Gastroenterology in 2016

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Case 1

21 Yrs, Male

Recent holiday to Thailand

Suffered an acute gastroenteritis

2 months of Abdominal discomfort, relieved by defecation

Episodes of frequent lose stool, Bloating

No weight loss

Recently stopped smoking

Normal FBC, U/E, LFT

CRP : <5, Stool cultures and microscopy : Normal,

Calprotectin 70

Differentials

- Post infective IBS
- Post infective bile acid diarrhoea
- Post infective carbohydrate intolerance
- Early IBD

Is IBD likely?

- What is the pre-test probability ?
- Probably no more than 25% that there will be endoscopic evidence of inflammatory bowel disease.

Test predictive values based on pre-test probability of endoscopically active IBD

Prevalence of endoscopic activity	Sensitivity	Specificity	Positive predictive value	Negative predictive value
FAECAL CALPROTECTIN				
0.25	**0.88**	**0.73**	**0.52**	**0.95**
0.50	0.88	0.73	0.76	0.86
0.75	0.88	0.73	0.91	0.67
CRP				
0.25	0.49	0.92	0.67	0.84
0.50	0.49	0.92	0.86	0.64
0.75	0.49	0.92	0.95	0.38

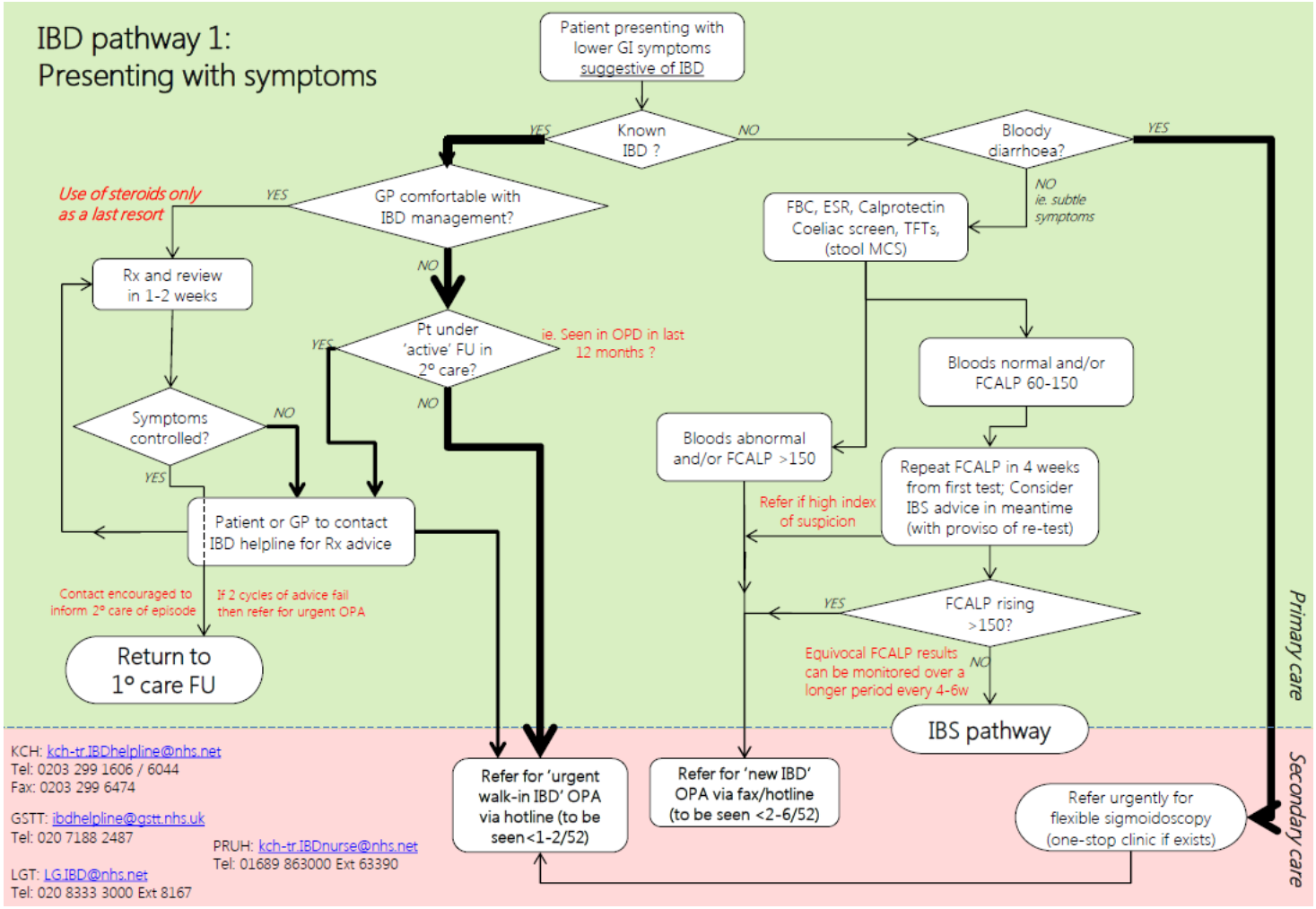
Mosli M H et al, *C- reactive protein, Fecal calprotectin and stool lactoferrin for detection of Endoscopic activity in symptomatic inflammatory bowel disease patients: A systematic review and meta analysis*. Am J Gastroenterol 2015. 110 (6)

Next step ?

- Symptomatic treatment
- Exclude food triggers
- Review ?
- Retest calprotectin ?

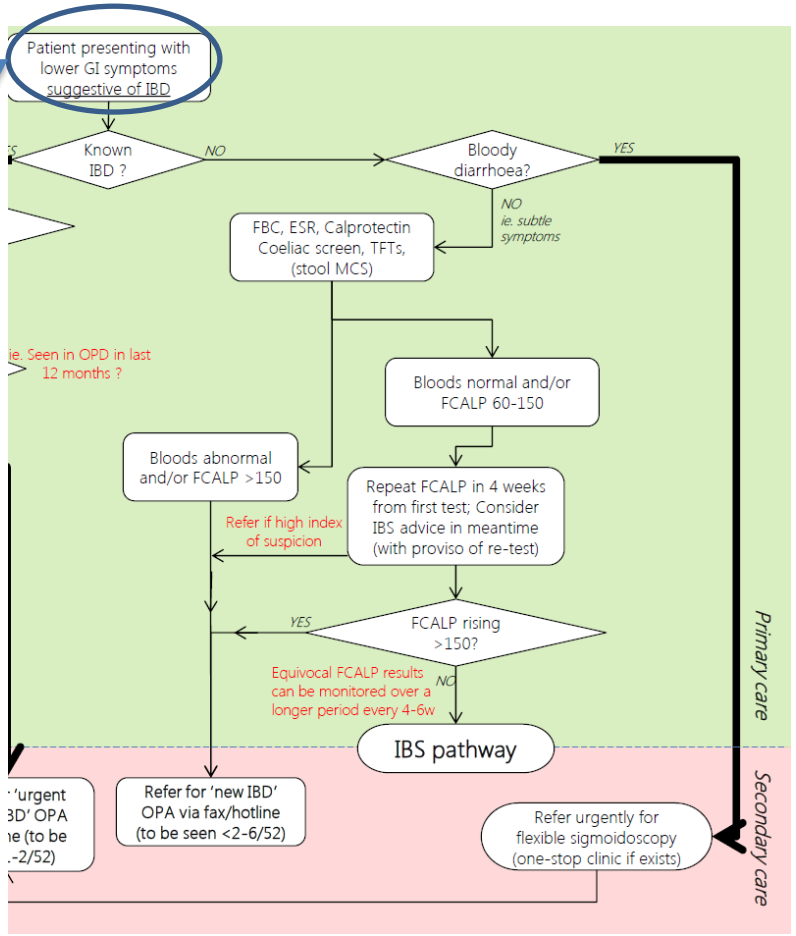
- Outcome: Remains in primary care at the end of 12 months. Treated for IBS

IBD pathway 1: Presenting with symptoms



Was the history suggestive of IBD ?

Probably NOT



South East London Area Prescribing Committee:

Primary & Secondary Care Inflammatory Bowel Disease Pathway January 2015

Authors:

Dr Bu Hayee, Consultant Gastroenterologist
Caroline Cheng, Lead Clinical Pharmacist,
Kings College Hospital NHS Foundation Trust

kch-tr.IBDhelpline@nhs.net Tel: 0203 299 1606 / 6044 Fax: 0203 299 6474

Dr Peter Irving, Consultant Gastroenterologist
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ibdhelpline@gstt.nhs.uk Tel: 020 7188 2487

Approved: 20 January 2015

Review date: 20 January 2017

Case 2

55 Yrs,Female	2 weeks of abdominal pain Initially, 2 days of constipation followed by diarrhoea, intermittent fresh rectal bleeding
	Recent dental extraction Metronidazole/Amoxicillin for 5 days Ibuprofen 400 mg bd for 5 days
	No weight loss
	Normal Hb, Coeliac screen, stool cultures, CRP 15, Calprotectin 125

Next step ?

