Management of IBS and IBD

Cynthia Ko, MD

November 4, 2023

Disclosures

- I have no conflicts of interest to disclose.

Outline

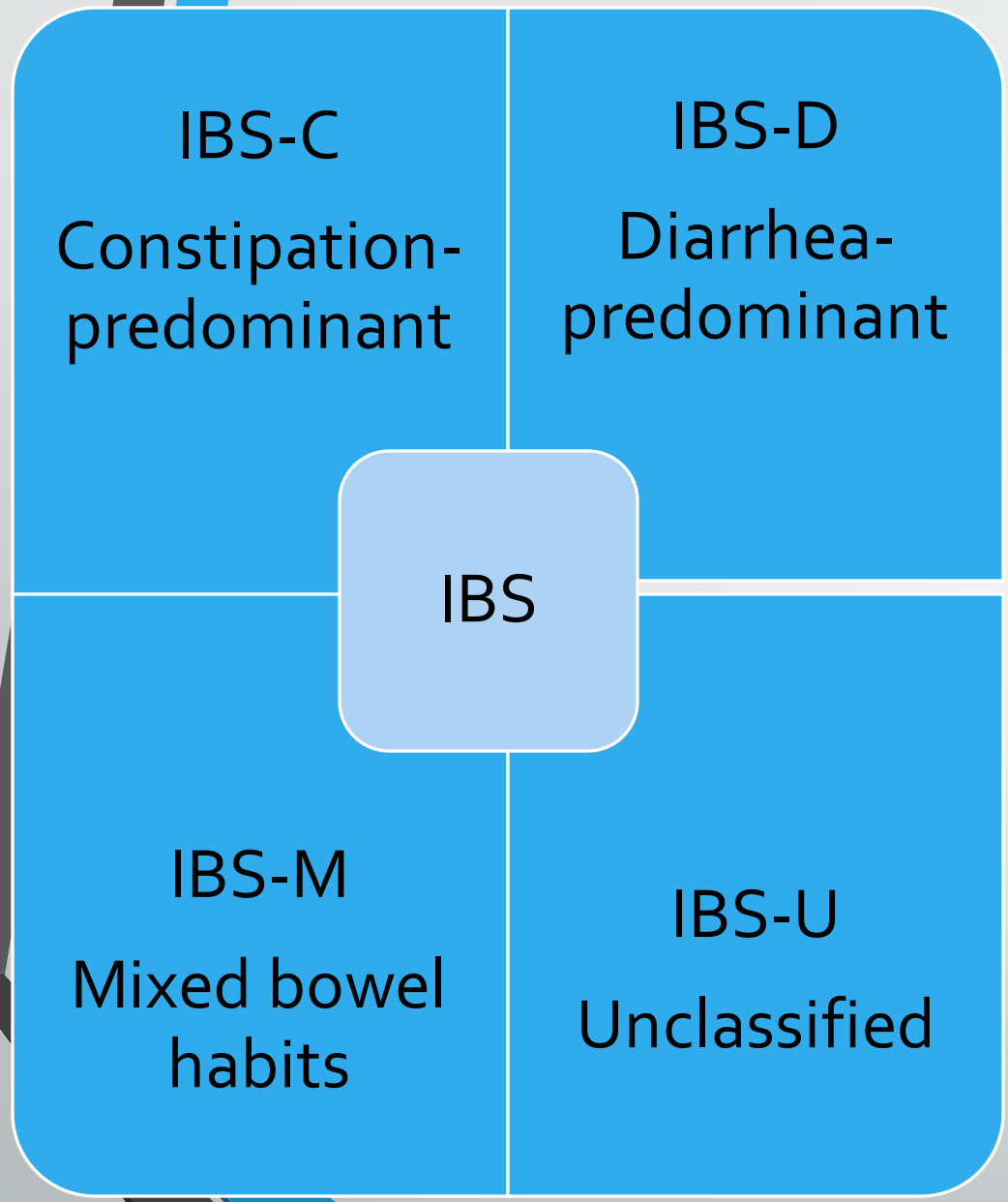
- Diagnosis and management of irritable bowel syndrome
- Diagnosis and management of inflammatory bowel disease

Case

- 23yo female presents with lower abdominal cramping, non-bloody diarrhea, and bloating occurring several days per week over the past 6 months. She has not had any weight loss or blood in her stools.
- PMH – anxiety, fibromyalgia
- Medications – none currently
- FH – no CRC or IBD

Epidemiology of IBS

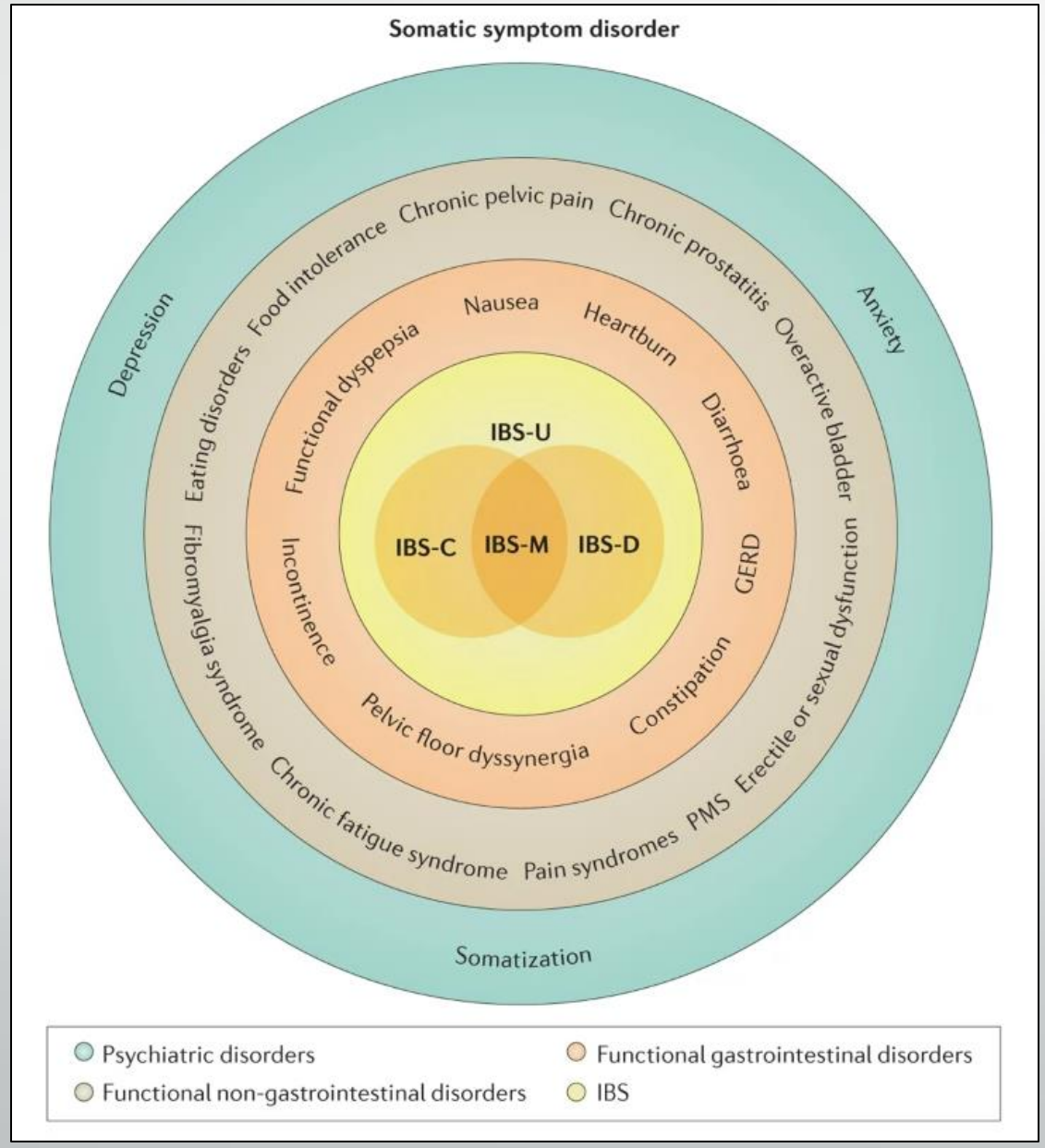
- 10-15% of U.S. population
  - Women > men
  - Younger > older
  - Frequent cause of work absenteeism
  - Decreased quality of life
- 25-50% of gastroenterology referrals



