

Functional Gastrointestinal Disease Pediatrics

Small Group Session: March 1, 2020

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Conflict of Interest Disclosure

(over the past 24 months)

- No relevant relationships with any commercial or non-profit organizations

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Conflict of Interest Disclosure

(over the past 24 months)

Commercial or Non-Profit Interest	Relationship
American Neurogastroenterology and Motility Society	Member, ANMS Council

CanMEDS Roles Covered

✓	Medical Expert (as <i>Medical Experts</i> , physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. <i>Medical Expert</i> is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
✓	Communicator (as <i>Communicators</i> , physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
✓	Collaborator (as <i>Collaborators</i> , physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as <i>Leaders</i> , physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
✓	Health Advocate (as <i>Health Advocates</i> , physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
✓	Scholar (as <i>Scholars</i> , physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as <i>Professionals</i> , physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Learning Objectives

At the end of this session participants will be able to:

1. Recognize the continuum of clinical presentations of functional constipation and irritable bowel syndrome in pediatric patients.
2. Identify psychosocial factors that play a role in the genesis/exacerbation of pediatric IBS.
3. Describe management approaches, both pharmacologic and non-pharmacologic, used in the care of pediatric patients with IBS.

Case

- 12 year old female
- Referred for “constipation”
- 2 year history
 - Abdominal pain
 - Vomiting
 - Constipation

Case

- Multiple admissions for “constipation” presenting with abdominal pain and vomiting
 - NG inserted; clean out with PEG + electrolytes
- Daily bowel movements; Bristol Type 6
- Decreased appetite; feels “full”
- Abdominal pain day and night; moderate 4-7 on pain scale

Does she have functional constipation or IBS with constipation?

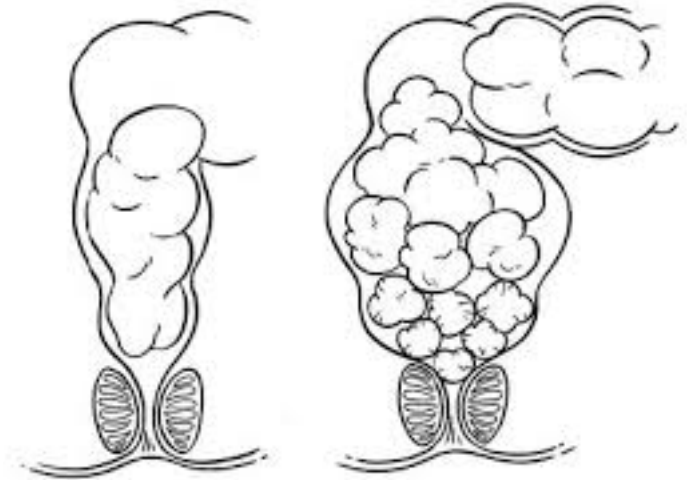
Functional Constipation

Rome IV Diagnostic Criteria for Functional Constipation (Child/Adolescent)