- C difficile toxin ?
- Stop Ibuprofen?
- What about the calprotectin ?
- Retest ?

Test predictive values based on pre-test probability of endoscopically active IBD

Prevalence of endoscopic activity	Sensitivity	Specificity	Positive predictive value	Negative predictive value
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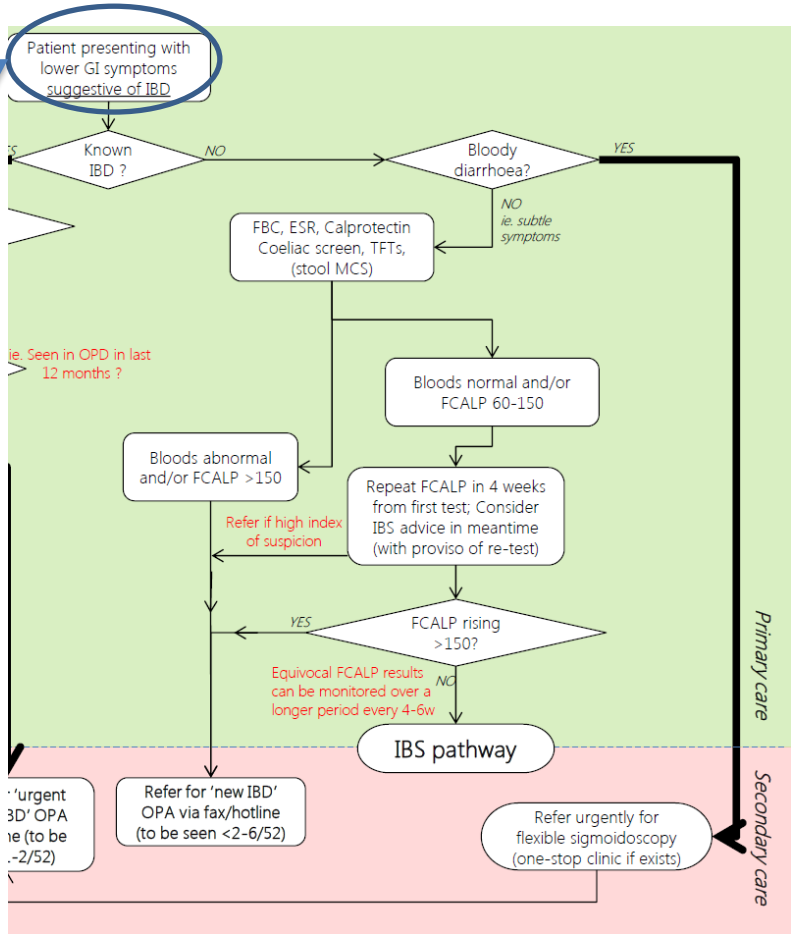
Was the history suggestive of IBD ?

Possibly



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Outcome

- Referred for Flexible sigmoidoscopy for rectal bleeding
- Had a colonoscopy after being seen in Gastro OPD
- Mild diverticular disease.
- Apthous ulcers in terminal ileum
- Stopped Ibuprofen.
- Discharged to primary care in 3 months
- Recovered completely

Case 3

60 Yrs, Female

Known Ulcerative Colitis, Diagnosed 10 years back

Has never required steroids

Usually takes Mesalazine 400 mg bd

More stress than usual recently

No weight loss

Normal Hb, Coeliac screen, stool cultures

CRP 10, Calprotectin 150

Test predictive values based on pre-test probability of endoscopically active IBD

Prevalence of endoscopic activity	Sensitivity	Specificity	Positive predictive value	Negative predictive value
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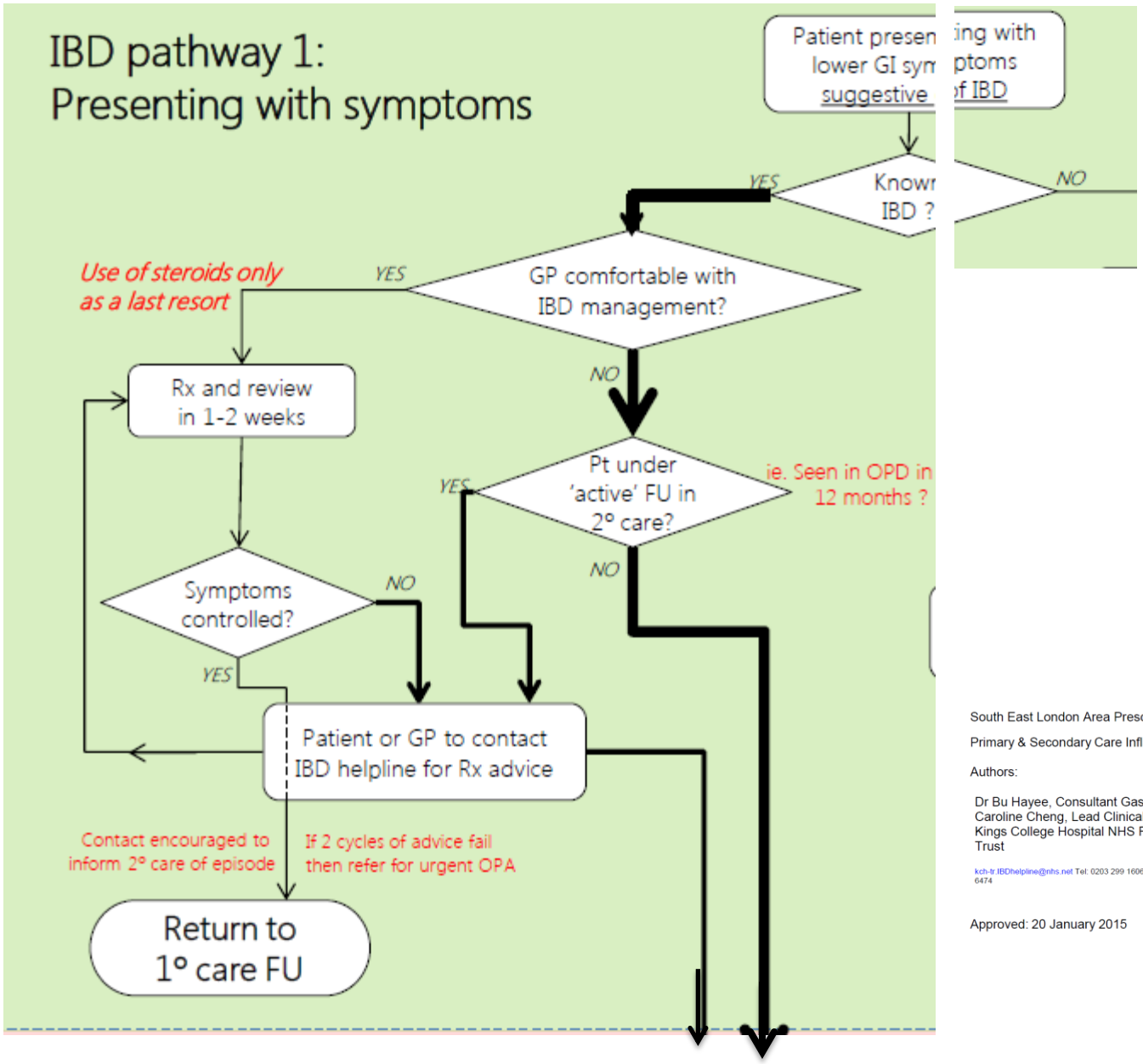

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Outcome

- Stool cultures repeated
- Increased mesalazine to 4.8 gms per day
- Added rectal mesalazine 1gm PR for 2 weeks
- Symptom free
- Increased maintenance to 2.4 gms per day
- Remained in primary care.
- No further flares over the next 12 months.
- Should she have been referred for a colonoscopy?

Colorectal cancer prevention: colonoscopic surveillance in adults with ulcerative colitis, Crohn's disease or adenomas

Clinical guideline [CG118] Published date: March 2011

1.1 List of all recommendations

People with inflammatory bowel disease

1.1.1 Offer colonoscopic surveillance to people with inflammatory bowel disease (IBD) whose symptoms started 10 years ago and who have:

- ulcerative colitis (but not proctitis alone) **or**
- Crohn's colitis involving more than one segment of colon.