Diagnostic criteria

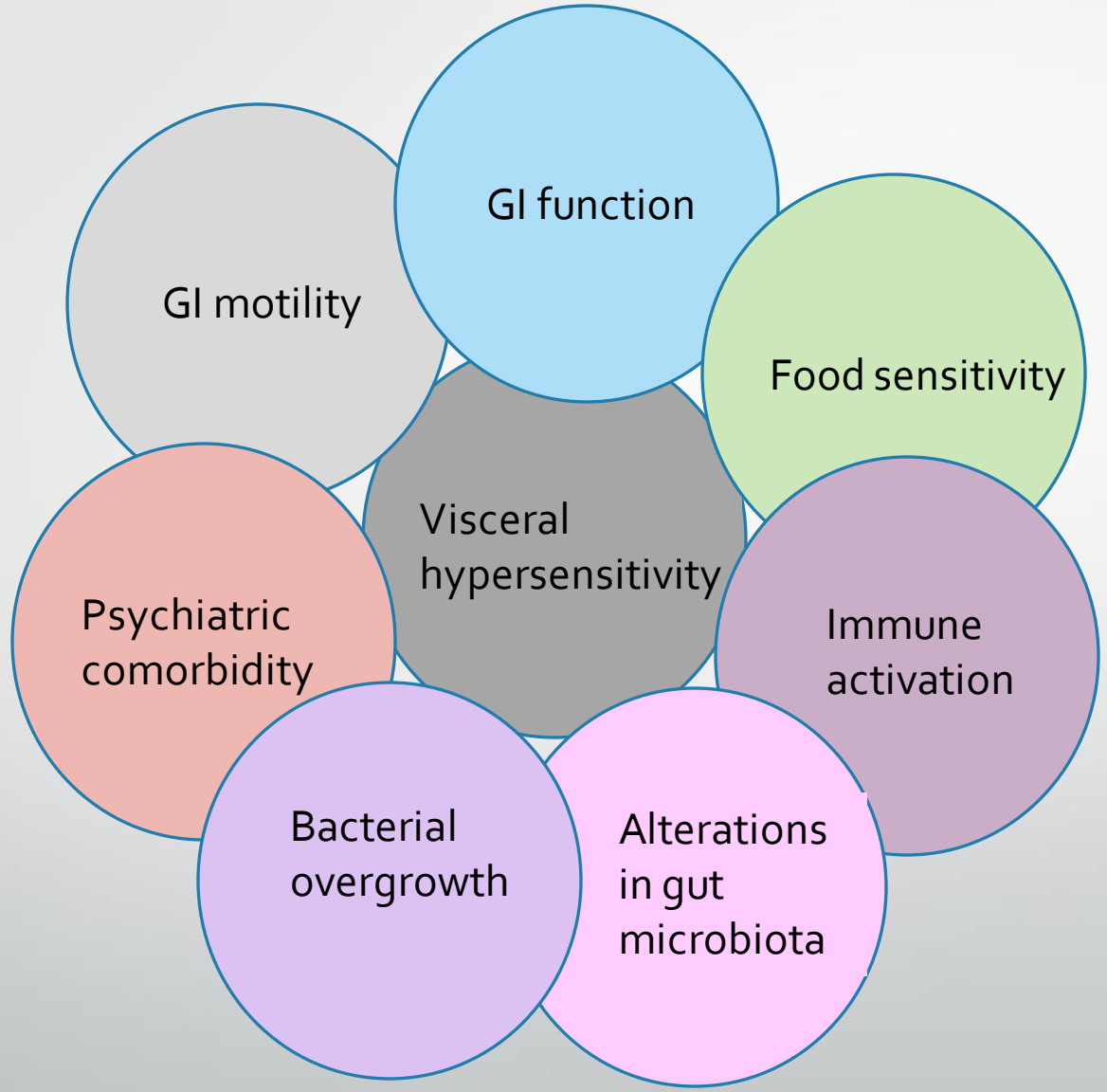
- Recurrent abdominal pain, at least one day per week over last 3 months, associated with 2 or more of the following:
  - Related to defecation
  - Change in stool frequency
  - Change in stool form or appearance

Frequent overlapping syndromes



Nature Reviews Disease Primers 2016; 2:16014

Pathophysiology



Which of the following is an appropriate step for her evaluation?

A. No further work-up needed

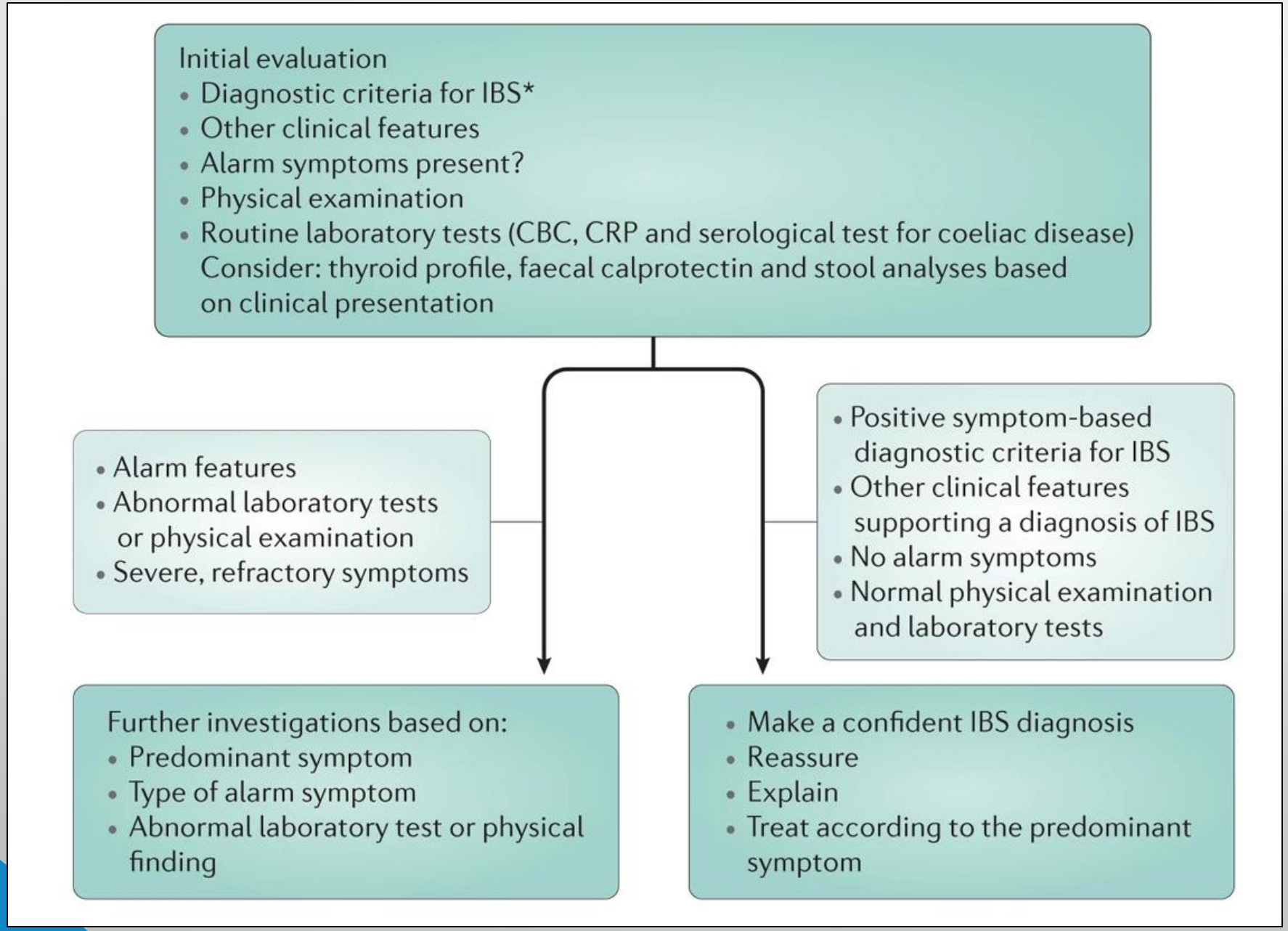
B. Celiac serologies

C. Fecal occult blood testing

D. CT abdomen/pelvis

E. Colonoscopy

Diagnosis of IBS



Nature Reviews Disease Primers 2016; 2:16014

Additional work-up based on presentation

All patients

- Age-appropriate colorectal cancer screening, if needed

Constipation

- If severe, consider:
  - Abdominal radiograph
  - Anorectal manometry

Diarrhea

- Giardia or enteric pathogen panel
- Fecal calprotectin

If no alarm features, limited diagnostic approach rules out organic disease in >95%

Reasons for GI referral

- Need for endoscopic evaluation
  - Alarm features
  - Family history of selected conditions including CRC, IBD, celiac disease
- Severity
- Lack of response to initial management

Principles of treatment

- NOT a diagnosis of exclusion
  - Benefit from "positive" diagnosis based on symptom criteria
- Assess impact on quality of life and activities of daily living
- Realistic expectations

What initial management strategy would you recommend?

A. Dietary modifications, including fiber supplementation

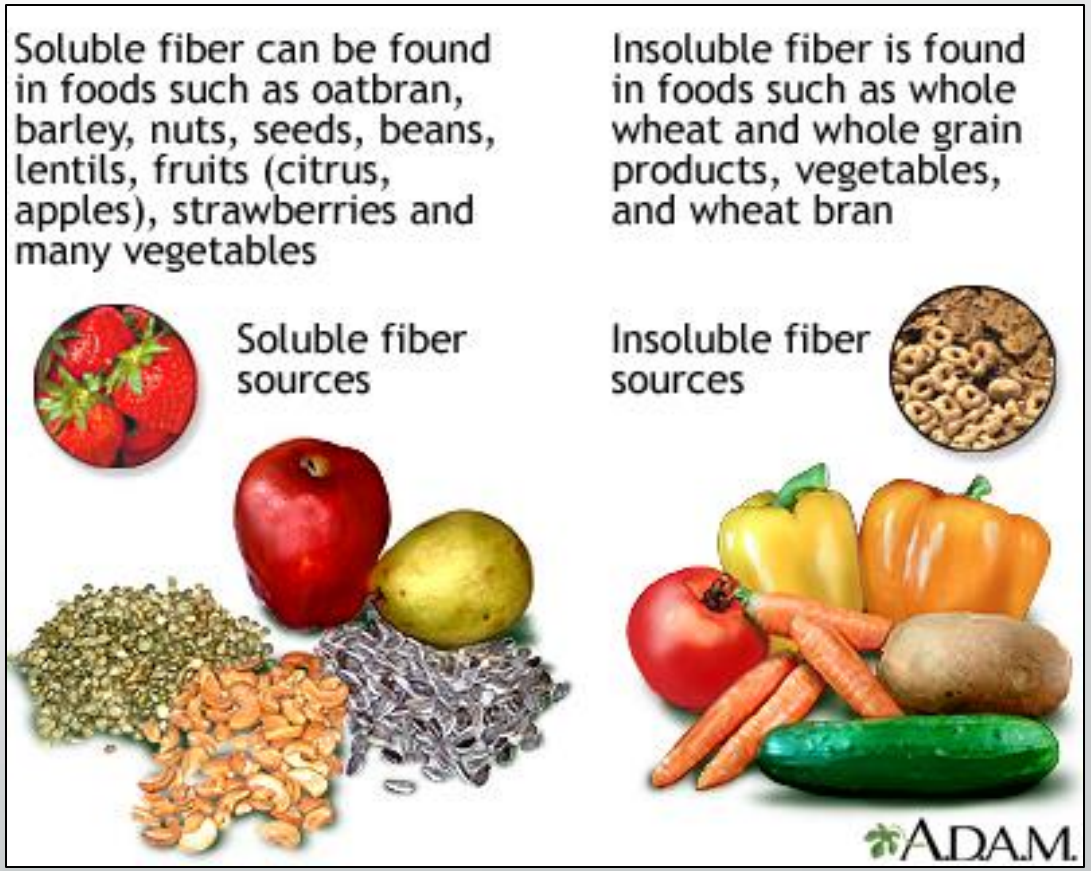
B. Loperamide

C. Rifaximin

D. Eluxadoline

Fiber supplementation

- Can be beneficial for any IBS sub-types
- Less benefit if already eating high-fiber diet
  - Generally aim for 25-35 grams total fiber intake
- Increased bloating and gas with initiation of treatment
  - Start low dose, titrate to effect



https://medlineplus.gov

Diet

- Traditional IBS diet
  - Regular meal pattern
  - Avoid large meals
  - Reduce intake of fat, spicy foods, caffeine, alcohol
  - Reduce gas-producing foods such as beans, cabbage onions
  - Lactose elimination
- Low FODMAP diet
  - Can use if no response to more traditional dietary recommendations
  - 4-6 week elimination period followed by gradual reintroduction of foods