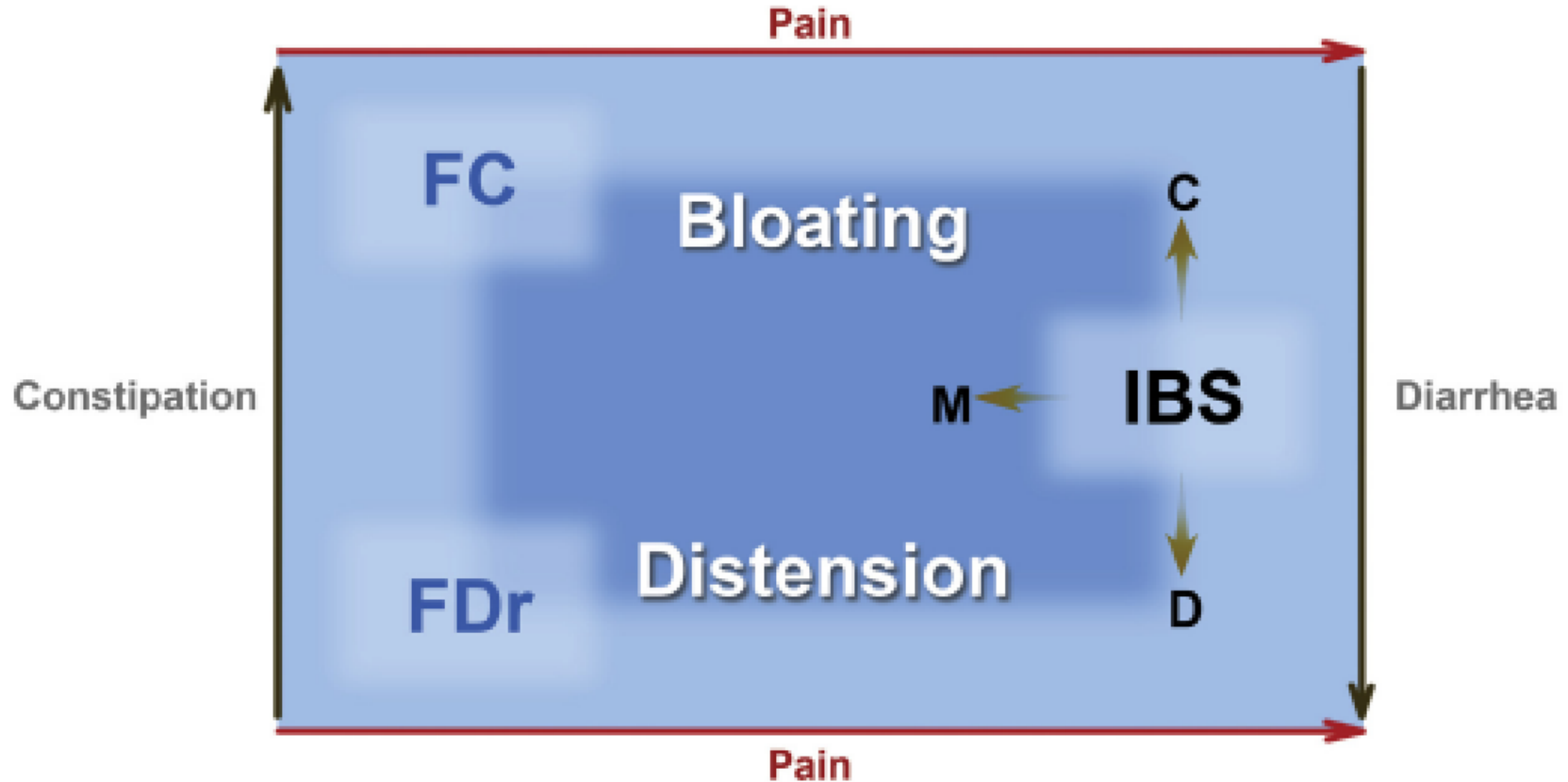
Must include 2 or more of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of irritable bowel syndrome

1. 2 or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years
2. At least 1 episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of large fecal mass in the rectum
6. History of large diameter stools that can obstruct the toilet

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.



IBS – Part of FBD Continuum



Irritable Bowel Syndrome

Rome IV Diagnostic Criteria for Irritable Bowel Syndrome (Child/Adolescent)

Must include all of the following:

1. Abdominal pain at least 4 days per month associated with one or more of the following:
 - a. Related to defecation
 - b. A change in frequency of stool
 - c. A change in form (appearance) of stool
2. In children with constipation, the pain does not resolve with resolution of constipation (children in whom the pain resolves have functional constipation)
3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Criteria fulfilled for at least 2 months before diagnosis.



Prevalence of FGIDs according to Rome IV

Table III. Functional GI disorder prevalence in children greater than 4 years old according to Rome III and Rome IV criteria

Diagnoses	Rome IV, N (%)	Rome III*
Functional constipation	135 (14.10%)	122 (12.90%)
Functional dyspepsia – postprandial distress syndrome [†]	69 (7.20%)	-
Functional dyspepsia – epigastric pain syndrome [†]	4 (0.40%)	-
Functional dyspepsia – unspecified [†]	N/A	2 (0.20%)
IBS	49 (5.10%)	27 (2.80%)
FAP NOS	30 (3.1%)	FAP 2 (0.3%) FAPS 8 (0.8%)
Aerophagia	25 (2.60%)	41 (4.30%)
Cyclic vomiting syndrome	19 (2.00%)	10 (1.10%)
Functional vomiting	13 (1.40%)	-
Abdominal migraine	11 (1.10%)	87 (9.20%)
Functional nausea	5 (0.50%)	-
Nonretentive fecal incontinence	2 (0.20%)	17 (1.80%)
Rumination	0 (0%)	0.00%
Any functional GI disorder	25.00%	23.10%

