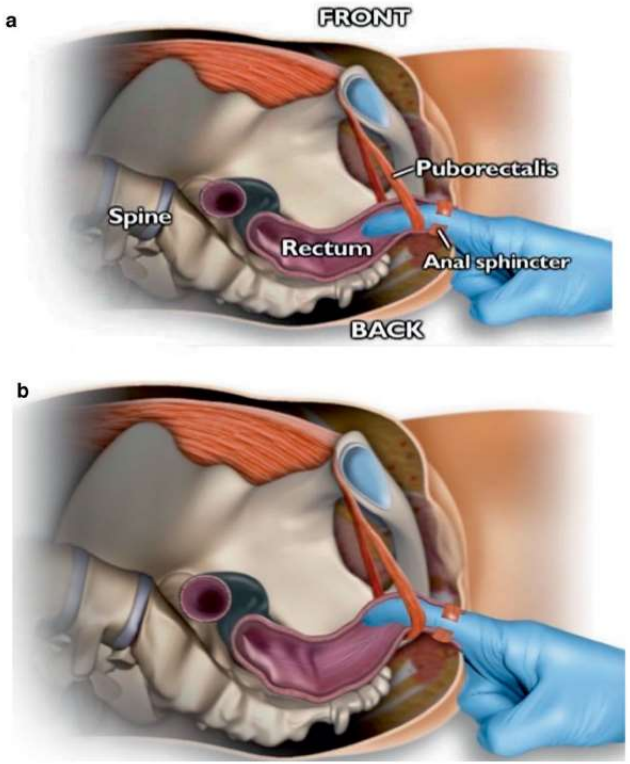
Further testing - BSG 2021

• Colonoscopy	• No
• BT for SIBO	• No
• 7α-hydroxy-4-cholesten-3-one	• Yes
• ARM	• Maybe
• Fecal elastase	• No

"… specificity of DRE for identifying dyssynergia when compared to anorectal manometry were 75 and 87%, respectively, and the positive predictive value was 97%."





Rao, AJG 2018

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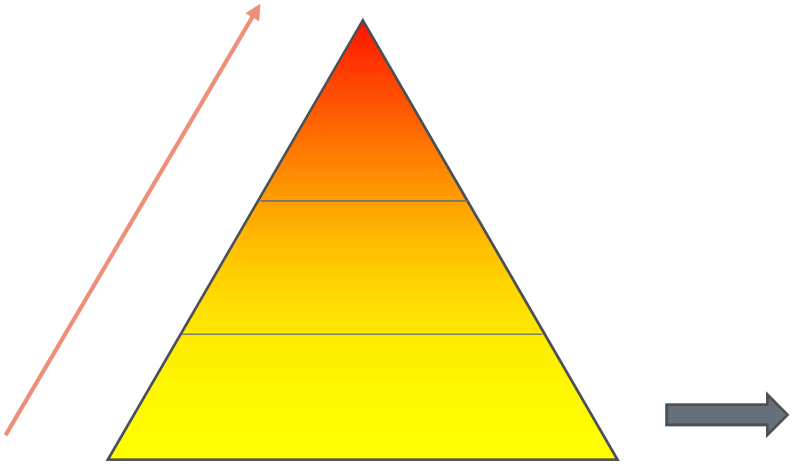
Ms. B.

- Fullfills IBS-C ROME IV Criteria. What first line measures do you propose?



Explain, reassure, positive diagnosis, diet, lifestyle advice

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MDCP - Rome Foundation

- A. The categorical Rome diagnosis - symptom-based, may include physiological criteria
  - Irritable bowel syndrome
- B. Clinical modifier
  - IBS-C, exacerbation post antibiotics, multiple chronic pain diagnoses
- C. The personal impact of the disorder on the patient
  - Moderate
- D. Psychosocial influences
  - Cultural, psychosocial context
- E. Physiological abnormalities or biomarkers
  - Normal labs findings, endoscopy, normal Transit, normal DRE and no outlet symptoms

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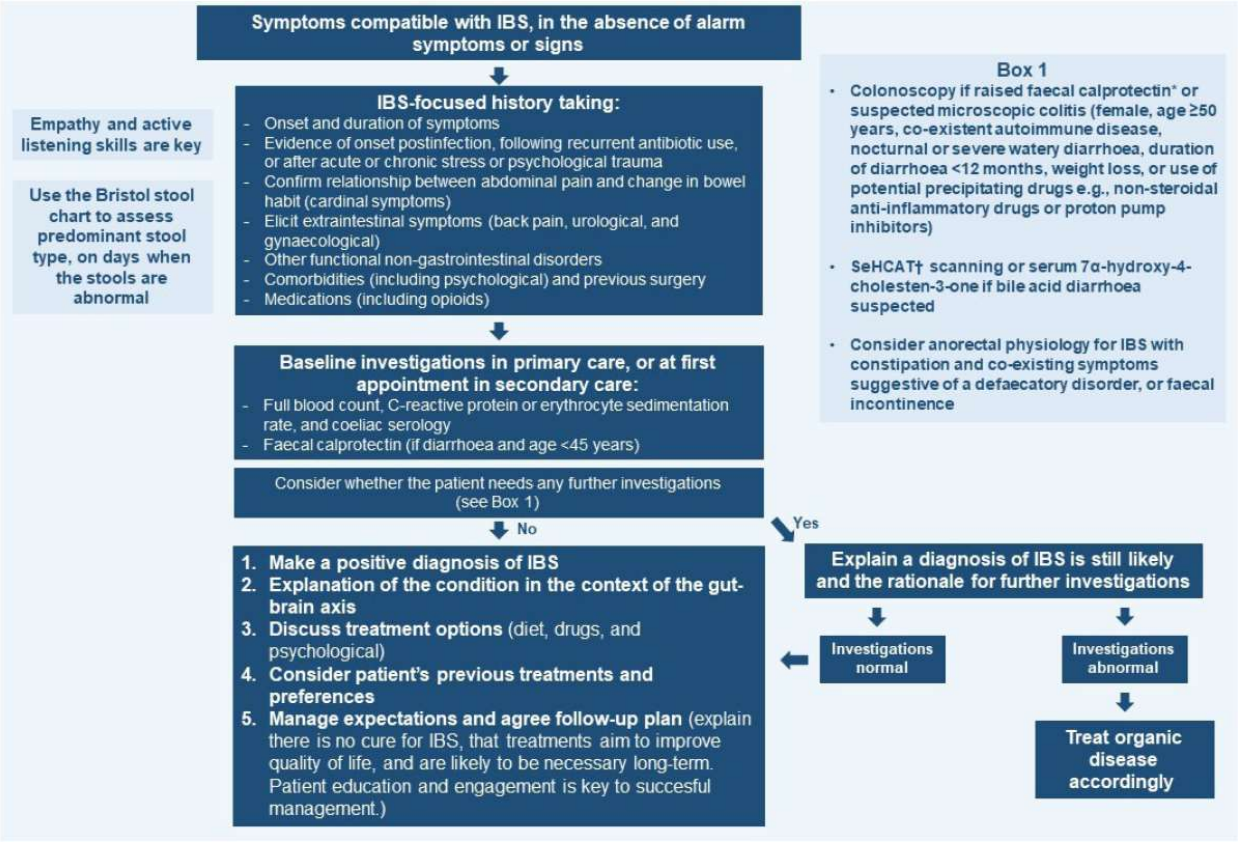
Communication

- Positive diagnosis of IBS and patient education => reduction in IBS symptom severity and gastrointestinal (GI)-specific anxiety, improvement in perceived knowledge of IBS and HRQoL

  Ringström, G. et al., Structured patient education is superior to written information in the management of patients with irritable bowel syndrome: a randomized controlled study. European Journal of Gastroenterology & Hepatology 22(4):p 420-428, April 2010.