Table 1 Risk of developing colorectal cancer in people with IBD

Low risk:

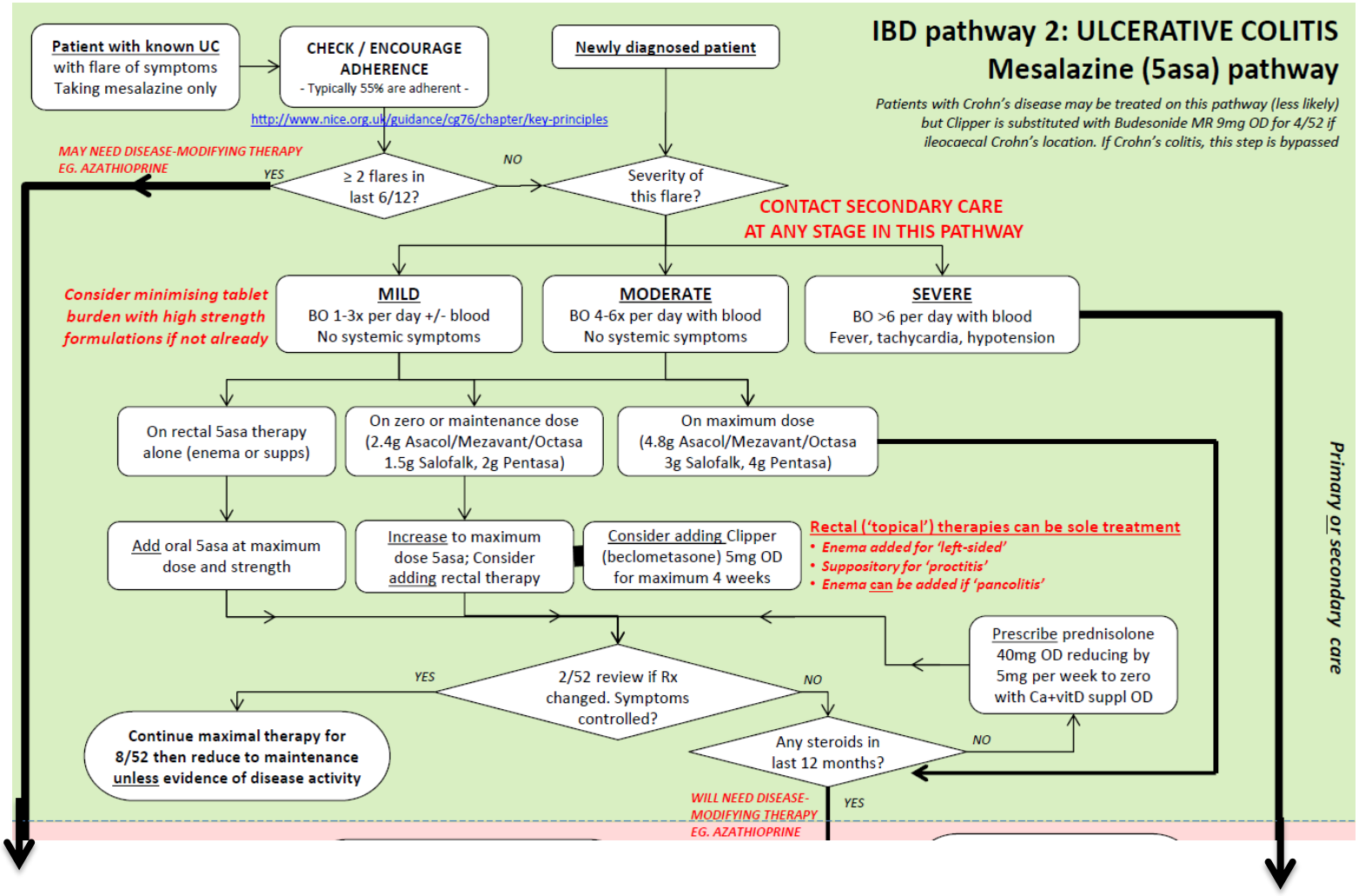
- extensive but quiescent ulcerative colitis **or**
- extensive but quiescent Crohn's colitis **or**
- left-sided ulcerative colitis (but not proctitis alone) or Crohn's colitis of a similar extent.

Intermediate risk:

- extensive ulcerative or Crohn's colitis with mild active inflammation that has been confirmed endoscopically or histologically **or**
- post-inflammatory polyps **or**
- family history of colorectal cancer in a first-degree relative aged 50 years or over.

High risk:

- extensive ulcerative or Crohn's colitis with moderate or severe active inflammation that has been confirmed endoscopically or histologically **or**
- primary sclerosing cholangitis (including after liver transplant) **or**
- colonic stricture in the past 5 years **or**
- any grade of dysplasia in the past 5 years **or**
- family history of colorectal cancer in a first-degree relative aged under 50 years.



OP Referral

Early OP Referral

Urgent Admission

Case 4

25 Yrs,Female	Known Crohn's, Small bowel resection age 18 Well over the last 7 years, Finishing university Usually takes Azathioprine 100 mg PO daily
	Abdominal pain, bloating, pale stools Pain relieved by defecation Recent acute gastroenteritis
	No weight loss Smoking 3 cigarettes a day over last 3 years
	Normal Hb, Coeliac screen, stool cultures CRP 25, Calprotectin 120

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Outcome

- Colonoscopy: Deep ulcers at neo terminal ileum. Anastomotic stricturing
- 15 cms of inflammatory stricturing in neo terminal ileum and another 20 cms of inflammatory stricturing. Small collection.
- Oral antibiotics and elemental diet for 4 weeks. Optimised azathioprine dosage

- Resolution of collection on follow up MRI in 6 weeks.
- Commenced Adalumimab
- Fibrotic stricturing and more pain in 6 months.
- Laparoscopic resection
- Currently on maintenance Adalumimab after 12 months.

Surprised at how aggressive the disease was ?

- Calprotectin was only 120
- Normal CRP
- No weight loss

CRP

- CRP
  - Produced in the liver
  - Stimulation by interleukin (IL)-6, tumor necrosis factor (TNF)-alpha and IL-1-beta produced at the site of inflammation.
  - CRP-level is a marker for inflammation, but is not specific for CD or UC

Table 2. Diagnostic accuracy of fecal calprotectin, stool lactoferrin, and C-reactive protein for endoscopically active disease

Marker	Sensitivity	Specificity	Positive LR	Negative LR	AUC	Diagnostic OR
C-reactive protein						
IBD	0.49 (0.34, 0.64)	0.92 (0.72, 0.98)	6.3 (1.9, 21.3)	0.56 (0.44, 0.71)	0.72 (0.68, 0.76)	11 (3, 38)
Fecal calprotectin						
IBD	0.88 (0.84, 0.90)	0.73 (0.66, 0.79)	3.2 (2.6, 4.1)	0.17 (0.14, 0.21)	0.89 (0.86, 0.91)	19 (13, 27)
CD	0.87 (0.82, 0.91)	0.67 (0.58, 0.75)	2.7 (2.1, 3.4)	0.19 (0.14, 0.27)	0.85 (0.82, 0.88)	14 (9,22)
UC	0.88 (0.84, 0.92)	0.79 (0.68, 0.87)	4.2 (2.8, 6.4)	0.15 (0.11, 0.20)	0.91(0.89, 0.94)	28 (18, 46)
Sensitivity analysis 1[a]	0.87 (0.82, 0.90)	0.71 (0.62, 0.78)	3 (2.3, 3.8)	0.19 (0.14, 0.24)	0.87 (0.84, 0.90)	16 (11, 23)
Sensitivity analysis 2[a]	0.87 (0.83, 0.91)	0.71 (0.63, 0.78)	3 (2.3, 3.9)	0.18 (0.13, 0.24)	0.88 (0.85, 0.91)	19 (14, 28)
Sensitivity analysis 3[a]	0.88 (0.84, 0.91)	0.73 (0.66, 0.79)	3.2 (2.5, 4.1)	0.17 (0.13, 0.21)	0.89 (0.86, 0.92)	19 (14, 28)
Sensitivity analysis 4[a]	0.87 (0.83, 0.90)	0.72 (0.65, 0.78)	3.1 (2.5, 3.9)	0.18 (0.14, 0.23)	0.88 (0.85, 0.91)	17 (12, 24)
Stool lactoferrin						
IBD	0.82 (0.73, 0.88)	0.79 (0.62, 0.89)	3.8 (2.0, 7.5)	0.23 (0.14, 0.38)	0.87 (0.84, 0.90)	16 (6, 48)

AUC, area under the curve; CD, Crohn's disease; IBD, inflammatory bowel disease; LR, likelihood ratio; OR, odds ratio; UC, ulcerative colitis.