Low FODMAP diet

High FODMAP Foods

Vegetables
Artichoke, asparagus, cauliflower, garlic, green peas, mushrooms, onion, sugar snap peas

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

Dairy & alternatives
Milk, ice cream, soy milk (made from whole soybeans), sweetened condensed milk, yogurt

Protein sources
Legumes, some marinated meats/ poultry/seafood, some processed meats

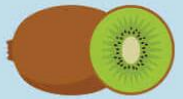
Breads & cereals
Wheat/rye/barley based breads, breakfast cereals, biscuits and snack products

Sugars & sweeteners
High fructose corn syrup, honey, sugar free confectionery

Nuts & seeds
Cashews, pistachios

Low FODMAP Alternatives

Vegetables
Eggplant, green beans, bok choy, bell pepper, carrots, cucumber, lettuce, potato, tomato, zucchini



Fruits
Cantaloupe, grapes, kiwi fruit, mandarin, orange, pineapple, strawberries

Dairy & alternatives
Almond milk, brie/camembert cheese, feta cheese, hard cheeses, lactose-free milk, soy milk (made from soy protein)

Protein sources
Eggs, firm tofu, meats/poultry/seafood (marinated in lemon juice with olive oil, black pepper or Italian herbs), tempeh

Breads & cereals
Corn flakes, oats, rice cakes (plain), sourdough spelt bread, wheat/rye/ barley free breads

Sugars & sweeteners
Dark chocolate, maple syrup, rice malt syrup, table sugar

Nuts & seeds
Macadamias, peanuts, pumpkin seeds, walnuts

Tips for dietary management

- Short-term trials only
  - Discontinue if no symptom improvement
- Use with caution if:
  - At risk for malnutrition
  - At risk for or diagnosed with an eating disorder
  - Food insecure
  - Poorly controlled psychiatric disorder
- Refer to registered dietician or provide high-quality resources
  - www.monashfodmap.com

https://gastro.org/clinical-guidance/the-role-of-diet-in-irritable-bowel-syndrome-ibs/

Pharmacologic management – IBS-C

	Polyethylene glycol	Dicyclomine, hyoscyamine, peppermint oil	Lubiprostone	Linaclotide, plecanatide	Tenapanor
Mechanism of action	- Osmotic laxative	- Gut smooth muscle relaxant	- Chloride channel activator	- Guanylate cyclase C receptor agonist	- Inhibits Na-H exchanger in small and large intestine
Dosage	- Initial 17 gm daily	-Dicyclomine 10-20 mg q6 hrs prn -Hyoscyamine 0.125-0.25 mg q4 hrs prn - Peppermint - unclear	- 8 mcg BID for IBS - 24 mcg BID for CIC	-Linaclotide 72, 145, or 290 mcg daily -Plecanatide 3 mg daily	50 mg BID
Precautions	- Diarrhea - Effect on abdominal pain unclear	- Most beneficial for abdominal pain	- Diarrhea	- Diarrhea	- Diarrhea

Pharmacologic management – IBS-D

	Loperamide	Dicyclomine, hyoscyamine	Bile acid sequestrants	Rifaximin	Alosetron	Eluxadoline
Mechanism	- Peripheral mu-opioid agonist - Prolong transit time	- Gut smooth muscle relaxant	- Inhibit bile acid-induced colonic secretion and motility	- Non-absorbable antibiotic	- 5-HT3 receptor antagonist - Decreases colonic motility and secretion	- Mixed mu-opioid receptor agonist and delta-opioid receptor antagonist
Dosage	- 2-16 mg/day	-Dicyclomine 10-20 mg q6 hrs prn -Hyoscyamine 0.125-0.25 mg q4 hrs prn	- As tolerated	550 mg TID x 14 days	0.5-1 mg BID	75-100 mg BID
Precautions and side effects	- Constipation	- Most beneficial for abdominal pain	- Side effects of constipation, bloating, flatulence	- Small degree of benefit - Need for retreatment	- Use only for severe IBS-D - Side effects – severe constipation, ischemic colitis	- Pancreatitis - Contraindicated in patients without a gallbladder or with >3 drinks/day

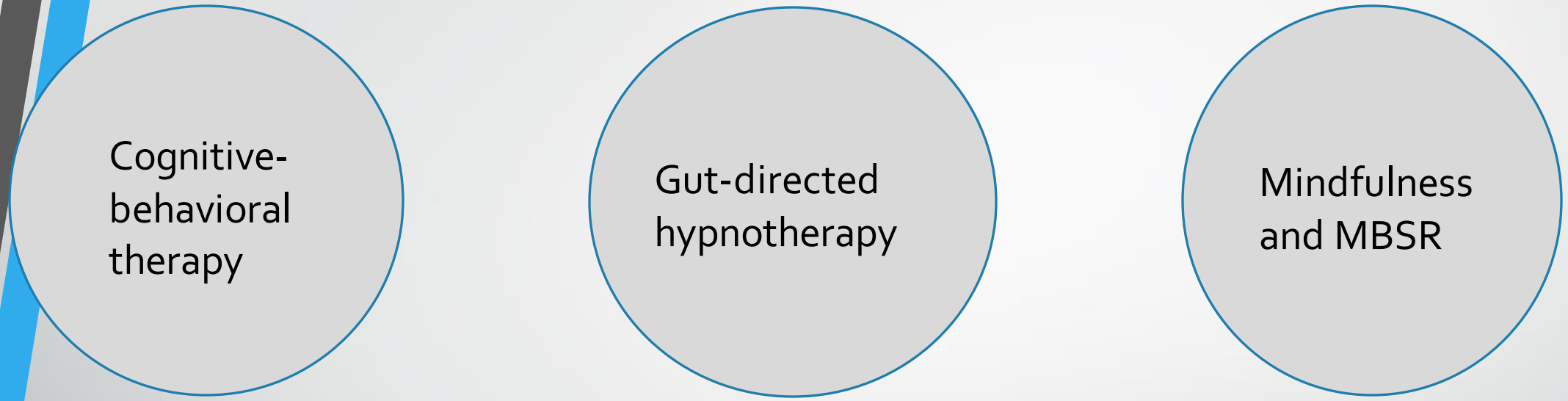
Neuromodulators

	Tricyclic antidepressants	**SSRIs**	**SNRIs**
Mechanism of action	- Effect on gut-brain interactions, altering motility, secretion, and sensation	- Centrally-mediated effects, increasing gastric and intestinal motility - No significant effect on visceral sensation	- Centrally mediated effects on motility - Unclear effect on visceral sensation
Benefits	- Independent of effects on depression - Often use lower doses - May take several weeks	- Likely minimal benefit	- Clinical evidence lacking
Precautions	- Side effects - Dose titration - Constipation	- Side effects - Can consider if coexisting anxiety or depression	- Side effects - Can consider if coexisting anxiety or depression