- Underline chronicity, possibility of recurrent fluctuating symptoms triggered by stress, drugs and often the act of eating
- IBS is not associated with an increased risk of cancer or mortality but QoL as affected by IBS than IBD

  Pace F, Molteni P, Bollani S, et al. Inflammatory bowel disease versus irritable bowel syndrome: a hospital-based, case-control study of disease impact on quality of life. Scand J Gastroenterol 2003;38:1031–8.


Symptoms compatible with IBS, in the absence of alarm symptoms or signs
Empathy and active listening skills are key
Use the Bristol stool chart to assess predominant stool type, on days when the stools are abnormal
IBS-focused history taking:
- Onset and duration of symptoms
- Evidence of onset postinfection, following recurrent antibiotic use, or after acute or chronic stress or psychological trauma
- Confirm relationship between abdominal pain and change in bowel habit (cardinal symptoms)
- Elicit extraintestinal symptoms (back pain, urological, and gynaecological)
- Other functional non-gastrointestinal disorders
- Comorbidities (including psychological) and previous surgery
- Medications (including opioids)
Baseline investigations in primary care, or at first appointment in secondary care:
- Full blood count, C-reactive protein or erythrocyte sedimentation rate, and coeliac serology
- Faecal calprotectin (if diarrhoea and age <45 years)
Consider whether the patient needs any further investigations (see Box 1)
No
Yes
1. Make a positive diagnosis of IBS
2. Explanation of the condition in the context of the gut-brain axis
3. Discuss treatment options (diet, drugs, and psychological)
4. Consider patient's previous treatments and preferences
5. Manage expectations and agree follow-up plan (explain there is no cure for IBS, that treatments aim to improve quality of life, and are likely to be necessary long-term. Patient education and engagement is key to succesful management.)
Explain a diagnosis of IBS is still likely and the rationale for further investigations
Investigations normal
Investigations abnormal
Treat organic disease accordingly
Box 1
• Colonoscopy if raised faecal calprotectin* or suspected microscopic colitis (female, age ≥50 years, co-existent autoimmune disease, nocturnal or severe watery diarrhoea, duration of diarrhoea <12 months, weight loss, or use of potential precipitating drugs e.g., non-steroidal anti-inflammatory drugs or proton pump inhibitors)
• SeHCAT† scanning or serum 7α-hydroxy-4-cholesten-3-one if bile acid diarrhoea suspected
• Consider anorectal physiology for IBS with constipation and co-existing symptoms suggestive of a defaecatory disorder, or faecal incontinence

Treamtent: general considerations

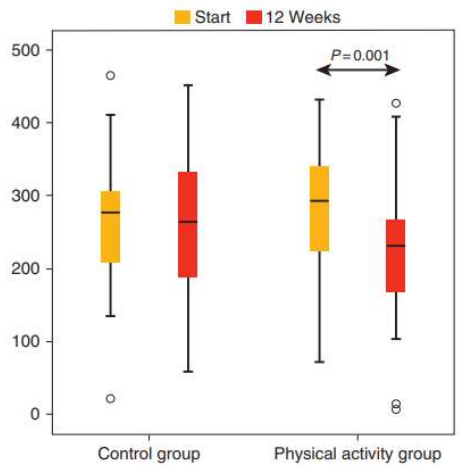


Figure 2. IBS-Severity Scoring System, IBS score.

Elisabet Johannesson, Am J Gastroenterol 2011

Recommendation	PEN Grade[14]	
1 Healthy eating & lifestyle		
Alcohol	Assess intake and screen for signs of binge drinking. Ensure alcohol intake is in keeping with safe national limits (2016)	C
Caffeine	Insufficient evidence to make a recommendation (2016)	D
Spicy food	If related to symptoms assess spicy food intake and trial restriction (2016)	C
Fat	If related to symptoms during or after eating, assess fat intake and ensure it is in line with national healthy eating	C
5 Gluten	At this time no recommendation can be made to treat IBS symptoms with a gluten-free diet (2016)	D
6 Probiotic products to improve IBS symptoms	Advise that probiotics are unlikely to provide substantial benefit to IBS symptoms. However, individuals choosing to try probiotics are advised to select one product at a time and monitor the effects. They should try it for a minimum of 4 weeks at the dose recommended by the manufacturer (2016)	B
	Taking a probiotic product is considered safe in IBS (2016)	B
7 Elimination diets/ food hypersensitivity	Non-specific elimination diets are no longer valid to improve IBS symptoms (2016)	D

FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; IBS, irritable bowel syndrome; IBS-C, IBS – constipation-predominant; PEN, Practice-based Evidence in Nutrition.

BSG/NICE:
“regular meals, maintain adequate nutrition, limit alcohol and caffeine intake, adjust fibre intake, reduce consumption of fatty and spicy foods”

McKenzie et al, Evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). J Hum Nutr Diet

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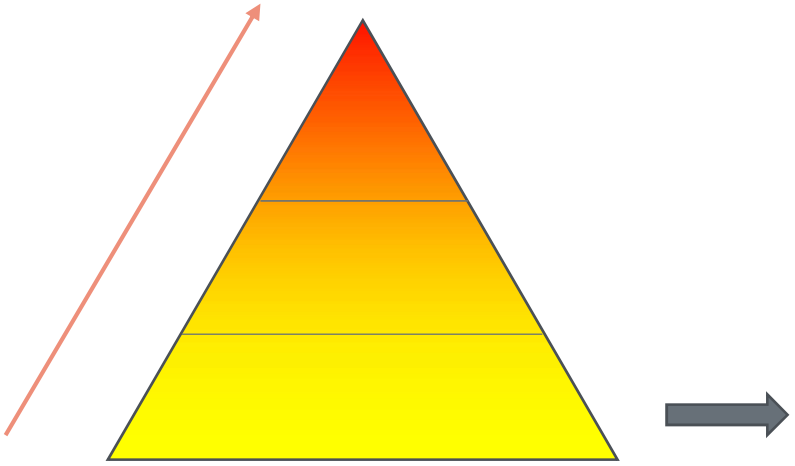
Ms. M.