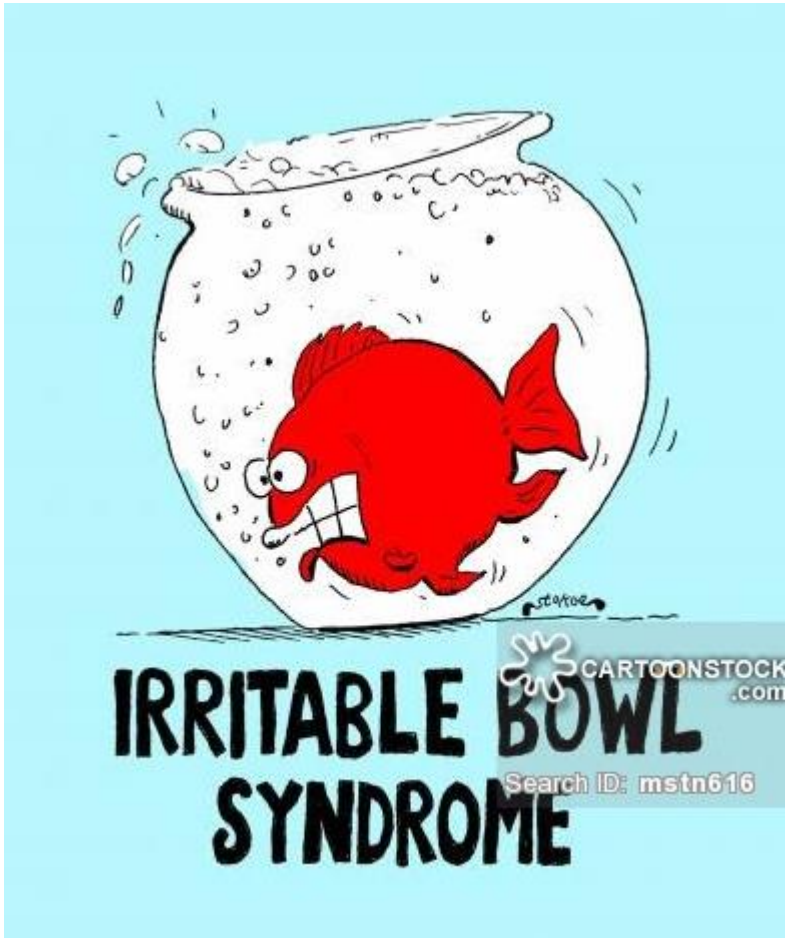
[a]Sensitivity analysis 1: excluding studies that included healthy controls that did not undergo colonoscopy; sensitivity analysis 2: excluding studies that included any patient not known to have a diagnosis of inflammatory bowel disease; sensitivity analysis 3: excluding one study that examined patients presenting with lower gastrointestinal symptoms; and sensitivity analysis 4: excluding two studies that were published in abstract form.

Mosli, M.H., et al., *C-Reactive Protein, Fecal Calprotectin, and Stool Lactoferrin for Detection of Endoscopic Activity in Symptomatic Inflammatory Bowel Disease Patients: A Systematic Review and Meta-Analysis.* Am J Gastroenterol, 2015. **110**(6): p. 802-19; quiz 820.

Stool markers

- Calprotectin is a calcium- and zinc-binding protein
- Large amounts in neutrophil granulocytes
- Very stable marker
- Resistant to colonic bacterial degradation
- Can be stored at room temperature for more than a week
- Stool concentration is proportional to the neutrophil cell infiltrate in the bowel mucosa
- It is a very sensitive marker for intestinal inflammation

- Not a specific marker for CD or UC
  - Neoplasia
  - Polyps
  - Diverticulitis
  - Infectious Colitis
  - Microscopic colitis
  - NSAID medication
  - Small intestinal bacterial overgrowth
  - Increasing age


IRRITABLE BOWL
SYNDROME
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Spectrum of Functional GI Disorders

Dyspepsia

Irritable bowel syndrome
Chronic constipation

Functional abdominal pain syndrome

Spectrum of Functional GI Disorders

Rumination
chest pain, heartburn

? Gallbladder dysfunction
? Sphincter of Oddi dysfuntion

Functional abdominal pain syndrome

Dyspepsia
Aerophagia
Vomiting

Irritable bowel syndrome
Chronic constipation

Pelvic floor dyssynergia

Clinical features (mainly symptoms) → phenotype
Precise phenotype → most appropriate management
Do NOT use IBS as a generic term for all functional GI disorders

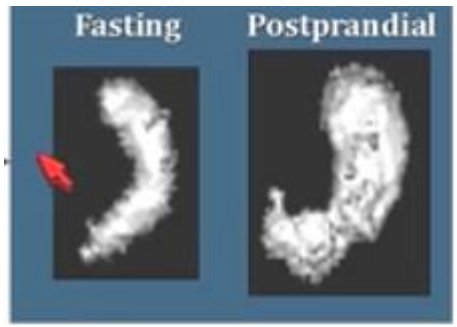
Diagnosing Functional GI Disorders

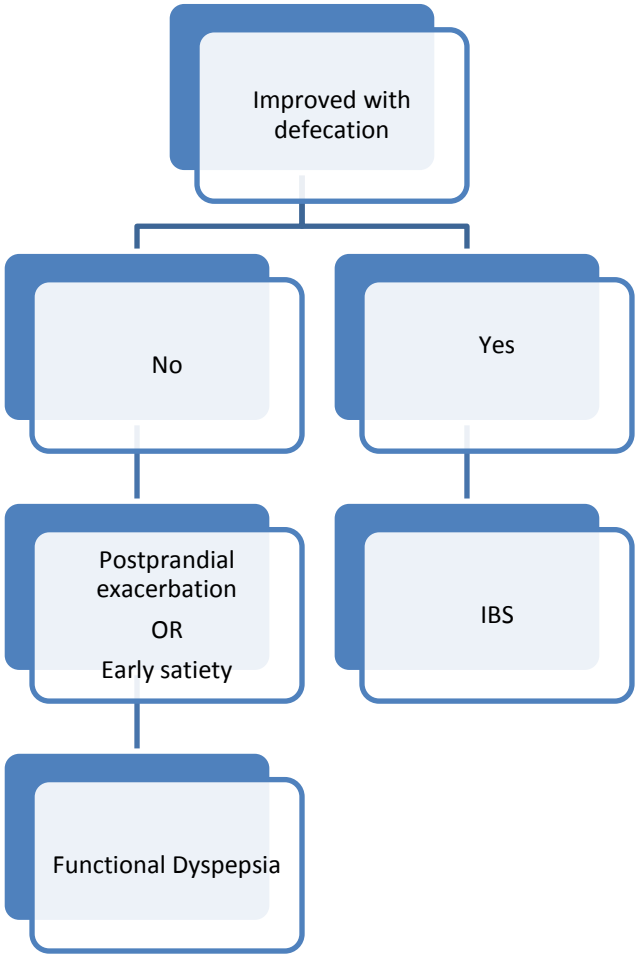
1. Listen
   - Ask the right questions
2. Characterise the phenotype
   - Dyspepsia, diarrhoea-IBS, Constipation, Defecatory disorders
3. Only perform selected tests
   - Another normal endoscopy will not help
4. Therapy (Not Opiods), dietary, pshychological and behavioural therapy