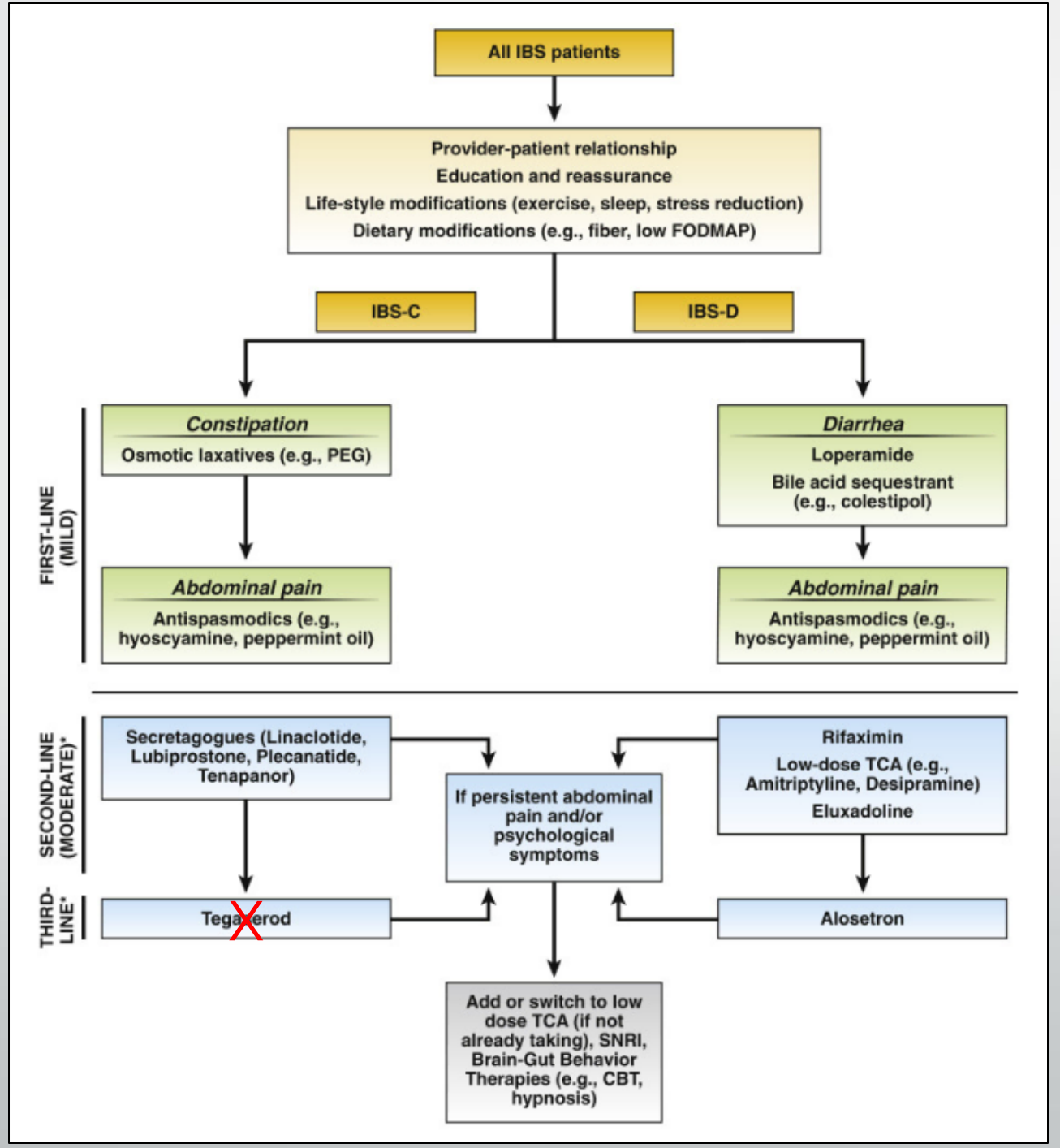
No evidence of benefit

- Prebiotics
- Probiotics
- Fecal microbiota transplantation

Brain-gut behavioral therapy

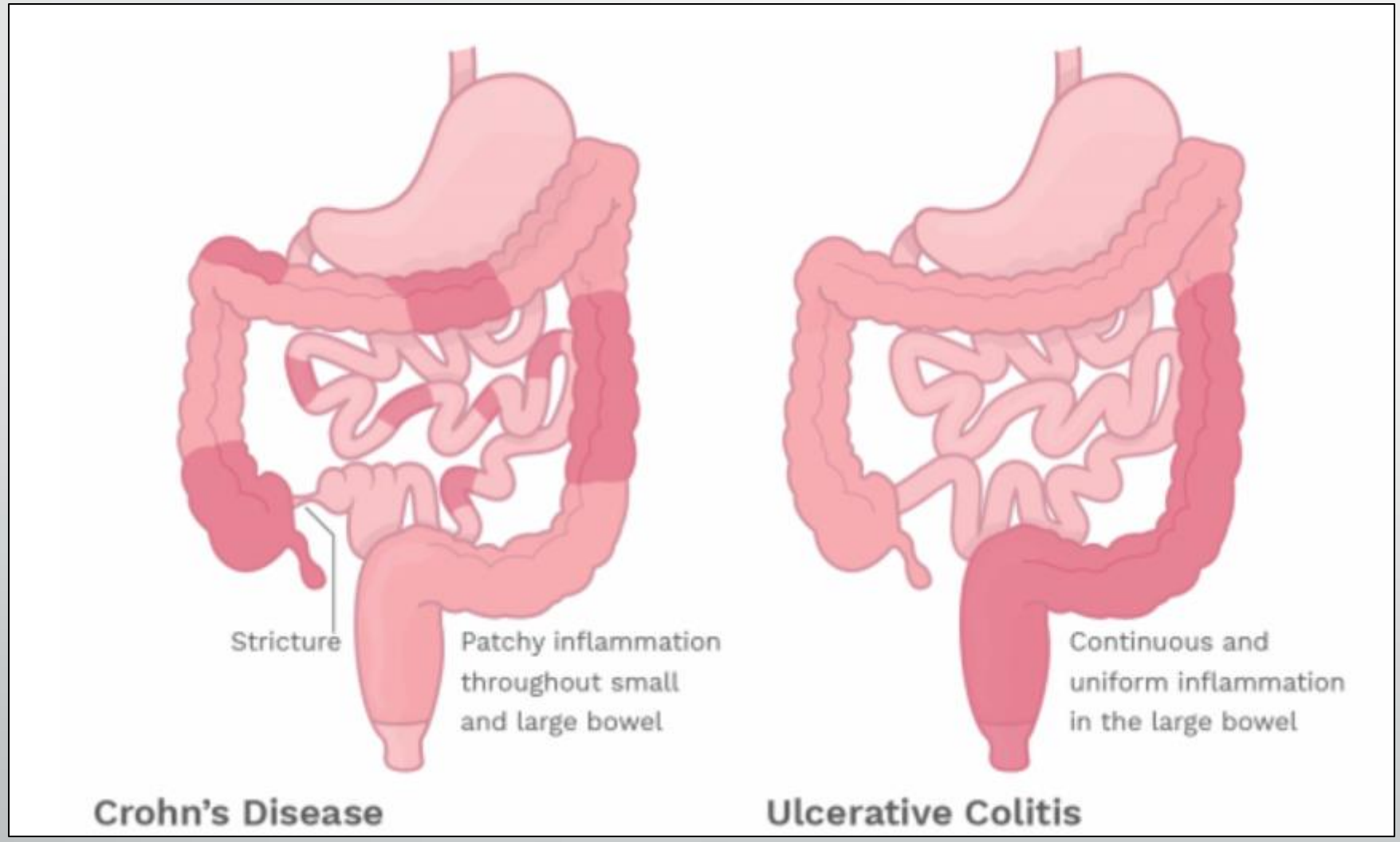


- Low risk
- Applicable to all IBS-subtypes
- Most useful if cognitive-affective drivers of IBS symptoms
- Prescription smart-phone apps available



https://gastro.org/clinical-guidance/pharmacological-management-of-irritable-bowel-syndrome-with-constipation-ibs-c/

Inflammatory bowel disease



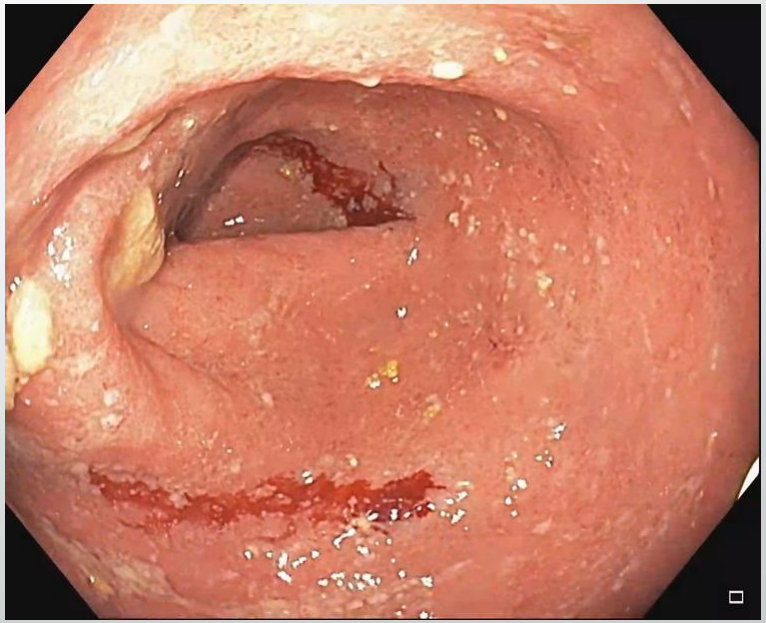
crohnscolitisfoundation.org

Case presentation

- 30yo male presents with lower abdominal pain, diarrhea 10 times per day, and rectal bleeding x 4 months. He has anorexia, fatigue, and a 15 pound weight loss.
- PMH – sacroiliitis
- Medications – ibuprofen
- Labs- ESR 40, CRP 25, Hgb 10.1

Epidemiology of IBD

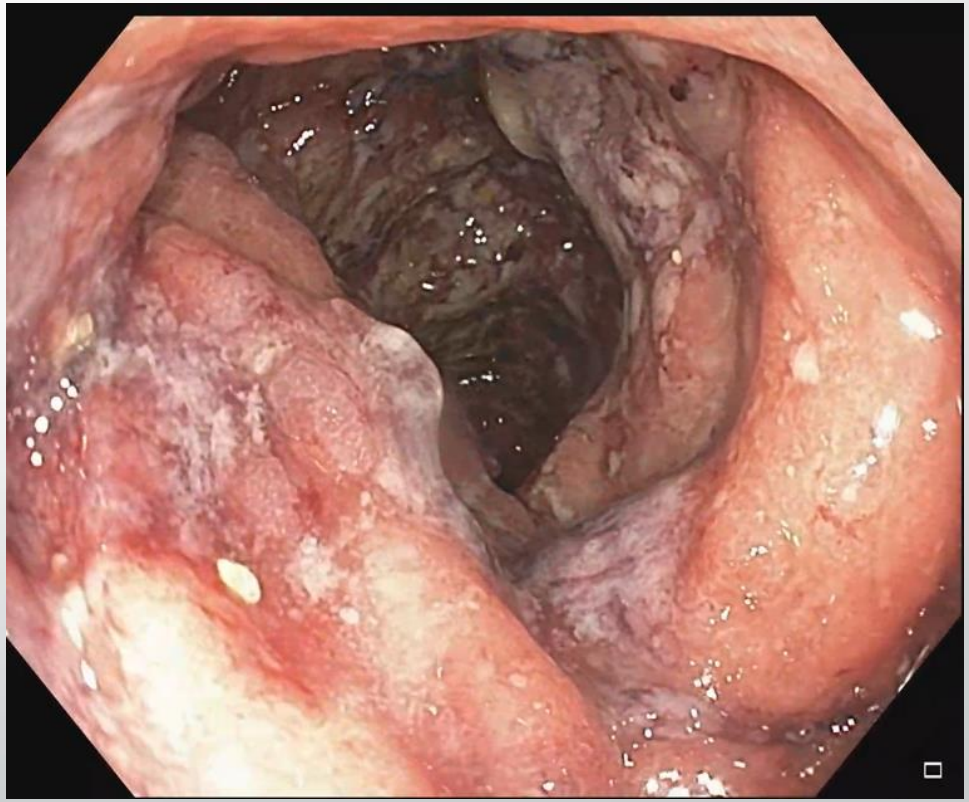
- Two peaks of onset: age 15-35, age 55-70
- M = F
- Prevalence in U.S. ~1%
- Familial clustering