SST: Metamucile, BT, Nifedipine cream for anal fissures. PT already ongoing for chronic pelvic pain (OBGYN). G+K (FA+)

- IgG based exclusion diets ?
- GFD?
- How much fibre in 1 metamucile teaspoon (g)?



Communication, fibre, physical activity, +/- FODMAP

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Ms. B.

- 3M FUP:
  - 1 SBM/d, no manual evacuation anymore but BSS still 1-2 in >25%
  - In the meantime: UTI, ttt/Ciprofloxacin with good GI symptomatic response, is very concerned a chronic GI infection might have been missed
  - BT: + (post Cipro)

  - … What now?

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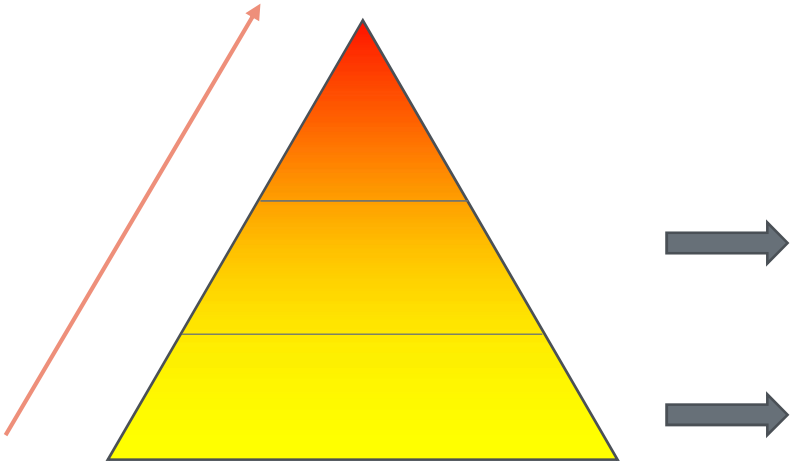
Ms. M.

- BT+, still some pain and hard stool



FUP visit, adress anxiety/stress (screening!), gut pharmacotherapy

Explain, reassure, positive diagnosis, diet, lifestyle advice

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PHQ-4: THE FOUR-ITEM PATIENT HEALTH QUESTIONNAIRE FOR ANXIETY AND DEPRESSION

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious or on edge	0	1	2	3
Not being able to stop or control worrying	0	1	2	3
Feeling down, depressed or hopeless	0	1	2	3
Little interest or pleasure in doing things	0	1	2	3
TOTALS				

Total score is determined by adding together the scores of each of the 4 items.
Scores are rated as normal (0-2), mild (3-5), moderate (6-8), and severe (9-12).
Total score ≥3 for first 2 questions suggests anxiety.
Total score ≥3 for last 2 questions suggests depression.

Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. Psychosomatics. 2009

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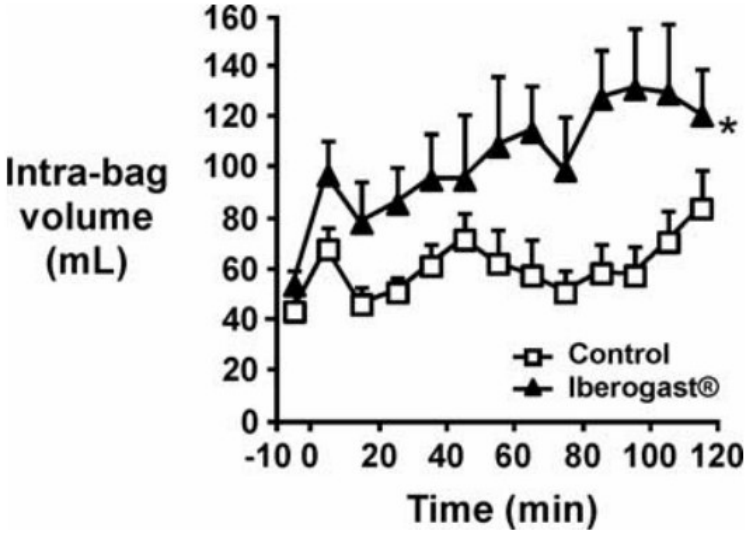
1. Line pharmacotherapy

	IBS-C	IBS-D
Loperamide	-	(+)
Antispasmodics	(+)	(+)
Peppermint oil	+	+
PEG/laxatives	(+) pain!	-

Antimuscarinics (butylscopolamin/buscopan) => slow transit, dry mouth
Smooth muscle relaxants (mebevirine/duspatalin)



Pilichiewicz et al. Am J Gastroenterol 2007;102:1276–1283

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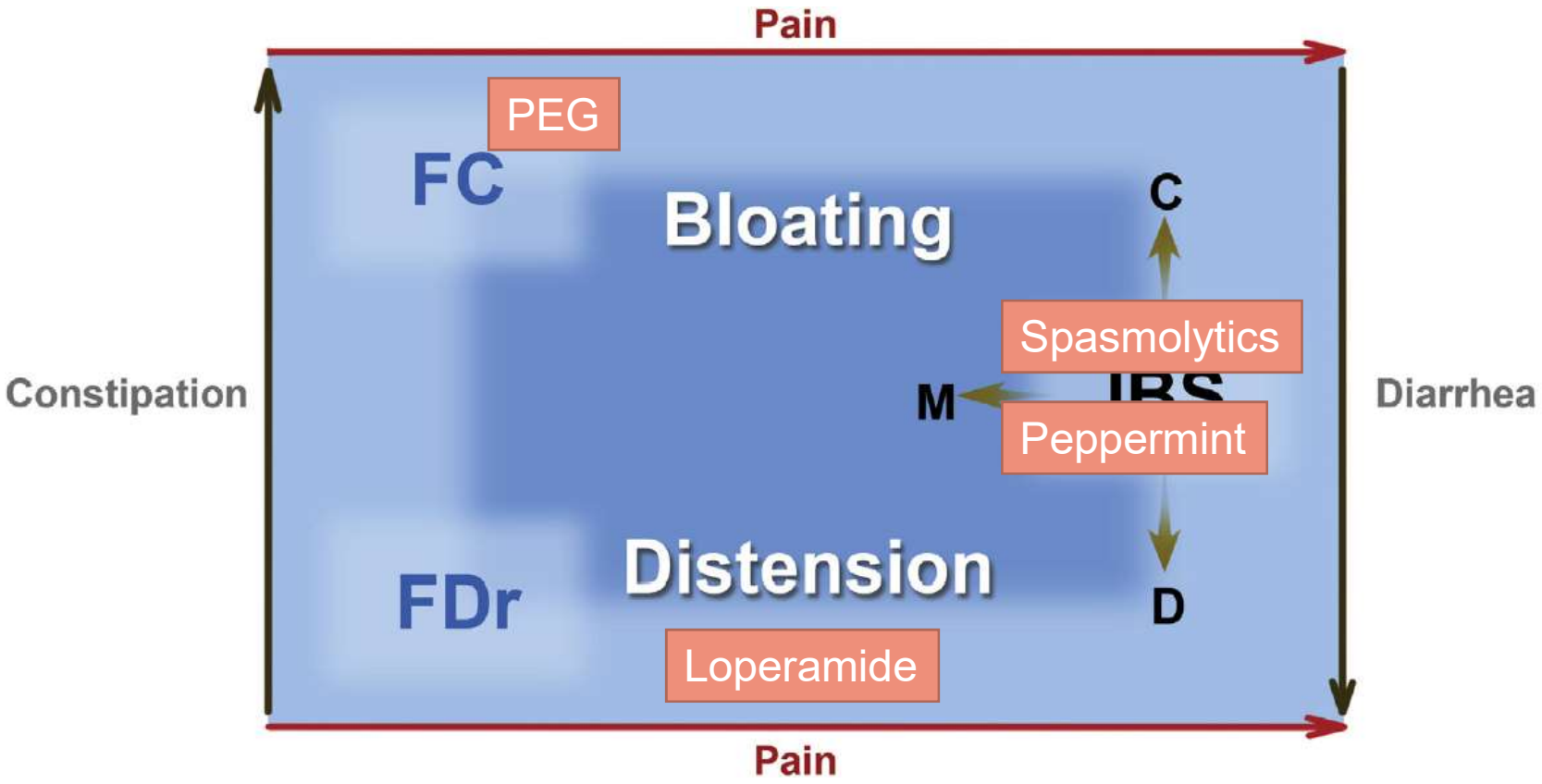
SST: SDDs caspules, optimiziation of fiber dosis