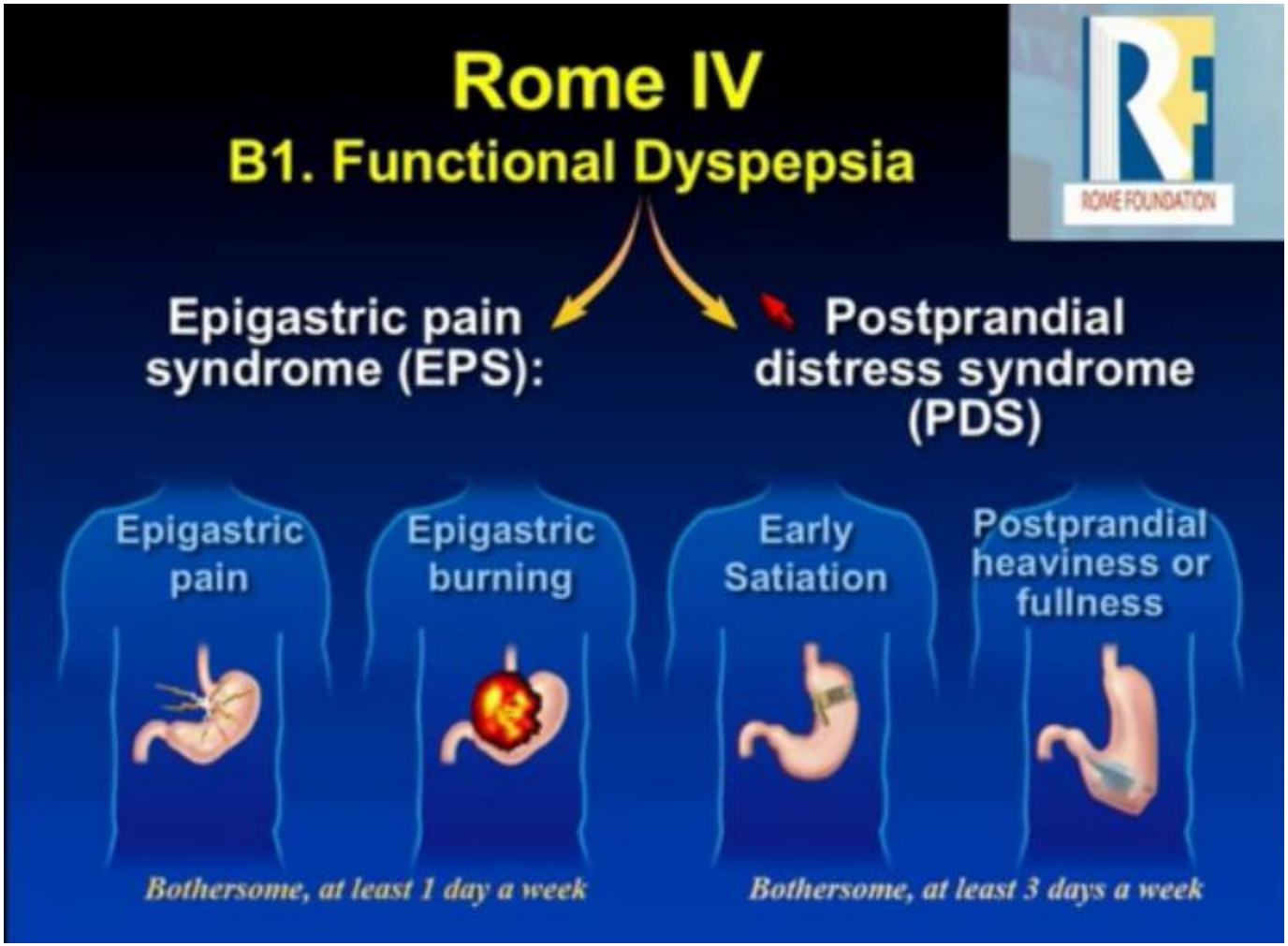
Case 1: Functional Dyspepsia

35 Yrs, Female	Postprandial epigastric distress, early satiety, nausea and bloating for 5 years
	Abdominal discomfort not relieved by defecation or associated with abnormal bowel movements
	10 lbs weight loss
	Medications: Pantoprazole- ineffective
	Normal FBC, U/E, LFT
	OGD: Reactive gastritis. No inflammation on biopsy, negative CLO

Abdominal Pain

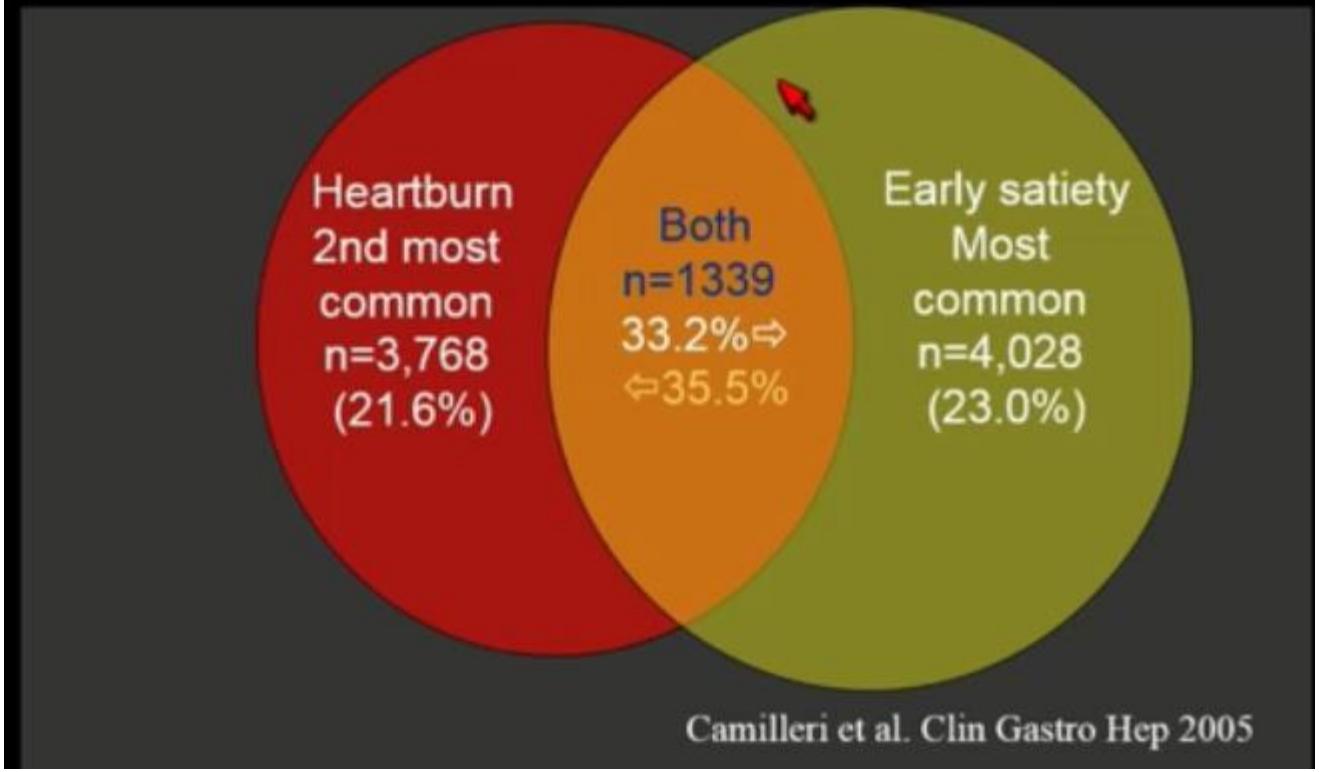




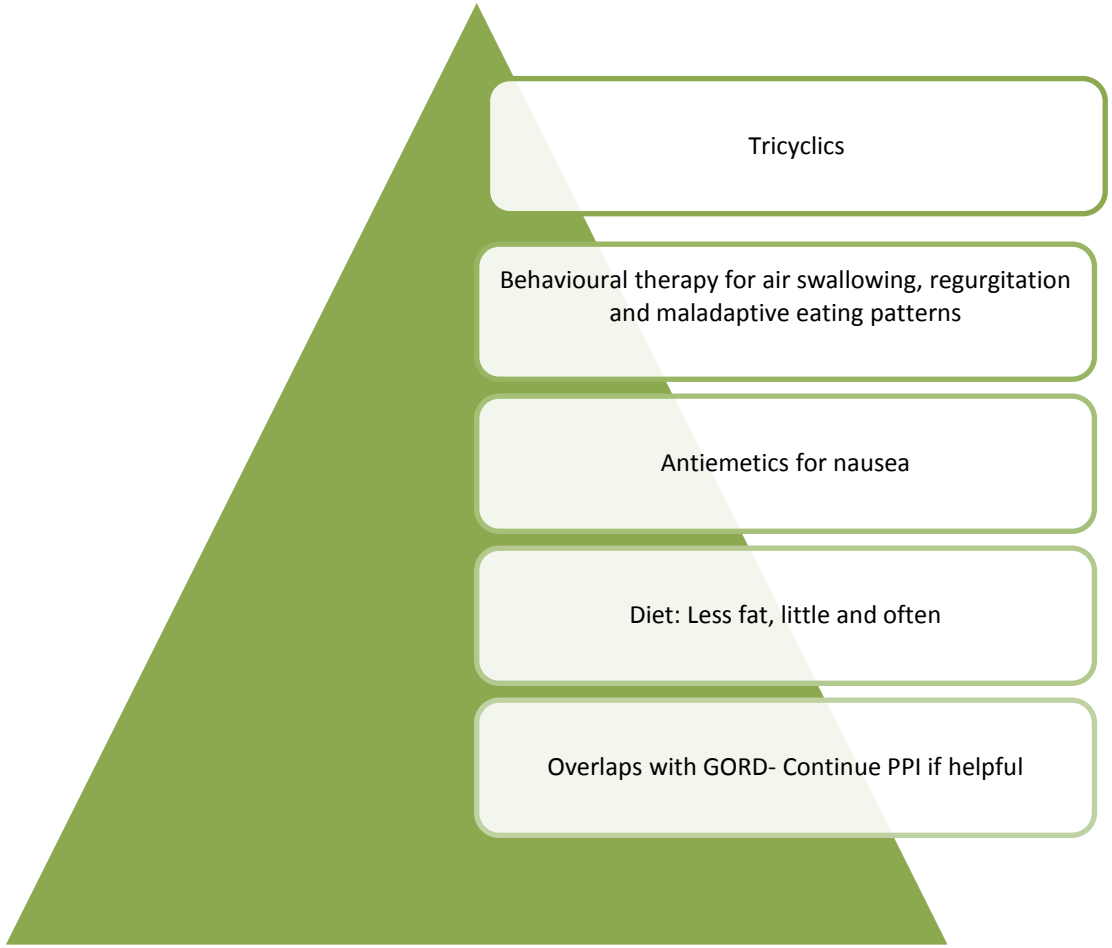

Rome IV
B1. Functional Dyspepsia
ROME FOUNDATION
Epigastric pain syndrome (EPS):
Postprandial distress syndrome (PDS)
Epigastric pain
Epigastric burning
Early Satiation
Postprandial heaviness or fullness
Bothersome, at least 1 day a week
Bothersome, at least 3 days a week