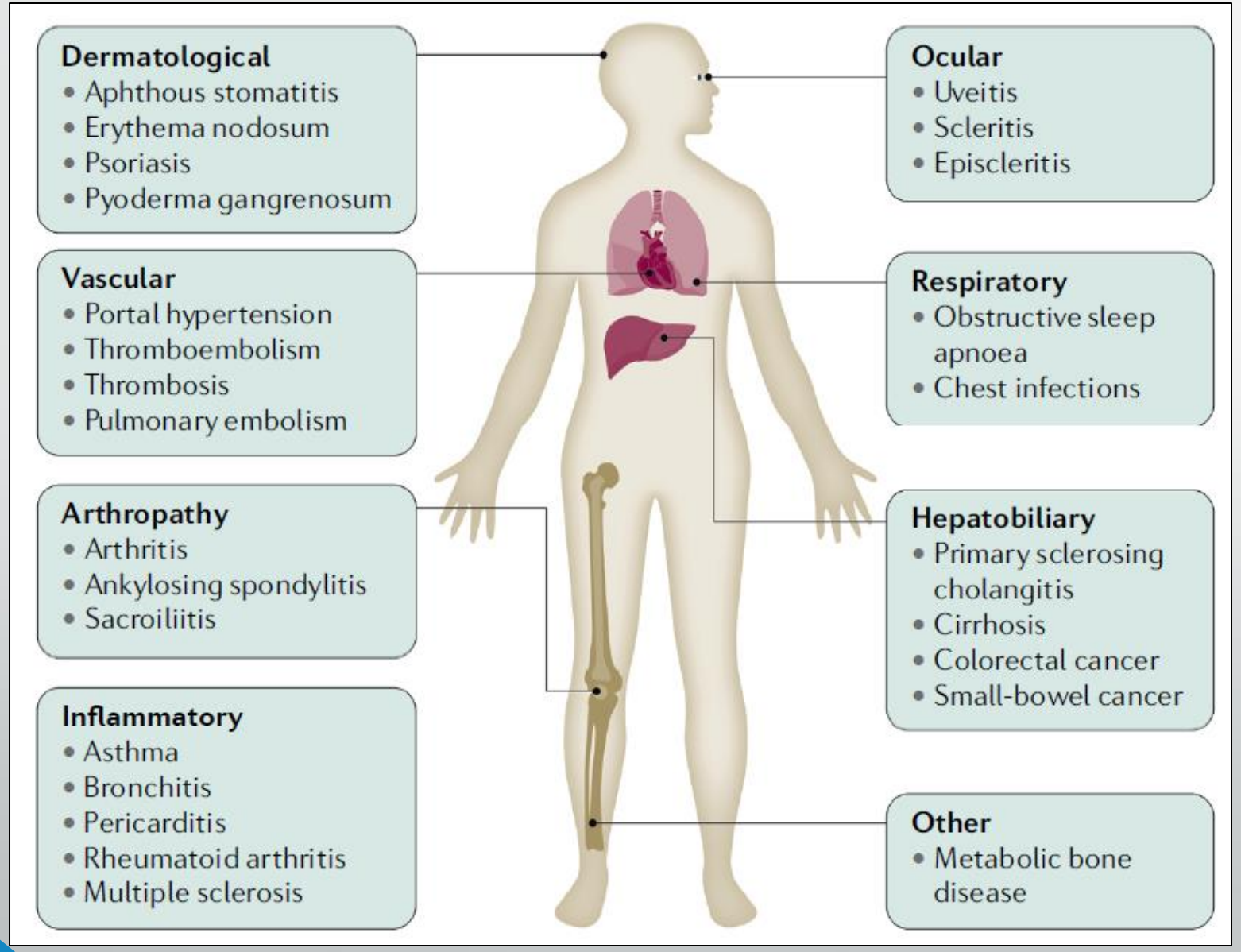
Symptoms

- Abdominal pain
- Diarrhea
- GI bleeding
- Fatigue

- Fever
- Weight loss
- Malnutrition



Extraintestinal manifestations of IBD



Nature Rev Dis Primers 2020; 6:22

Which of the following is an appropriate step for his evaluation?

A. No further work-up needed

B. Enteric pathogen panel

C. Upper endoscopy

D. Colonoscopy

E. CT abdomen/pelvis

Diagnosis

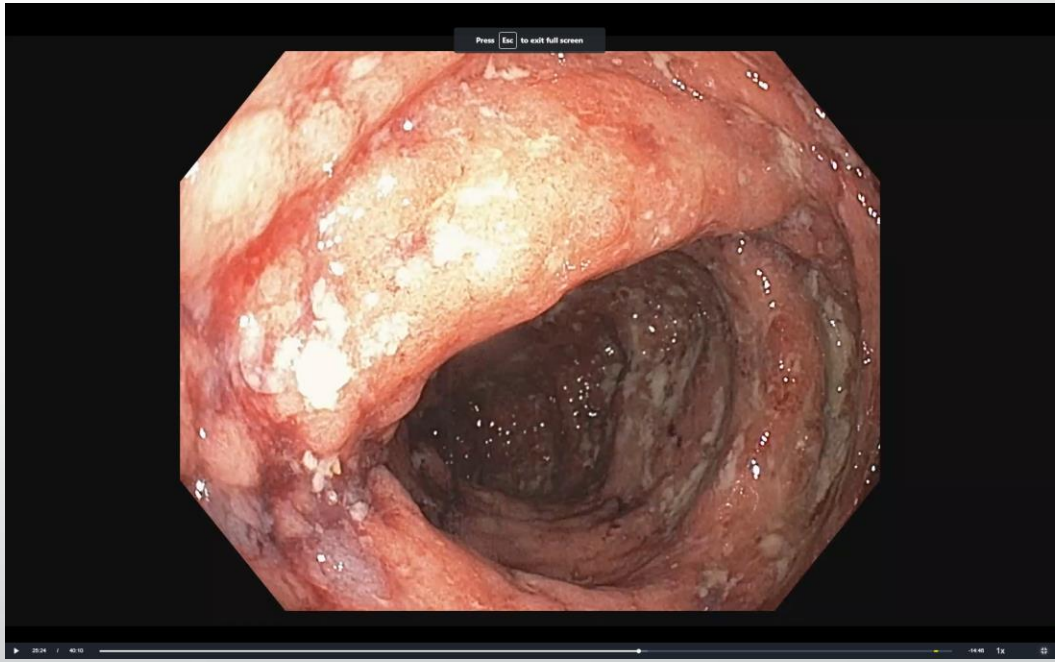
- Suspect if diarrhea with rectal bleeding, abdominal pain, weight loss
- Consider screening with fecal calprotectin
- Colonoscopy
  - +/- EGD if suspected Crohn's
- If findings suspicious for Crohn’s, consider:
  - Small bowel capsule endoscopy – increased risk of small bowel obstruction
  - CT or MR enterography

Colonoscopy

Diffuse, circumferential inflammation starting in the rectum and extending to the transverse colon

Normal right colon and terminal ileum

Consistent with extensive ulcerative colitis



What is an appropriate initial management strategy?

A. Mesalamine suppository

B. Mesalamine enema

C. Azathioprine

D. Prednisone

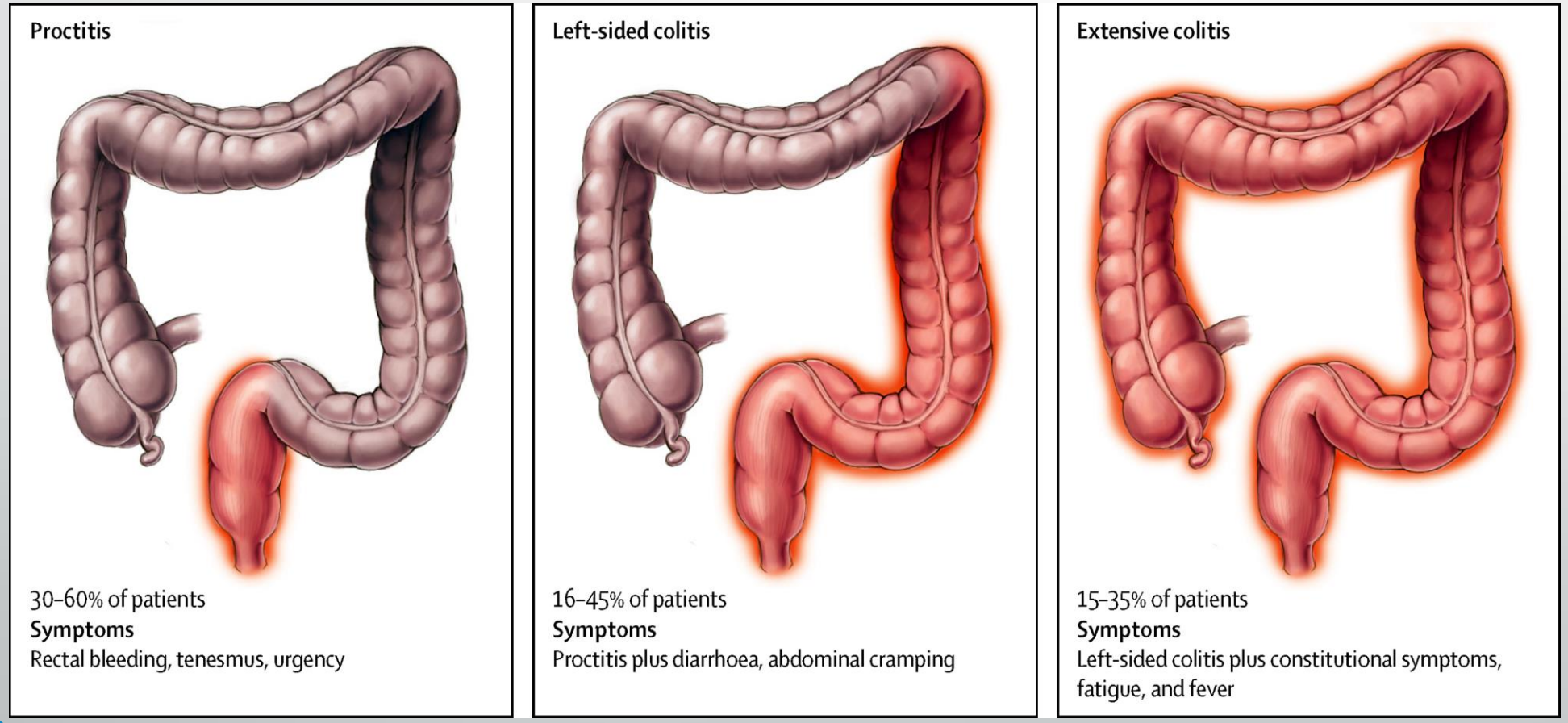
Goals of therapy

- Clinical remission
- Endoscopic remission
- Avoidance of repeated or long-term steroid exposure
- Avoidance of disease and therapy-related complications