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Frau B.N., 1974

- 4M FUP:
  - Post SDD Significant decrease in pain and increase in stool consistency, but persistent symptoms
  - Metamucile not that well tolerated anymore
  - Laxoberon initiated by the patient (not reported before?)
  - Pain partially responded to bowel prep (colonoscopy)

  - … What now?

2. Line pharmacotherapy

	IBS-C	IBS-D
TCA	+	+
Rifaximin	-	+
SSRI	(+)	(+)
5HT4 agonists	(+)	-
Linaclotide	+	-
5HT3 antagonists	-	+
Eluxadoline	-	+

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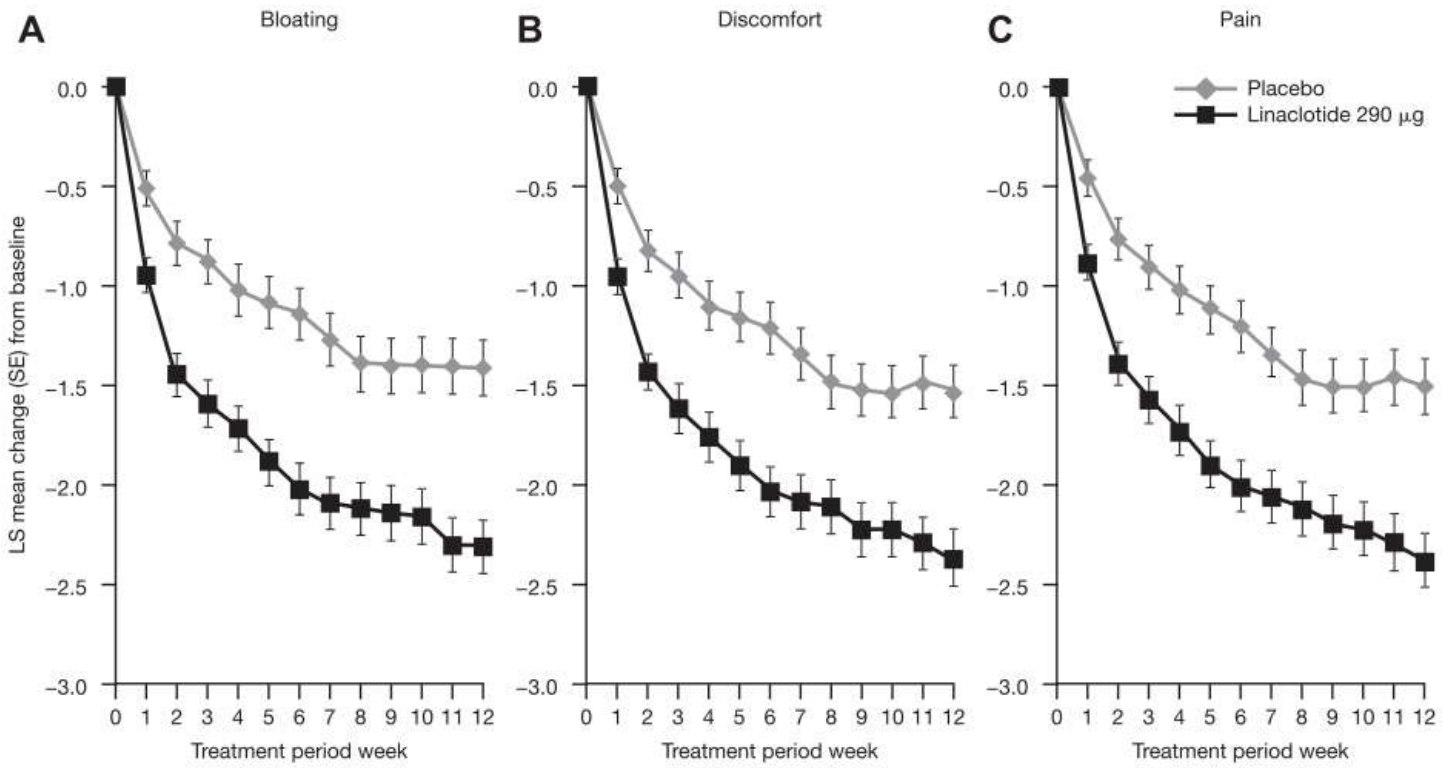
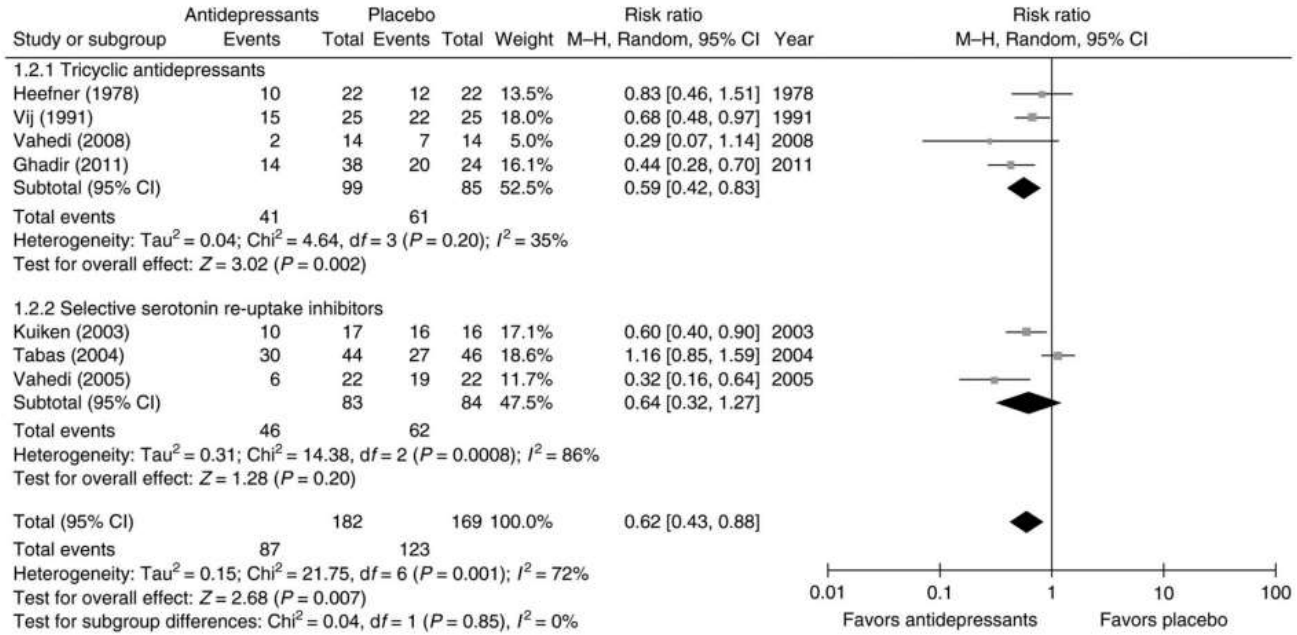
Linaclotide: yes for IBS-C