Overlap of Upper GI Symptoms in USA

Symptom prevalence (≥1x/month) n=17,484



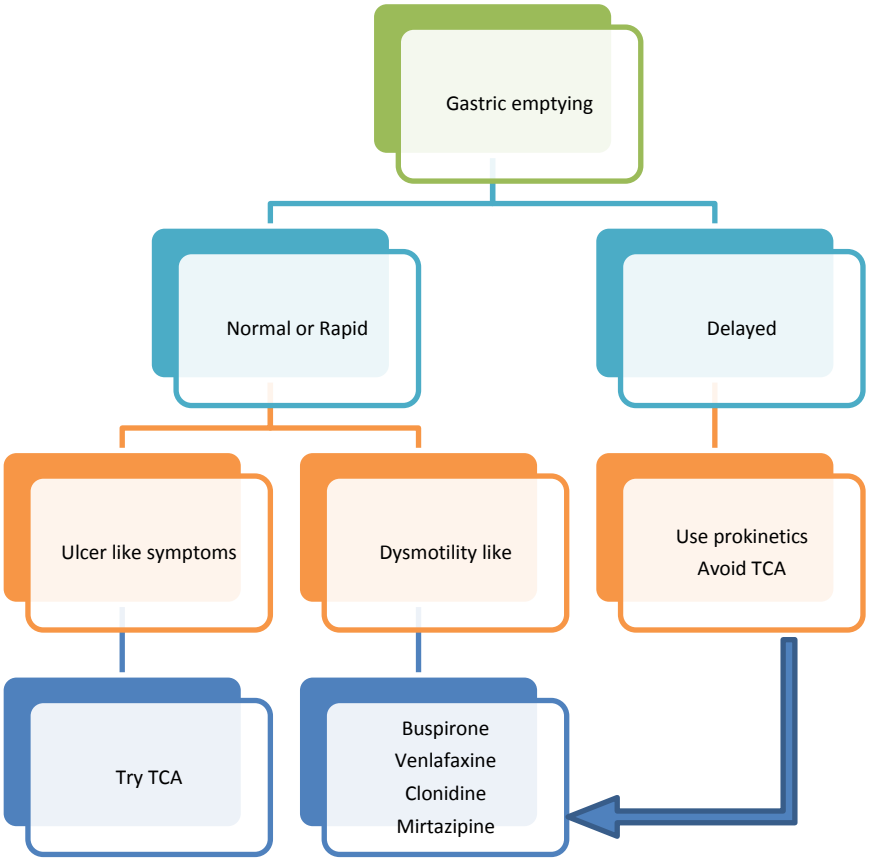
Managing Dyspepsia



Therapeutic options

Drug (Class, Dose)	Acute effects	Trials
Buspirone (5-HT agonist, 10 mg b.i.d- t.i.d)	Reduce acute postprandial symptoms Increase accommodation	Reduce bloating, postprandial fullness
Venlafaxine-XR (SNRI- 75 – 150 mg)	Increase accommodation	None
Mitrazipine NaSSA	Accommodation	Reduced early satiety, Up to 4 kg weight gain
Clonidine (alpha 2 adrenergic agonist, 0.1 mg b.i.d)	Increase compliance, reduced sensation, unchanged gastric emptying	None

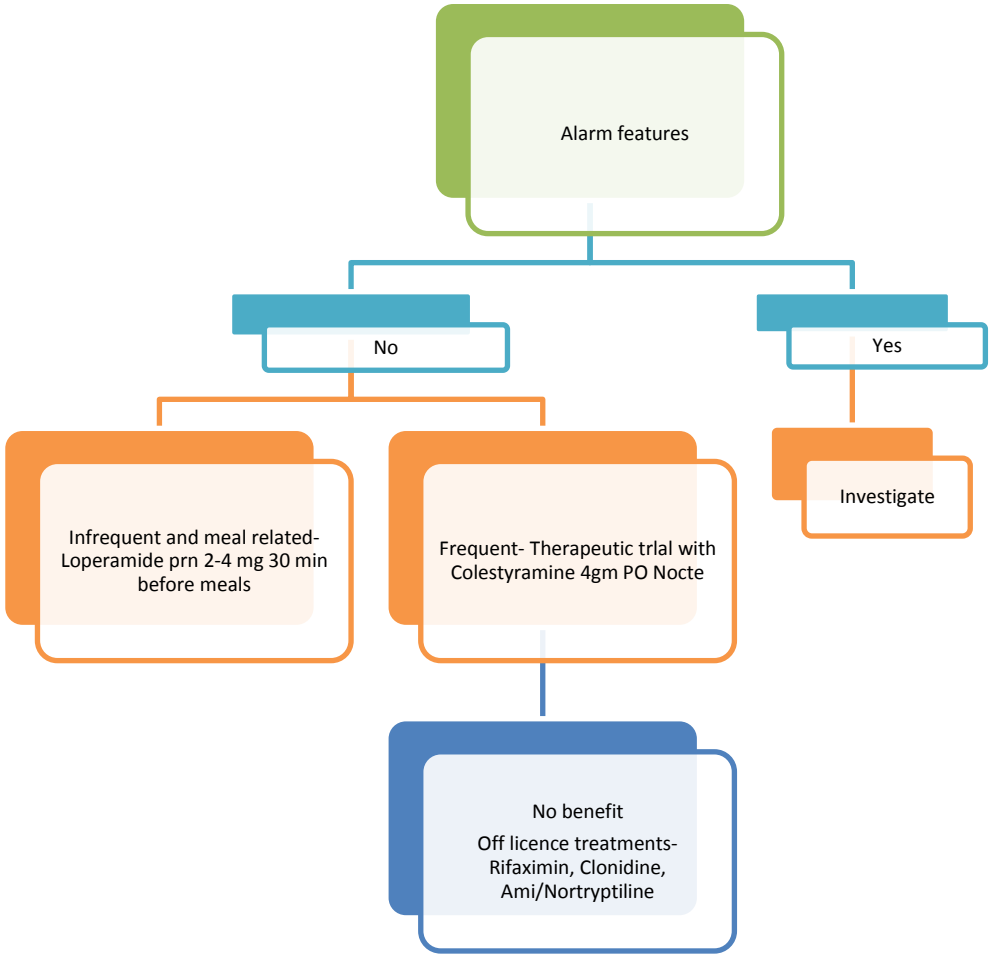
Managing REFRACTORY dyspepsia



Case 2: Irritable Bowel Syndrome

22 Yrs, Female	
	Diarrhoea for 3 years
	Followed acute gastroenteritis
	Postprandial abdo discomfort, semi formed stools, frequent faecal incontinence, urgency
	Relief with defecation
	Weight gain (23 lbs) in the same time, No alarm symptoms
	OGD: Reactive gastritis. No inflammation on biopsy, negative CLO
	Normal FBC, Chemistry, TTG, Faecal calprotectin
	Tried Probiotics

Managing Diarrhoea



Diaphragmatic Breathing

Technique 1:
Diaphragmatic breathing
Chitkara, MD et al., Am J Gastroenterol 2006;101:2449–2452

image from Miranda VanTilburg

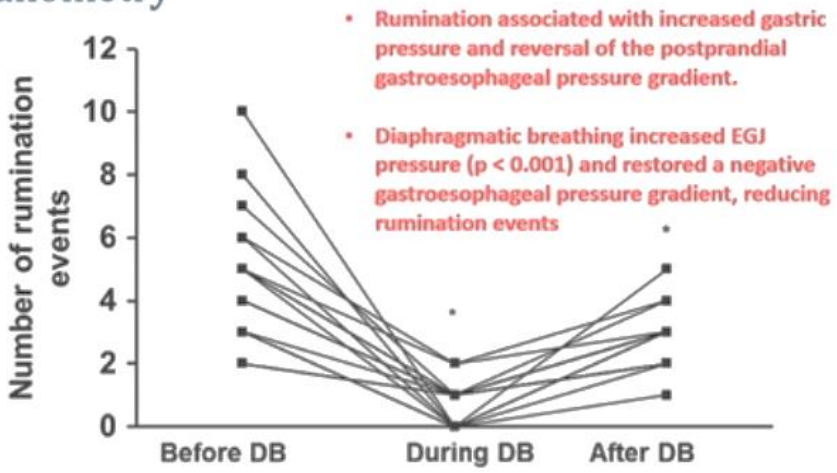
- Indications
  - Rumination
  - Urgency

The Prescription to the Patient

- Practice breathing exercise midway through the meal (if regurgitation occurs during the meal) or after meals for three different 5 min periods of inactivity with 10 min in between periods
- Repeat breathing after each episode of re- gurgitation.

- The **goal is for diaphragmatic breathing to occur unconsciously during events that may precipitate regurgitation [conditioning].**

Diaphragmatic breathing for rumination syndrome during high resolution esophageal manometry



- Rumination associated with increased gastric pressure and reversal of the postprandial gastroesophageal pressure gradient.
- Diaphragmatic breathing increased EGJ pressure ($p < 0.001$) and restored a negative gastroesophageal pressure gradient, reducing rumination events

Diaphragmatic Breathing for Urgency

Bowel Urgency + **Fear** Elicits the Fight or Flight Response

- **Increase in distal colonic motility**
- **Acceleration of intestinal transit**

- Relieves physical muscle tension/abdominal wall pressure
- Activates parasympathetic nervous system
- Releases CO2/Increases 02 to all cells
- Slows heart rate/ Lowers blood pressure

Bottom Line:
You cannot be tense and out of control AND relaxed and in control at the same time!

carnett sign - Google | Carnett sign.pdf | diaphragmatic breath

https://www.youtube.com/results?search_query=diaphragmatic+breathing+exercises

YouTube GB

diaphragmatic breathing exercises

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CioffrediPT
3 years ago • 172,990 views
In this video, Whitney Zweeres, PTA teaches the diaphragmatic breathing technique. This technique can be used for pain ...