Ulcerative colitis - severity

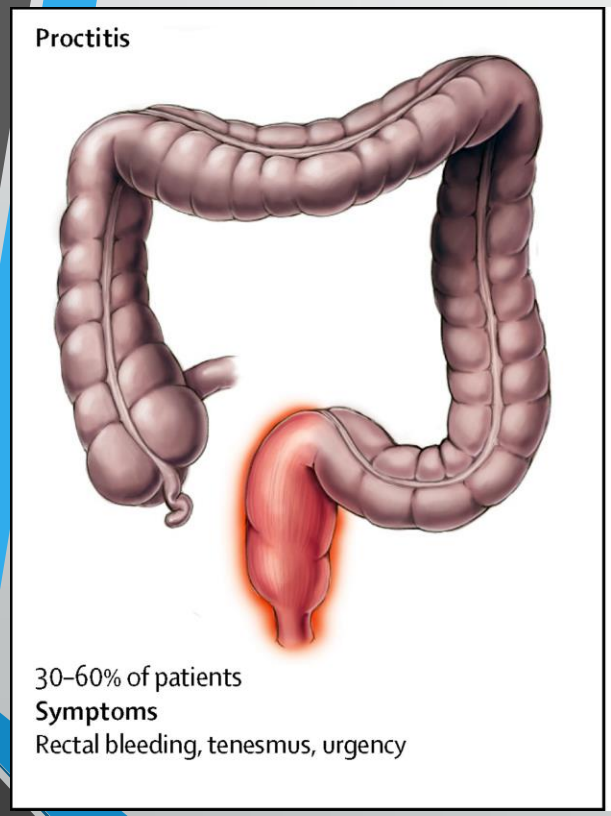
	Mild	**Moderate**	**Severe**
BMs/day	<4	4-6	>6
Rectal bleeding	None or small amounts	Yes	Severe, anemia
Systemic toxicity	None	Mild	Yes
Weight	Maintained	Maintained	Weight loss, malnutrition

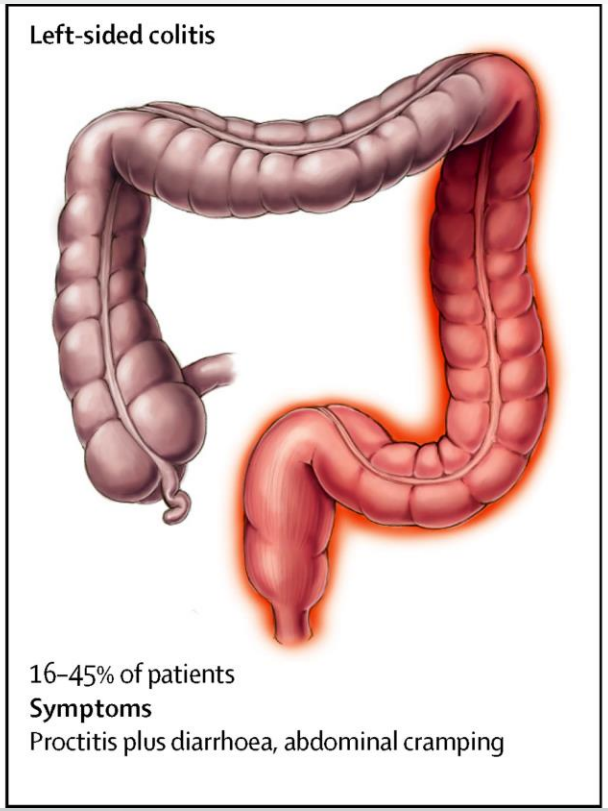
Disease extent - ulcerative colitis



Lancet 2016 389:1756-1770

Mild-moderate proctitis or limited left-sided colitis





Induction of remission

First-line:

- Topical mesalamine (suppository or enema)

Second-line:

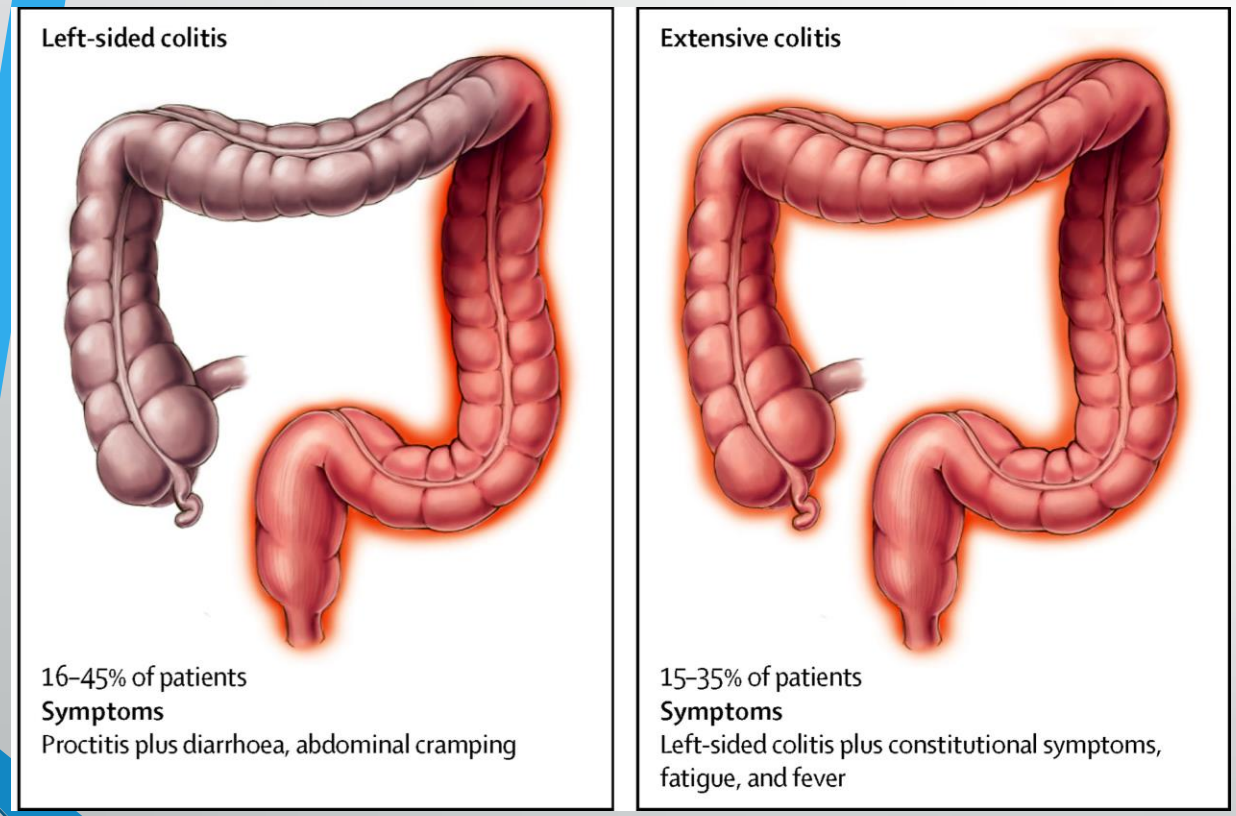
- Oral mesalamine
- Topical glucocorticoids (suppository, foam, or enema)

Maintenance therapy if:

- Involvement above the rectum
- Proctitis with frequent flares

Lancet 2016 389:1756-1770

Mild-moderate left-sided or extensive UC



Induction of remission
First-line therapy:
Oral +/- topical mesalamine

If no or inadequate response:
- Budesonide
- Prednisone

Maintenance of remission
- Taper off steroids (if used)
- Continue mesalamine

Lancet 2016 389:1756-1770

Moderate-to-severe UC

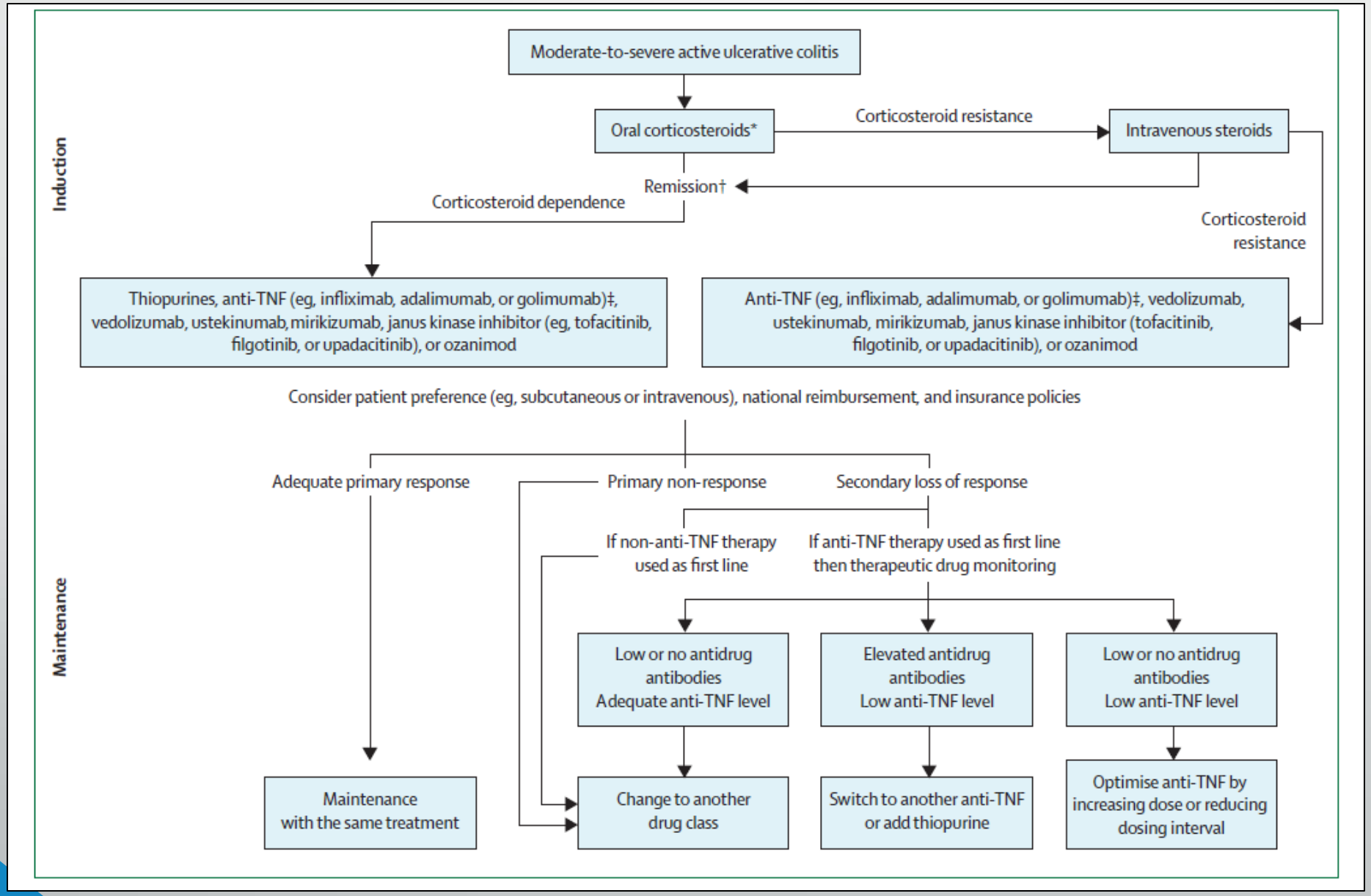
- More intensive therapy needed if:
  - Moderate-severe symptoms
  - Inadequate response or relapse for patients with mild-moderate symptoms
- Goal of therapy: steroid-free clinical and endoscopic remission
- Multiple options depending on patient characteristics, preferences, and cost

Lancet 2016 389:1756-1770

Immunosuppressive therapies for UC

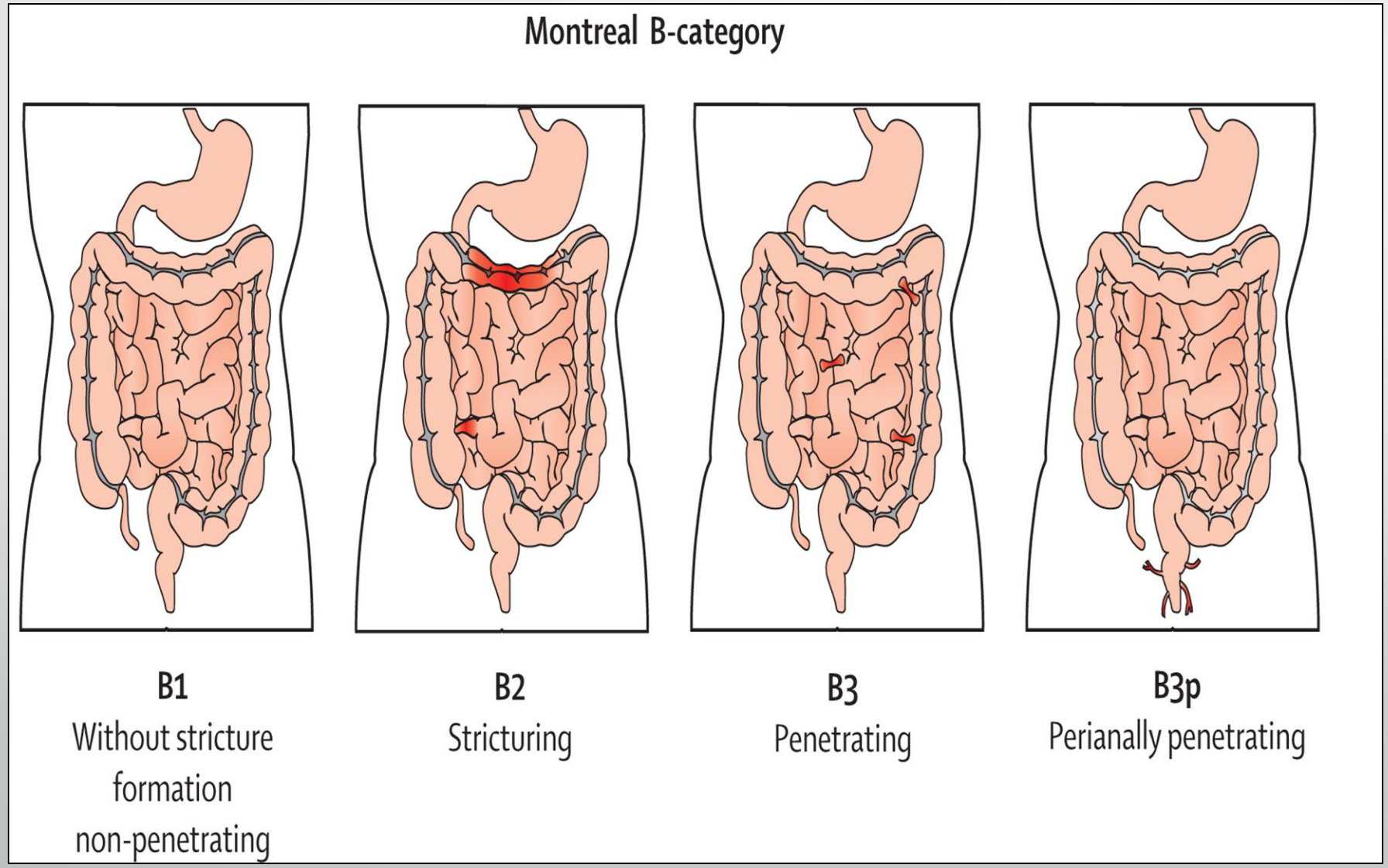
Biologics		Small molecules	
TNF inhibitors	Infliximab Adalimumab Certolizumab Golimumab	Glucocorticoids	Prednisone Budesonide
Anti-$\alpha 4 B7$ integrin	Vedolizumab	Immunomodulator	Azathioprine/6-MP Methotrexate
Anti-IL 12/23 antibody	Ustekinumab	JAK inhibitor	Tofacitinib Upadacitinib
		Sphingosine-1-phosphate receptor modulator	Ozanimod Etrasimod