Chang et al., AJG 2021

SSRIs: suboptimal for pain



Study or subgroup	Antidepressants Events	Total	Placebo Events	Total	Weight	Risk ratio M–H, Random, 95% CI	Year
1.2.1 Tricyclic antidepressants							
Heefner (1978)	10	22	12	22	13.5%	0.83 [0.46, 1.51]	1978
Vij (1991)	15	25	22	25	18.0%	0.68 [0.48, 0.97]	1991
Vahedi (2008)	2	14	7	14	5.0%	0.29 [0.07, 1.14]	2008
Ghadir (2011)	14	38	20	24	16.1%	0.44 [0.28, 0.70]	2011
Subtotal (95% CI)		99		85	52.5%	0.59 [0.42, 0.83]	
Total events	41		61				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 4.64$, $df = 3$ ($P = 0.20$); $I^2 = 35\%$							
Test for overall effect: $Z = 3.02$ ($P = 0.002$)							
1.2.2 Selective serotonin re-uptake inhibitors							
Kuiken (2003)	10	17	16	16	17.1%	0.60 [0.40, 0.90]	2003
Tabas (2004)	30	44	27	46	18.6%	1.16 [0.85, 1.59]	2004
Vahedi (2005)	6	22	19	22	11.7%	0.32 [0.16, 0.64]	2005
Subtotal (95% CI)		83		84	47.5%	0.64 [0.32, 1.27]	
Total events	46		62				
Heterogeneity: $Tau^2 = 0.31$; $Chi^2 = 14.38$, $df = 2$ ($P = 0.0008$); $I^2 = 86\%$							
Test for overall effect: $Z = 1.28$ ($P = 0.20$)							
Total (95% CI)		182		169	100.0%	0.62 [0.43, 0.88]	
Total events	87		123				
Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 21.75$, $df = 6$ ($P = 0.001$); $I^2 = 72\%$							
Test for overall effect: $Z = 2.68$ ($P = 0.007$)							
Test for subgroup differences: $Chi^2 = 0.04$, $df = 1$ ($P = 0.85$), $I^2 = 0\%$							

Fig. 3 Forest plot of randomized controlled trials of antidepressants versus placebo in terms of effect on abdominal pain in irritable bowel syndrome

Ford et al., Effect of Antidepressants and Psychological Therapies in Irritable Bowel Syndrome: An Updated Systematic Review and Meta-Analysis, AJG 2021