Case

- Additional symptoms of headaches, blurred vision, dizziness, weaknesses
- Parents separated; family stressed by admissions/appointments and lack of progress
- Due to constellation of symptoms and prominence of abdominal pain – referred to Pediatric Chronic Pain Program

Should we worried be about anything else?

Clinical Assessment

- Establish a working and therapeutic alliance with patient and family
- Take time +++
- Patient's history
- Pain history
- Stressful episode or infectious episode associated with onset of symptoms
- Psychosocial history of patient and family
- Family history of GI disorders
- Dietary association with pain episodes

Red Flags: neither sensitive nor specific...

- Pain

- Nocturnal Pain
- Persistent right upper or right lower quadrant pain

- Associated GI symptoms

- Persistent vomiting
- Nocturnal diarrhea
- Dysphagia
- Hematochezia
- Perirectal disease

- General symptoms

- Fever, arthritis, aphthous ulcers
- Involuntary Weight loss
- Deceleration of linear growth, delayed puberty

- Family history of IBD

- Family history of celiac disease

- Family history of peptic ulcer

...but the greater the number present, the greater the likelihood of organic disease

Work-Up?

- Directed by history of the child and family and by physical examination
- Initial screening can include:
 - CBC, CRP, albumin
 - IgA tTG
 - ALT, lipase/amylase
 - Urinalysis
 - Fecal calprotectin
 - Stool for ova and parasites

IBS and Celiac Disease

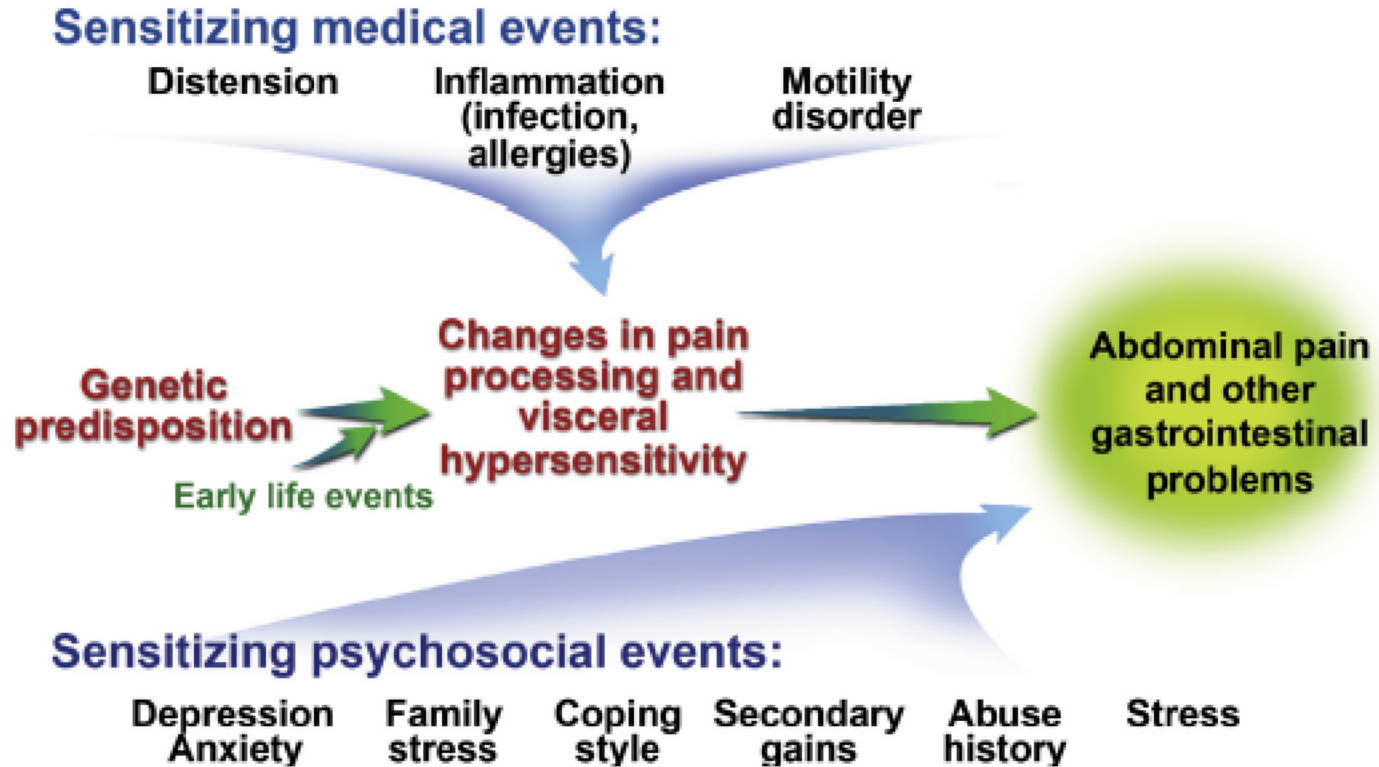
IBS: 4 times higher risk of having celiac disease than the general pediatric population
($P < .001$; odds ratio, 4.19 [95% CI, 2.03-8.49])