4-7-8 Breathing Exercise by GoZen
gozenonline
3 years ago • 230,445 views
http://www.gozen.com - This is a great breathing exercise for both adults and children to help alleviate anxiety. Basic breathing ...

Diaphragmatic Breathing Exercises For Anxiety
Fitness Oriented
1 year ago • 1,645 views
The diaphragm is a very important muscle located between your lungs and abdominal cavity which is critical for breathing.

Proper Breathing Exercise to Strengthen Lungs to Keep Healthy - Dr Mandell
motivationaldoc
6 months ago • 22,698 views
Belly breathing is a fundamental exercise to strengthen the lungs. Belly breathing refers to breathing that uses the diaphragm, ...

Breathing Exercises for Singing: How to Sing from Your Diaphragm Properly | Singing Lessons
Marnell Sample
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This simple breathing exercise will show you: (1) how to breathe from your diaphragm properly, (2) how to SING from your ...
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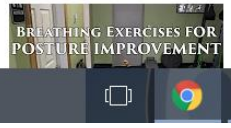

Breathing Exercises For Posture | Diaphragm Activation
GuerrillaZen Fitness
10 months ago • 4,207 views

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Case 3: Constipation

19 Yrs, Female

Constipation for 2 years

Infrequent hard bowel movements: Bristol 1

No urge to stool

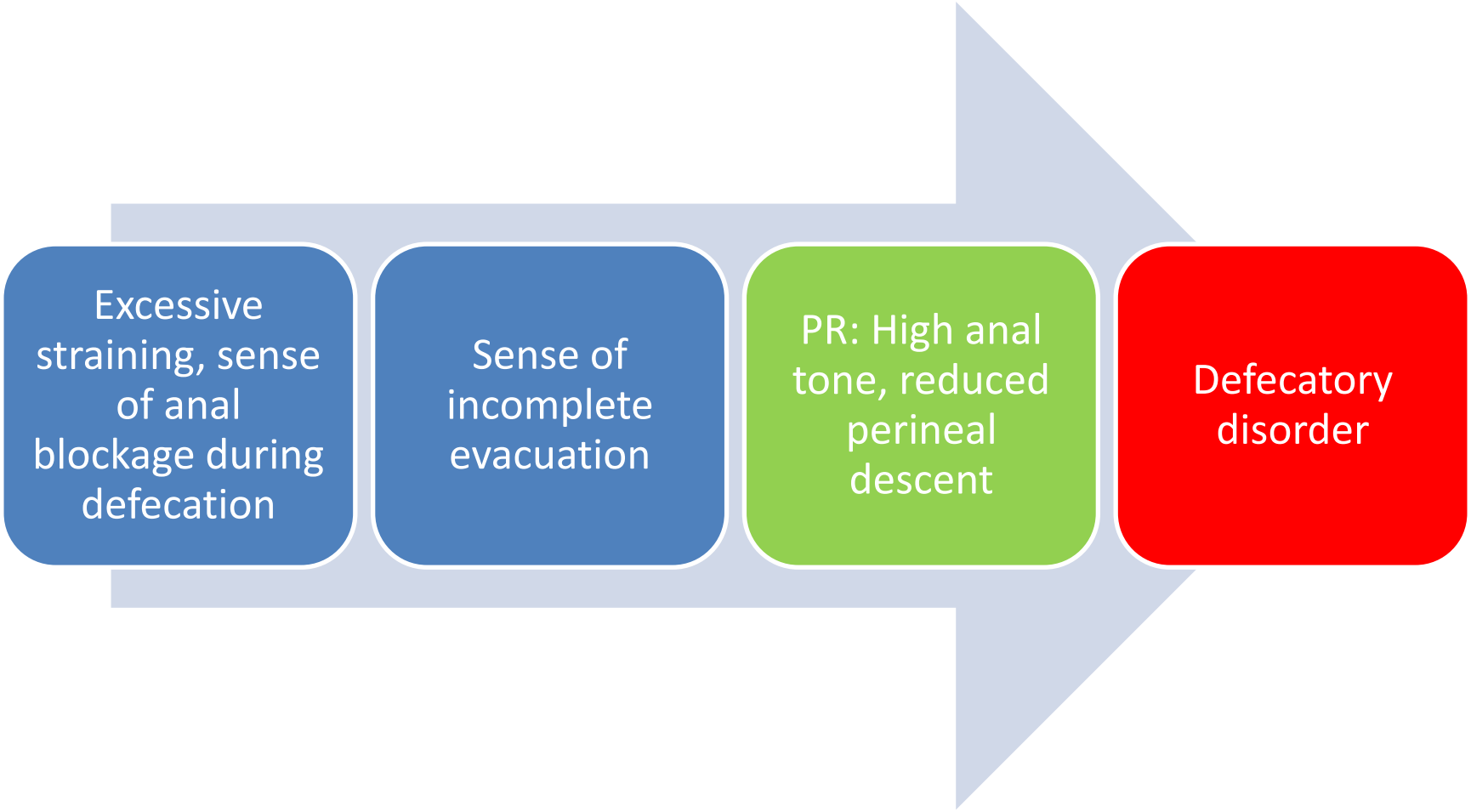
Right abdo pain with bloating: Not post prandial

Lower abdominal tenderness

Normal FBC, chemistry, faecal calprotectin: 150

Diagnosis: IBS ?

Back to the clinical features



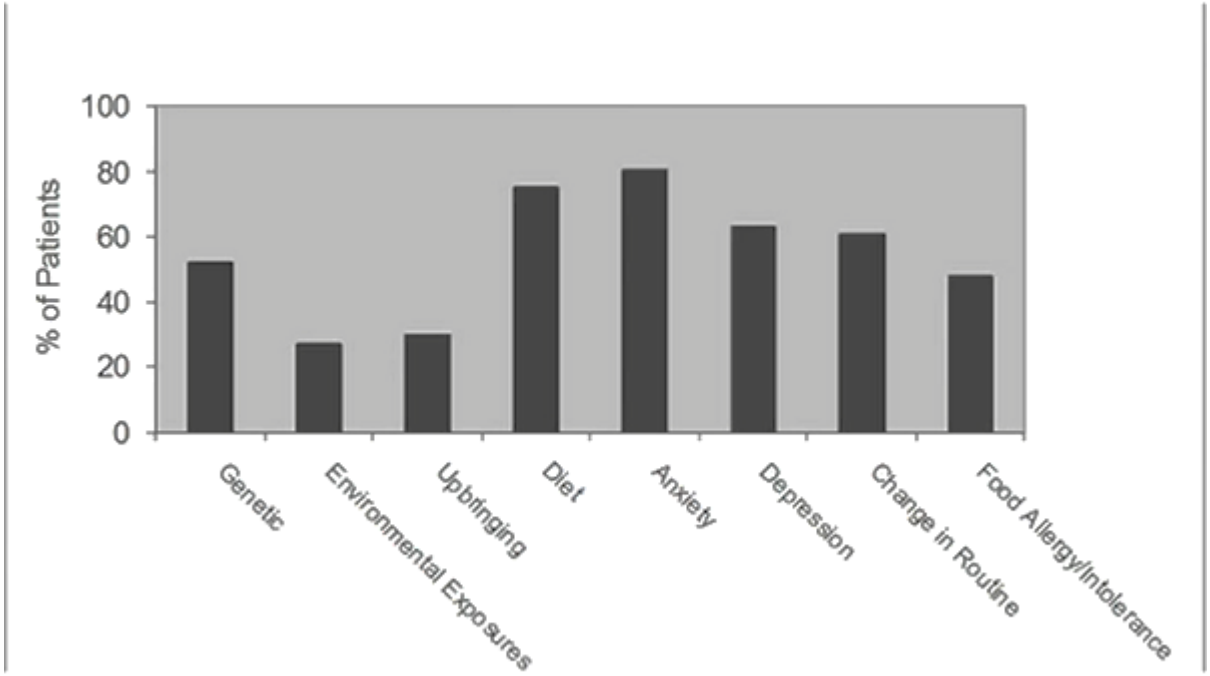
Chronic Constipation

- Chronic constipation : Distension of the right colon can cause abdominal pain
- Amenable to pelvic floor retraining
- Osmotic laxatives rarely provide patient satisfaction
- Stimulant laxatives may help