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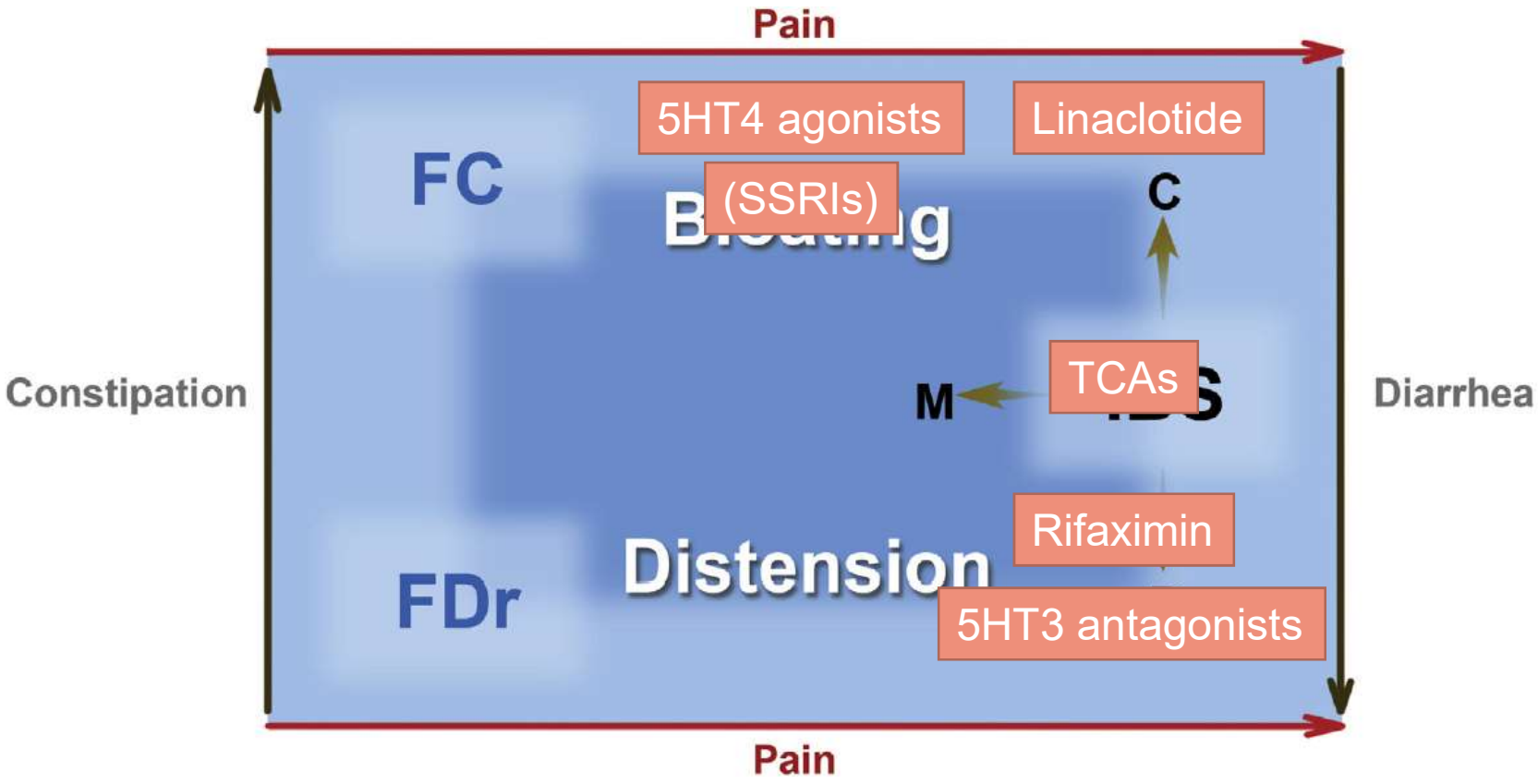
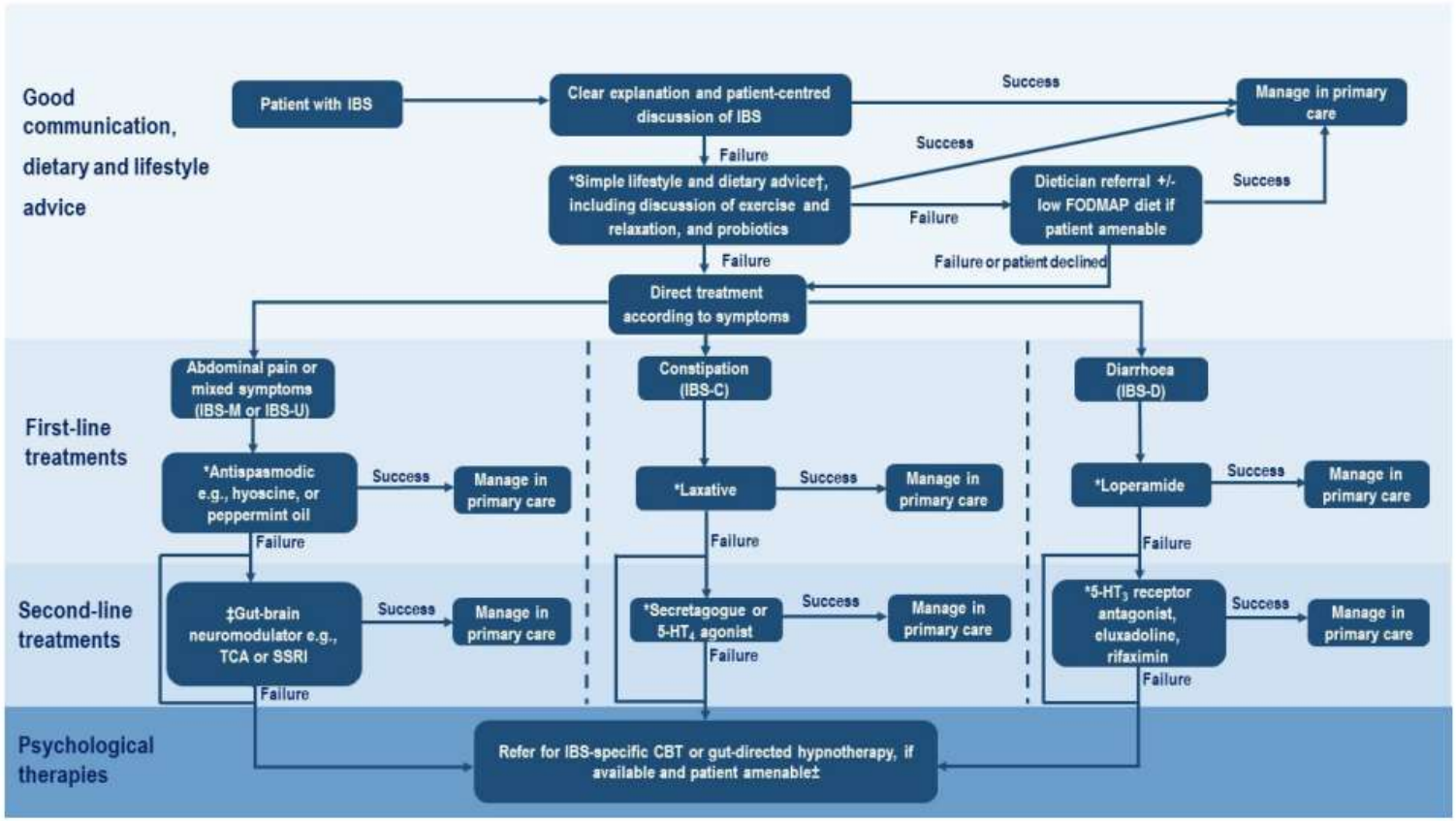
SST: NM = no way, PEG, 5HT4?




Good communication, dietary and lifestyle advice
Patient with IBS
Clear explanation and patient-centred discussion of IBS
Success
Manage in primary care
Failure
Success
*Simple lifestyle and dietary advice†, including discussion of exercise and relaxation, and probiotics
Dietician referral +/- low FODMAP diet if patient amenable
Success
Failure
Failure
Failure or patient declined
Direct treatment according to symptoms
First-line treatments
Abdominal pain or mixed symptoms (IBS-M or IBS-U)
Constipation (IBS-C)
Diarrhoea (IBS-D)
*Antispasmodic e.g., hyoscine, or peppermint oil
Success
Manage in primary care
*Laxative
Success
Manage in primary care
*Loperamide
Success
Manage in primary care
Failure
Failure
Failure
Second-line treatments
‡Gut-brain neuromodulator e.g., TCA or SSRI
Success
Manage in primary care
*Secretagogue or 5-HT4 agonist
Success
Manage in primary care
*5-HT3 receptor antagonist, eluxadoline, rifaximin
Success
Manage in primary care
Failure
Failure
Failure
Psychological therapies
Refer for IBS-specific CBT or gut-directed hypnotherapy, if available and patient amenable‡

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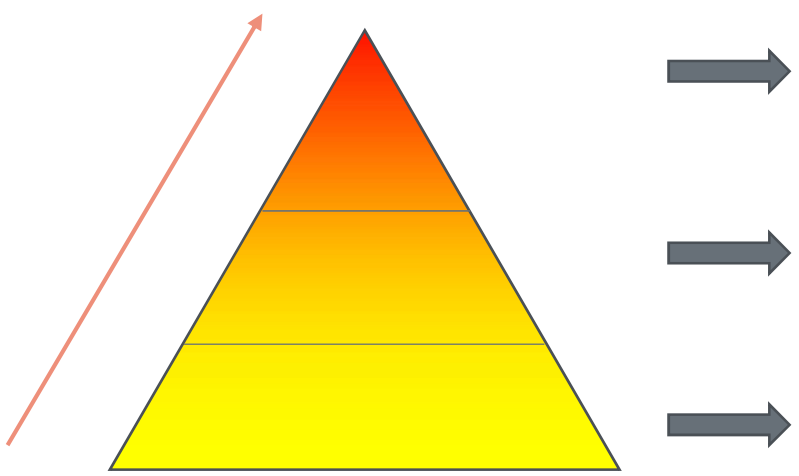
Ms. M.