Table 1. Prevalence of Celiac Disease in the Different Diagnostic Subgroups

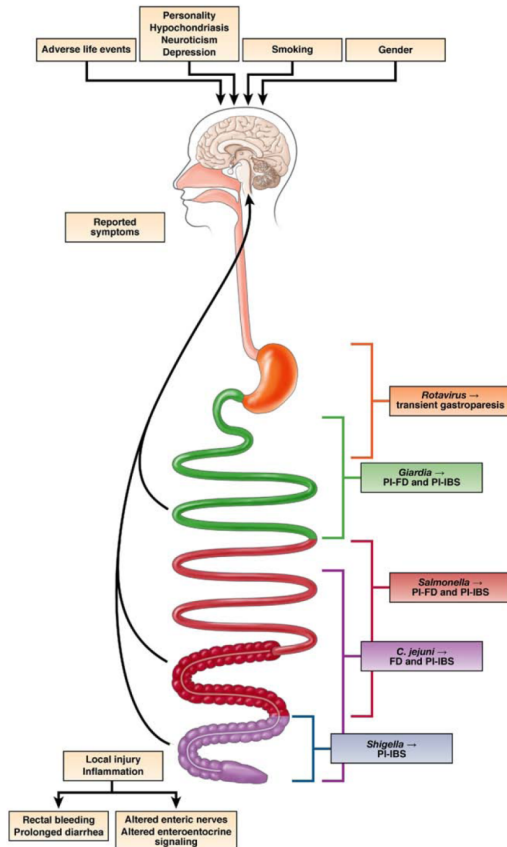
Functional Gastrointestinal Disorder	Patients, No.	Patients With Celiac Disease, No.	Prevalence of Celiac Disease, % (95% CI)
Irritable bowel syndrome	270	12	4.4 (2.5-7.6)
Functional dyspepsia	201	2	1.0 (0.2-3.5)
Functional abdominal pain	311	1	0.3 (0.1-1.7)

What caused her to be like this?

FBD – Sensitizing Events



Post-infectious FGID



- **Norovirus** : No pediatric data

- IBS (OR 11.40; 95 % CI 3.44 – 37.82; Zanini et al. Am J Gastroenterol 2012),
- FD, constipation (Porter et al. Clin Infect Dis 2012)

- **Giardia** :

- IBS RR=3.4 (95% CI 2.9 to 3.8) after infection (Wensaas et al. Gut 2012)
- Diarrhea, flatulence in preschool children (Mellingen et al. BMC Public Health 2010)

- **C. jejuni** (IBS, FD)

- **Salmonella** (IBS, FD)

- **Shigella** (IBS)