Dietary Treatments for IBS and Other FGID: Limited Evidence

Diet	Evidence for use
Low fat	Limited
Gluten-free	Limited
Specific carbohydrate intolerance	Little to **none**
Low FODMAP	Limited
Paleolithic	Minimal
Candida	None
Elimination	Little to none

Cause of IBS: Patients' Beliefs



Lacy, B et al, Am J Gastroenterol, 2006

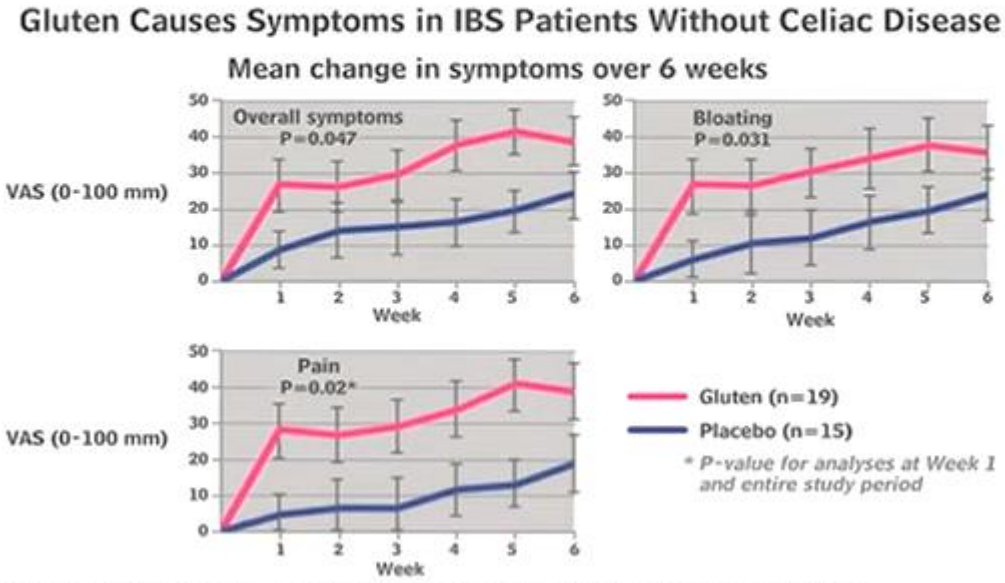
Food Allergy and IBS

- Controversial area studies for and against food allergy role in IBS
- One study suggested benefit of food-specific elimination diet:
  - 150 outpatients with IBS & various food-specific serum IgG
  - Randomized to 3 month of specific elimination versus sham elimination diet
  - Primary outcomes of IBS symptom severity (10% reduction) & global rating scores significantly improved with specific diet
  - Trend to benefit with secondary outcomes including QOL

However food-specific IgG is no longer recommended in the USA and Europe

W. Atkinson et al, Gut, 53:1459, 2004

Gluten Causes Symptoms in IBS Patients Without Celiac Disease



Adapted from Biesiekierski JR, et al. Am J Gastroenterol, Jan. 11, 2011 [Epub ahead of print]

No Effect of Gluten after Reduced FODMAP Diet in IBS Patients

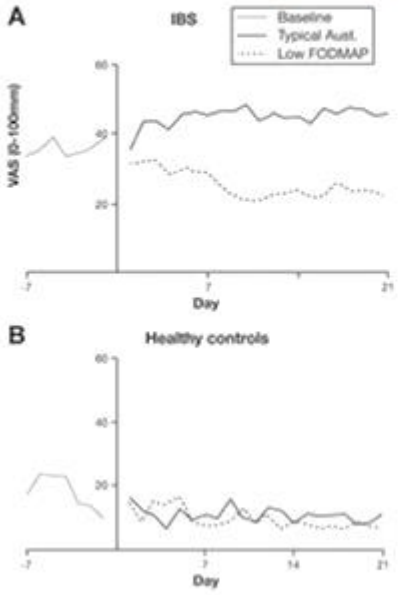
- 37 subjects with IBS (Rome III) reporting NCGS (celiac disease meticulously excluded) underwent double-blind cross-over study
- 2 wks low FODMAP diet resulted in significant improvement of GI symptoms and fatigue
- Challenge with gluten (high, low or control) did not result in symptomatic or biological changes
- Suggests sensitivity may not be due to gluten

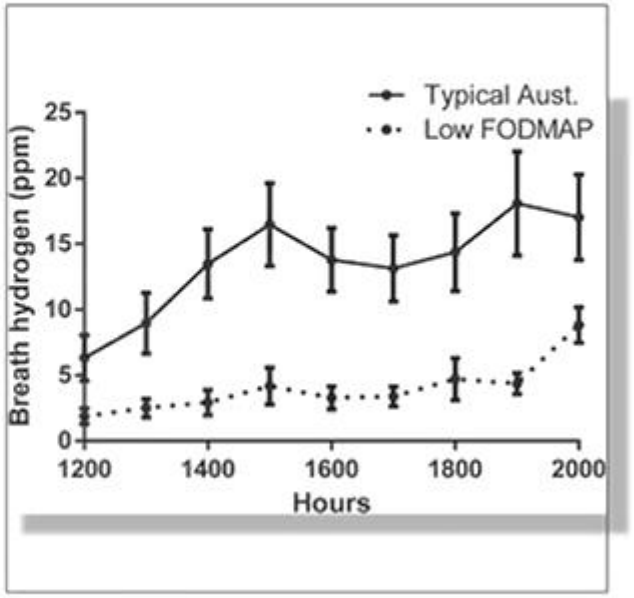
J. Biesiekierski, et al, Gastroenterol, 145:320, 2013

Pathophysiology of FODMAPs

- Poor absorption in the small intestine
- Osmotic effects in the colon, increased water
- Fermentation with gas production
- Luminal distension
- Effects on microbiota
- Immune modulation
- Alteration of intestinal barrier

A Diet Low in FODMAPs Reduces Symptoms of IBS





Halmos, EP, et al, Gastroenterol: 2014, 146; 67.

Case 4: Chronic abdominal pain

33 Yrs, Female	Unemployed, applied for disability
	Previous full employment, supportive family
	4 years of chronic pain and constipation
	Gradual reduction ins stool frequency to 1 per week
	Misuse of laxatives- now stopped
	Near constant abdominal pain
	Pat history: Fibromyalgia, daily headaches, depression, alcohol abuse in the past

Chronic Abdominal pain

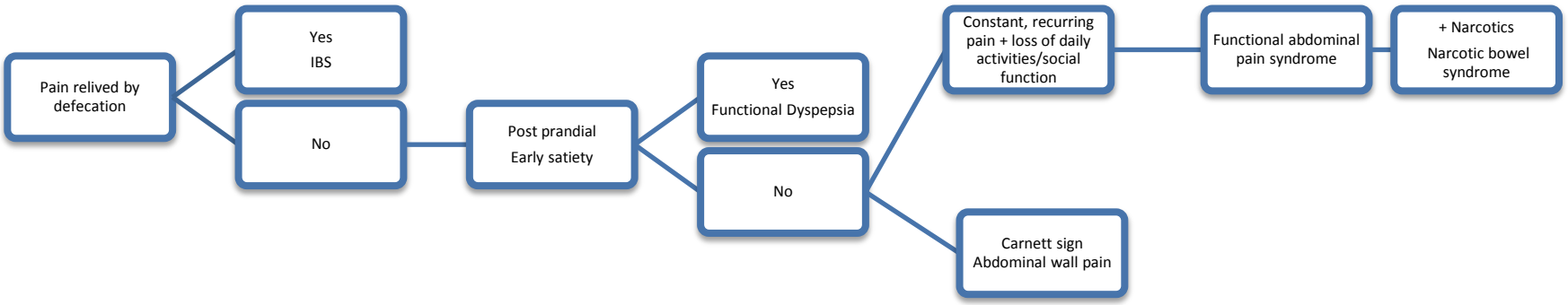


Figure 1. Carnett's sign for patients with pelvic pain. The examiner places his or her finger on the tender area of the patient's abdomen and asks the patient to raise both legs off the table. An increase in the patient's pain during this maneuver is considered a positive test.

Diagnoses

- Functional abdominal pain
- Narcotic Bowel syndrome
- Pelvic floor dysfunction

Therapy

- Chronic impairment
- Chronic Constipation
- Chronic pain
- Chronic headache
- Fibromyalgia
- Depression
- Addiction
- Disability
- NO ACUTE INTERVENTION CAN REVERSE THIS PROCESS
- Medications must be shifted to secondary role
- Therapeutic empathy
- Residential rehabilitation

Choosing the right antidepressant for Functional GI disease

- TCA
  - Best evidence
  - Amitryptiline
  - Desimipramine (n=261, 12 weeks, vs placebo)
  - Start low, check in 1 week, max dose 75 mg/day
- SSRI
  - Paroxetine (n=367, 2 studies)
  - Improved well being, less pain and anxiety
- SNRI
  - Duloxetine, venlafaxine- poor evidence

Snapshots at jasonlove.com

"I'm afraid that your irritable bowel syndrome has progressed. You now have furious and vindictive bowel syndrome."