- For next FUP:



Psychological ttts, central NM, continuity of care

FUP visit, adress anxiety/stress (screening!), gut pharmacotherapy

Explain, reassure, positive diagnosis, diet, lifestyle advice

Efficacy of Neuromodulators for IBS and Comorbid Pain Disorders

Treatment	IBS	Fibromyalgia	Chronic HA/ Migraine	Low back pain
Tricyclics (TCAs)	+	+	+	No effect
SSRI	No effect	+	±	No effect
SNRI	+?	+	+	+
Delta ligand agents	+	+	+	±
Azapirone	+		+	
Atypical antipsychotics	+	+	+	

Ford et al. Am J Gastroenterol 2018;113:1-18
Chang, Sultan, Lembo et al. *Gastroenterology*. 2022;163:118-136.
Drossman DA et al. Gastroenterology 2018;154:1140–1171

Macfarlane GJ et al. Ann Rheum Dis 2016;0:1–11
Saito Y et al. *Aliment Pharmacol Ther*. 2019;49:389–397
Burch, R. Curr Treat Options Neurol (2019) 21: 18

Chang, UEGW oral presentation, 2022

Efficacy of Behavioral Therapies for IBS and Comorbid Pain Disorders

Treatment	IBS/DGBI	Fibromyalgia	Chronic HA/ Migraine	Low back pain
Cognitive behavioral therapy (CBT)	+	+	+	+
Mindfulness based stress reduction (MBSR)	+	+	+	+
Hypnotherapy	+	+	+	+
Relaxation therapy	+	+	+	+
Psychotherapy	+	±		-

Ford et al. Am J Gastroenterol 2018;113:1-18
Laird KT et al. Clin Gastroenterol Hepatol 2016;14(7):937-947
Cherkin DC et al. JAMA 2016;315:1240-1249
Sullivan A. et al. J Neurol. 2016; 263(12): 2369–2377
Kropp P et al. Expert Rev Neurother 2017;17(11):1059-1068
Macfarlane GJ et al. Ann Rheum Dis 2016;0:1–11
Aman MM et al. Curr Pain Headache Rep (2018) 22: 3
Saito Y et al. *Aliment Pharmacol Ther.* 2019;49:389–397
Burch, R. Curr Treat Options Neurol (2019) 21: 18
Rizzo RRN et al. J Pain 2018;19(10):1103.e1-1103.e9.
Chou R. et al. Ann Intern Med 2017;166(7):493-505

Chang, UEGW oral presentation, 2022

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TAKE HOME MESSAGE - 1

- Take a good history - ABCDE model
- Distinguish categorical diagnosis and clinical modifiers
- Do a DRE
- 1. Line: communication, lifestyle, soluble fibre
- 2. Line: TCAs, SSRIs suboptimal for pain, Linaclotide/IBS-C, 5HT3a/IBS-D
- Have a low thresold for considering non pharmacological therapies

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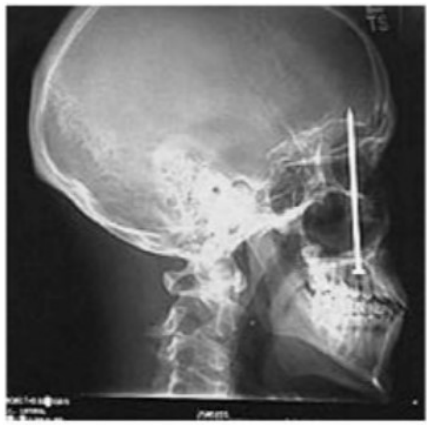
TAKE HOME MESSAGE - 2 - «a tale of 2 nails»

Fisher et al, BMJ 1995



Dimsdale & Dantzer, 2007

Thoughts, beliefs, perceptions, emotions, past experiences, context, and input from your body *all* affect your experience of pain

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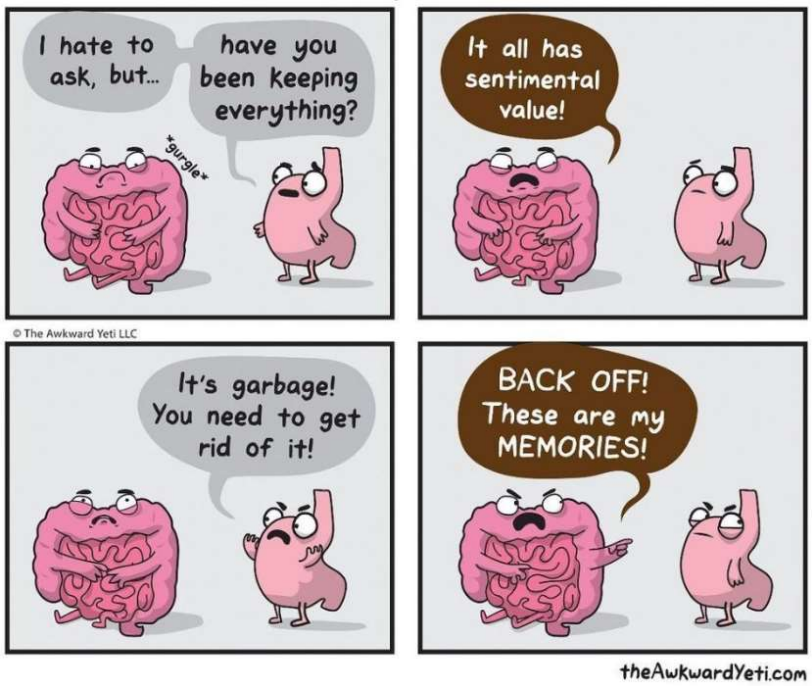
Thank you for your attention!