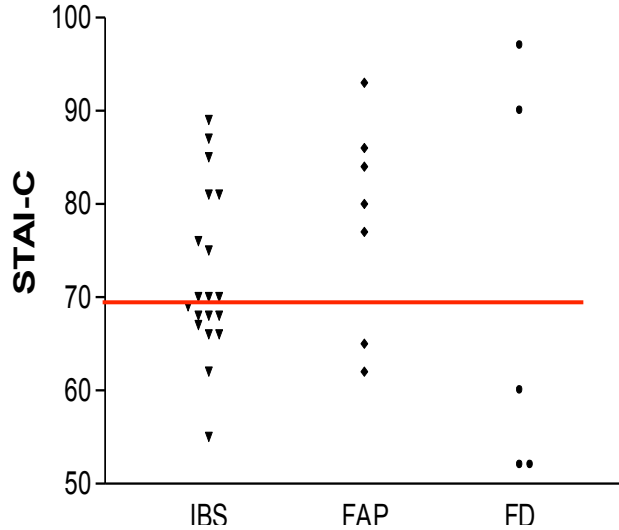
Spiller et al. Gastro 2009
Saps et al. J Pediatr 2008
Futagami et al. APT 2015

But she is not an anxious girl...

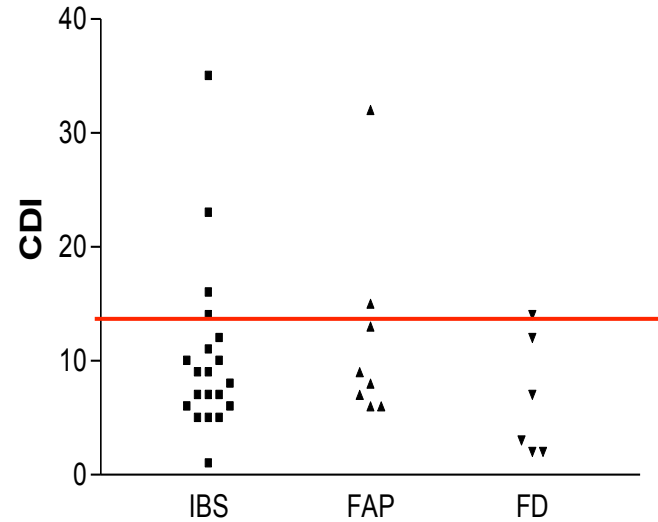
Visceral Hypersensitivity and Symptom Severity

- Psychological comorbidity is common in FGIDs
- Barostat testing in adult IBS and FD cohorts demonstrated increasing GI symptom severity with increasing visceral hypersensitivity
- Findings were independent of a tendency to report symptoms, or anxiety/depression comorbidities

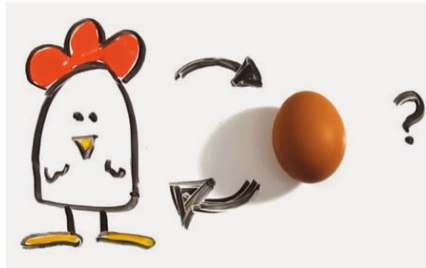
Psychological co-morbidities are frequent



Anxiety ~50 %



Depression ~10 %



Campo et al Pediatrics 2004
Faure et al J Pediatr 2007
Castilloux et al JPGN 2008

Family-child dynamics influence severity of symptoms

- Modeling
- Psychological distress
- Parental perception of:
 - Pain
 - Child's self-efficacy
- Parental protectiveness (e.g. keeping home from school when child in pain)
- Parental catastrophizing
- Coping style/self-efficacy

Tilburg et al, World J Gastroenterol 2015; 21(18): 5532-41

DuPenn et al, Children 2016; 3 (15)

Cunningham et al, JPGN 2014;59: 732–738

So, how do we treat this?

Treatment should be tailored to...