	IBS subgroup studied	Efficacy	Quality of data	Adverse events	Limitations of data
Diet, lifestyle, and probiotics					
Soluble fibre (eg, ispaghula 20–30 g/day)	No specific IBS subgroup recruited	Effective	Moderate	Total adverse events no more common with soluble fibre than with placebo in three RCTs	Only one RCT at low risk of bias; only a small number of patients in existing RCTs
Low FODMAP diet*	No specific IBS subgroup recruited	Might be effective	Very low	Total adverse events rarely reported	All RCTs at high risk of bias; heterogeneity between study designs; imprecision in estimate of effect; effect of FODMAP reintroduction not studied within the design
Exercise	No specific IBS subgroup recruited	Might be effective	Very low	Total adverse events not reported	Only two RCTs; high risk of bias in both RCTs; inconsistent effects on symptoms
Probiotics	No specific IBS subgroup recruited	Might be effective	Very low	Total adverse events no more common with probiotics than with placebo in a meta-analysis of 36 RCTs	Heterogeneity between studies; possible publication bias; only a small number of RCTs assessing each individual probiotic, meaning that it is difficult to know which species or strain is effective
First-line therapies					
Peppermint oil (200 mg three times a day)	No specific IBS subgroup recruited	Effective	Low	Total adverse events no more common with peppermint oil than with placebo in a meta-analysis of six RCTs	Only two RCTs at low risk of bias; heterogeneity between studies; trials used very specific formulations so data cannot be extrapolated to other available products; heartburn might be an adverse effect
Laxatives (eg, polyethylene glycol 13·8 g once a day and titrated)	Patients with IBS with constipation	Unclear efficacy	Low	Rates of abdominal pain numerically higher with polyethylene glycol than with placebo in one RCT	Only two RCTs; unclear risk of bias in both RCTs; unclear effect on abdominal pain
Antidiarrhoeals (eg, loperamide 4 mg as required)	Patients with IBS with diarrhoea and IBS with mixed stool pattern	Unclear efficacy	Very low	Total adverse events no more common with antidiarrhoeals than with placebo in two RCTs	Only two RCTs; unclear risk of bias in both RCTs; not all patients met criteria for IBS; no significant effect on IBS symptoms when data pooled; constipation might be an issue
Antispasmodics (eg, cimetropium 50 mg three times a day, hyoscine 10–20 mg three times a day, otilonium 20–40 mg three times a day, or pinaverium 50 mg three times a day)	No specific IBS subgroup selected, other than one RCT in patients with IBS with diarrhoea	Might be effective	Very low	Total adverse events significantly more common with antispasmodics than with placebo in a meta-analysis of 26 RCTs, particularly dry mouth, dizziness, and blurred vision	Only two RCTs at low risk of bias; heterogeneity between studies; possible publication bias; only a small number of RCTs assessing each individual antispasmodic

	IBS subgroup studied	Efficacy	Quality of data	Adverse events	Limitations of data
(Continued from previous page)					
Second-line therapies					
5-HT4 agonists (eg, tegaserod 6 mg twice a day)	IBS with constipation	Effective	High	Diarrhoea significantly more common with tegaserod than with placebo in a meta-analysis of six RCTs	Concerns regarding small excess of cardiovascular and cerebrovascular events led to withdrawal of tegaserod, which was reintroduced in 2018 but only for specific patients; no RCTs of prucalopride
5-HT3 antagonists (eg, alosetron 0·5–1·0 mg twice a day, ramosetron 2·5–5·0 µg once a day, or ondansetron 4 mg once a day and titrated)	IBS with diarrhoea and IBS with mixed stool pattern	Effective	High	Constipation significantly more common with alosetron than with placebo in a meta-analysis of three RCTs	All RCTs of ramosetron done in Japan; serious adverse events with alosetron included ischaemic colitis and severe constipation leading to restricted use; ramosetron is safer than alosetron, although constipation is still more common with active therapy
Tricyclic antidepressants (eg, amitriptyline 10–30 mg at night or desipramine 50 mg at night)	No specific IBS subgroup selected, other than one RCT in patients with IBS with diarrhoea	Effective	Moderate	Total adverse events significantly more common with tricyclic antidepressants than with placebo in a meta-analysis of six RCTs, particularly dry mouth and drowsiness	Only three RCTs at low risk of bias; possible publication bias; some atypical trials included
Eluxadoline (100 mg twice a day)	IBS with diarrhoea	Effective	Moderate	Rates of constipation, nausea, and vomiting numerically higher with eluxadoline than with placebo in a pooled analysis of two RCTs	Heterogeneity between studies; only a modest benefit over placebo in published RCTs; no benefit over placebo in terms of abdominal pain; serious adverse events include acute pancreatitis and sphincter of Oddi spasm
Antibiotic rifaximin (550 mg three times a day)	IBS with diarrhoea and IBS with mixed stool pattern	Effective	Moderate	Total adverse events no more common with rifaximin than with placebo in a pooled analysis of three RCTs	Only a modest benefit over placebo in published RCTs
Selective serotonin reuptake inhibitors (eg, fluoxetine 20 mg once a day)	No specific IBS subgroup selected, other than one RCT in patients with IBS with constipation	Might be effective	Low	Total adverse events no more common with selective serotonin reuptake inhibitors than with placebo	Only one RCT at low risk of bias; heterogeneity between studies
Pregabalin (225 mg twice a day)	No specific IBS subgroup recruited	Might be effective	Low	Total adverse events numerically higher with pregabalin than with placebo, particularly blurred vision, dizziness, and altered cognition	Only one single-centre RCT, although global symptoms, abdominal pain, diarrhoea, and bloating improved significantly

Intestinal secretagogues					
Linaclotide (290 µg once a day)	IBS with constipation	Effective	High	Diarrhoea significantly more common with linaclotide than with placebo in a meta-analysis of three RCTs	None
Lubiprostone (8 µg twice a day)	IBS with constipation	Effective	Moderate	Nausea significantly more common with lubiprostone than with placebo in a meta-analysis of three RCTs	Only a modest benefit over placebo in published RCTs
Plecanatide (3–6 mg once a day)	IBS with constipation	Effective	Moderate	Diarrhoea significantly more common with plecanatide than with placebo in a meta-analysis of two RCTs	Only a modest benefit over placebo in published RCTs
Tenapanor (50 mg twice a day)	IBS with constipation	Effective	Moderate	Diarrhoea more frequent with tenapanor than with placebo	Awaiting publication of all phase 3 trial data
Psychological therapies					
Cognitive behavioural therapy or gut-directed hypnotherapy	No specific IBS subgroup recruited	Effective	Very low	Adverse events not reported in individual RCTs, precluding their assessment in a meta-analysis of 36 RCTs	All RCTs at high risk of bias because of the nature of the interventions studied; heterogeneity between studies; possible publication bias; only a small number of RCTs assessing each intervention; time consuming because of need for therapist contact; minimal availability in some countries

Adapted from Ford and colleagues.[5] Most drugs should be trialled for 3 months, with their efficacy then reviewed (except for rifaximin, which is a 2 week treatment course). IBS=irritable bowel syndrome. RCT=randomised controlled trial. FODMAP=fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. *A low FODMAP diet should not be maintained in the long term; to date, the restriction phase in most published RCTs has been a maximum of 3–4 weeks.

Table 2: **Summary of evidence for efficacy of treatment approaches for IBS**