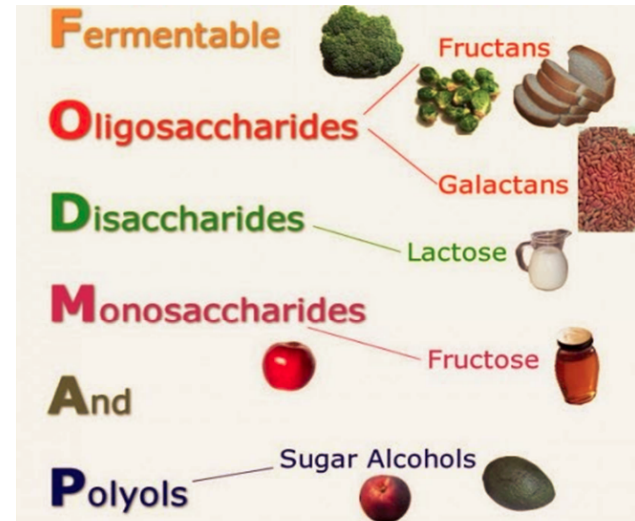
- IBS subtype : IBS-D, IBS-C
- IBS severity
- Associated psychological co-morbidities
- IBS pathophysiological mechanism (?)

Management of FGIDs

- Positive diagnosis
- Provide pathophysiological explanations
- Reassurance
 - Symptoms are real but are not life-threatening
 - Must learn to live/cope with the symptom
- Avoid triggers

IBS Treatment: Nutrition

- Reduce sorbitol, fructose, lactose?
- Low FODMAPs
- Fibres = age (years) + 5 g
- Avoid :
 - Fat
 - Tea, coffee, Coke
 - Spicy and acidic food



IBS: Symptomatic Treatments

- Constipation: mineral oil, lactulose, PEG 3350
- Diarrhea : loperamide (Imodium[®]), cholestyramine (Questran[®])...
- Pain : Antispasmodics : trimebutine, dicyclomine, Peppermint oil (Kline J Pediatr 2001)...
- Gas : simethicone...

IBS: Non-pharmacological Treatments

- Probiotics: *Lactobacillus GG*, *Lactobacillus rhamnosus GG*
JPGN 2010; 51:24-30 Gut 2010;59:325-32
- Hypnosis
Vlieger et al. Gastroenterology 2007
- Cognitive behavioural therapy (CBT)
Youssef et al. JPGN 2004

IBS: Treatment of Severe Forms

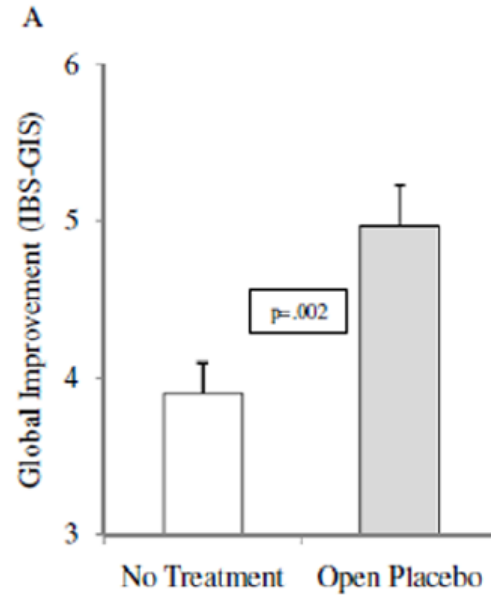
In most severe cases (school absenteeism)

- Amitriptyline 0.2 to 0.4 mg/kg HS, 10 to 50 mg/day; or
- Imipramine 0.2 to 0.4 mg/kg HS, 10 to 50 mg/day (less anticholinergic)
- Citalopram (5-HT reuptake inhibitor) 10 mg/day to 40 mg die
- Mirtazapine 7.5 to 15 mg HS

Check for
Suicidal
Ideation
and QT

Bahar et al. J Pediatr 2008 (RCT)
Saps et al. Gastroenterology 2009 (RCT)
Teitelbaum JPGN 2011 (Open)
Campo et al. 2004 (open study)
Roohafza et al NGM 2014 RCT
Hussain et al. JPGN 2014

Placebo



The placebo effect in IBS (even when placebo is announced)

What's next?

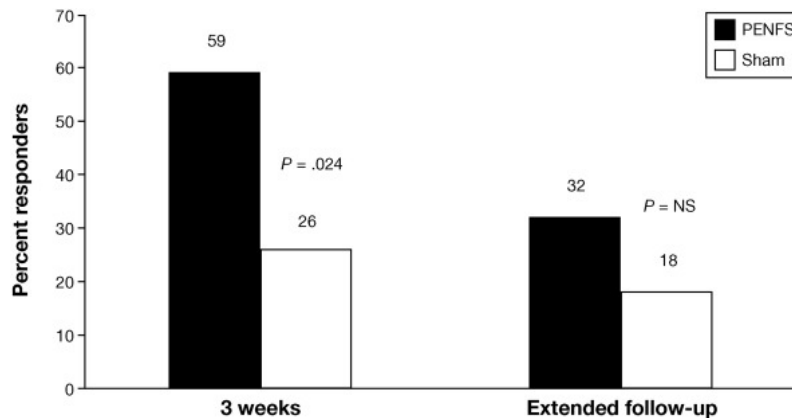
- IBS-C: Linaclotide : Guanylate-cylase C agonist
 - Improves visceral hypersensitivity; increases chloride secretion
- IBS-D: Eluxadoline: mu-opioid receptor agonist and a delta-opioid receptor antagonist
- IBS-D: Ondansetron : 5-HT₃R antagonist
- Larazotide: stimulation of tight junctions
- Ebastine (Aerius)(H1 antagonist) : TRPV1 desensibilisation (Wouters 2016)
- Pregabaline (Saito et al APT 2018)
- And... understand why some patients respond to FODMAPS and others do not

Auricular Neurostimulation

Controls activity of pain areas in the central nervous system particularly the amygdala and spinal cord



27 IBS adolescents (median age, 15.3 y): auricular neurostimulation
23 IBS adolescents (median age, 15.6 y): sham stimulation
5 days/week for 4 weeks

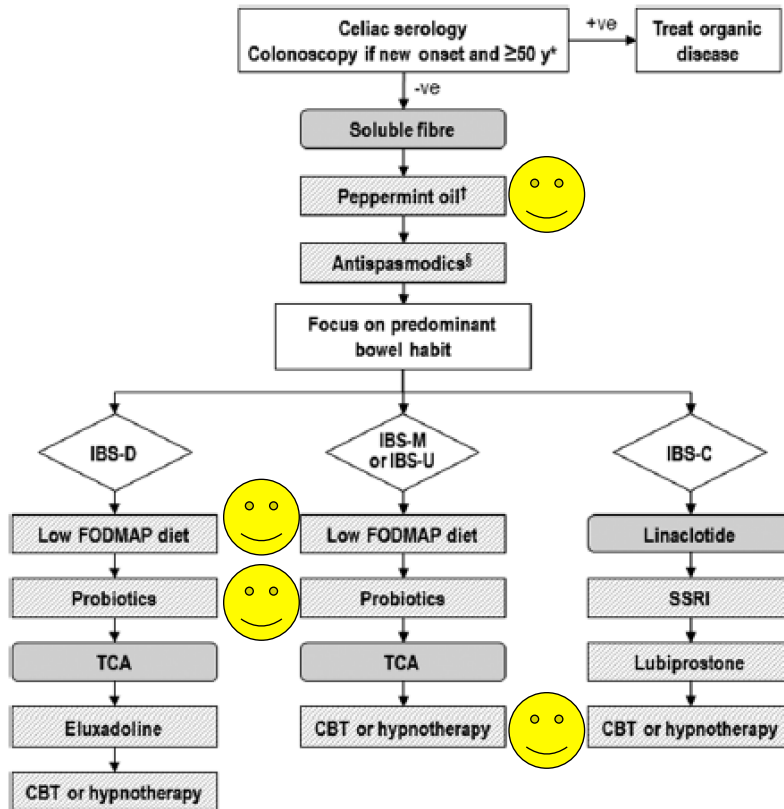


% with 30% improvement in worst pain severity in PENFS vs sham after 3 weeks and at extended follow-up 8–12 weeks after end of therapy

IB-STIM™



IBS Management - Pediatrics



Linaclotide: Safety and efficacy study of a range of doses administered orally to children aged 7-17 years, with irritable bowel syndrome with constipation (NCT02559817). Study completion date August 2019. Black box warning for < 6 years.