Moderate-severe UC



Lancet 2023 402:571-84

Crohn's disease



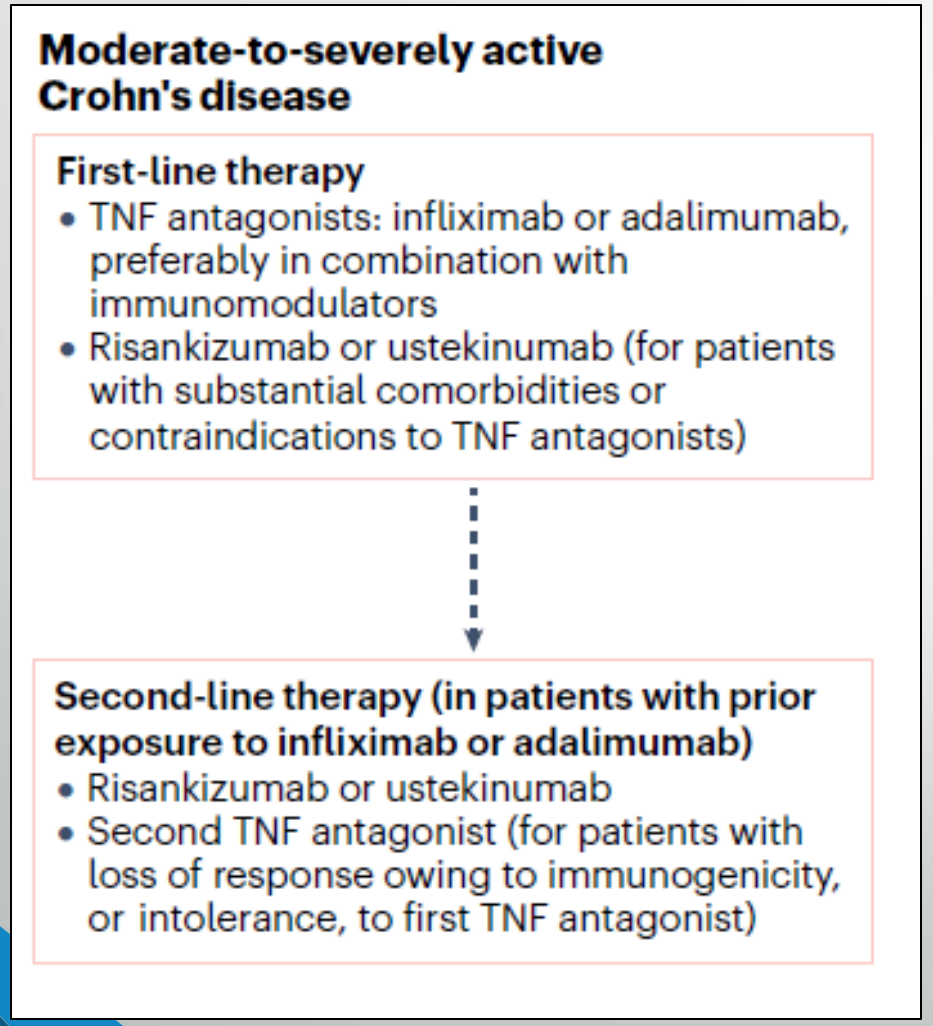
Lancet 2012; 3801590-1605

Therapy for Crohn's

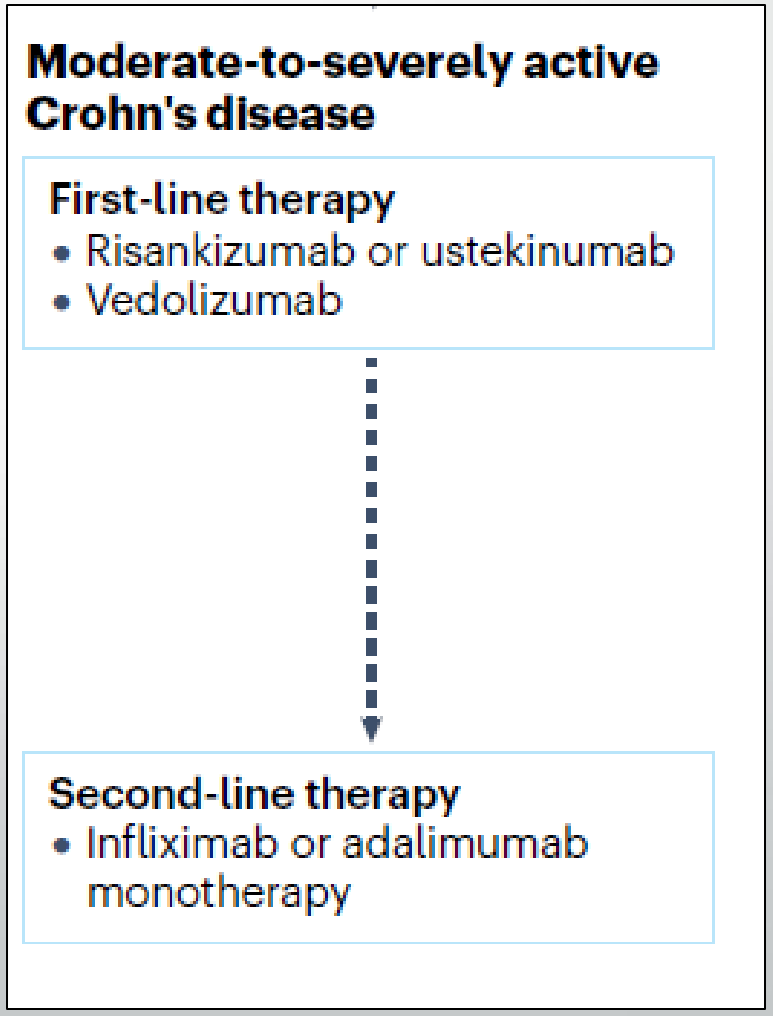
Biologics		Small molecules	
TNF inhibitors	Infliximab Adalimumab Certolizumab Golimumab	Glucocorticoids	Prednisone Budesonide
Anti-$\alpha 4\beta 7$ integrin	Vedolizumab	Immunomodulator	Azathioprine/6-MP Methotrexate
Anti-IL 12/23 antibody	Ustekinumab	JAK inhibitor	Upadacitinib
Anti-IL 23	Risankizumab		

Moderate-to-severe Crohn's

High risk of disease complications

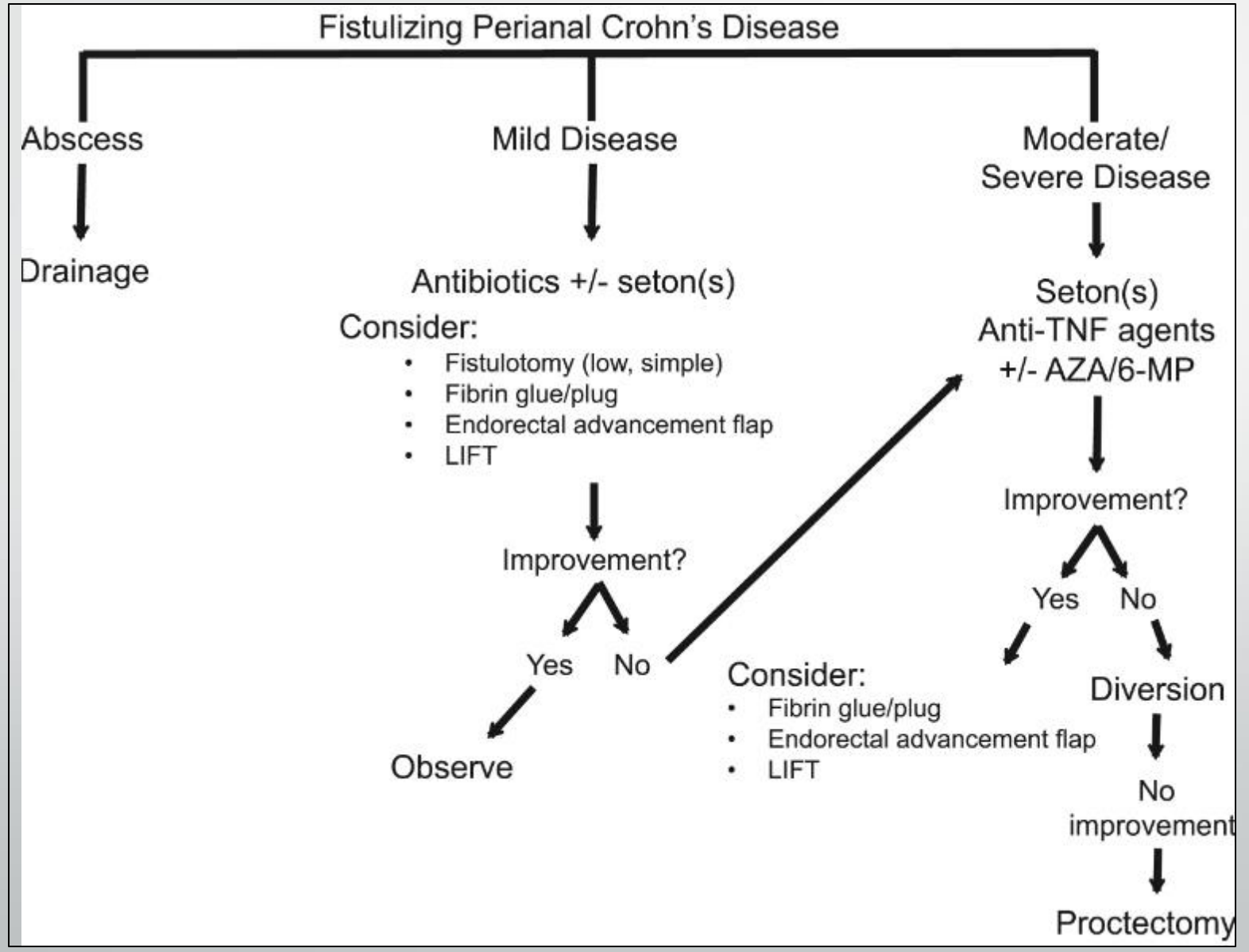


High risk of treatment complications



Nat Rev Gastroenterol Hepatol 2023; 20:411-12

Perianal fistulas



American Surgeon 2021; 87:1361-7

Health maintenance - vaccination

☐	COVID-19 vaccine (Moderna, Pfizer, Novavax)	All patients with IBD.
☐	Influenza, Fluzone High Dose, Flublok recombinant, Fluad adjuvanted	All adult patients with IBD should receive a standard dose. Those on Anti-TNF monotherapy should receive a high dose influenza vaccine.[1] Older Adults aged ≥65 should receive the high dose, recombinant or adjuvanted inactive influenza vaccine.[2]
☐	Pneumococcus (PCV 15, PCV 20 or PPSV23)	All patients ≥19 years age receiving systemic immunosuppression.*
☐	Recombinant Herpes Zoster (RZV) (adjuvanted- non-live) SHINGRIX	All patients with IBD ≥19 years of age.[3]

☐	Human Papilloma Virus (HPV) 9valent GARDASIL	All Adults 18–26. Adults 26-45* shared decision who are likely to have a new sexual partner.
☐	Hepatitis B Heplisav® Engerix® or Recombivax®:	All adult patients with IBD. Universal vaccination is recommended for all adults 19–59.[4]
☐	Measles, Mumps, and Rubella (MMR) two-dose live vaccine	Patients with IBD not immune to MMR. If immune status is uncertain, obtain immunization history. IgG antibody titer can be checked but not recommend by ACIP. MMR live vaccine should not be given to patients currently on systemic immunosuppressive therapy.[5]
☐	Varicella two-dose live vaccine	Documentation of two doses or varicella vaccine. Serology not recommended by ACIP for evaluation of vaccine induced immunity in those with appropriate documentation.[6]

https://www.crohnscolitisfoundation.org

Health maintenance – cancer screening

Cancer Screening	Which Patients	How Often
☐ Colorectal	All IBD patients with extensive colitis (>1/3 of the colon) for ≥8 years should undergo surveillance colonoscopy every 1–3 years, depending on cancer risk.	Patients with IBD with a diagnosis of PSC should undergo colonoscopy, starting at the time of PSC diagnosis, and annually thereafter. Patients with IBD with features that are high-risk for developing colon cancer (i.e. prior history of adenomatous polyps, dysplasia, family history of colon cancer and extensive colitis) should have colonoscopies more frequently than every 3 years.
☐ Cervical	All women with IBD who are being treated with systemic immunosuppression.*	Should undergo cervical cancer by cytology annually (if cytology alone) or every 3 years (if HPV negative).[7]
☐ Skin	All IBD patients being treated with systemic immunosuppression.*	Should have annual total body skin exams to screen for skin cancer.

https://www.crohnscolitisfoundation.org

Health maintenance - other

Other Screenings	Which Patients	How Often
☐ Mental Health	All	Annual; Depression (PHQ2) and anxiety (GAD7) at baseline, and then annually. Refer for counseling/ therapy when identified.
☐ Osteoporosis	All	Screen for osteoporosis by central (hip and spine) DXA scan in all patients with IBD if ANY risk factors for osteoporosis; low BMI, >3 months cumulative steroid exposure, smoker, post-menopausal, hypo-gonadism. Repeat in 5 years and no sooner than 2 years[1] if initial screen is normal. Vitamin D (800-1000 IU per day) and calcium (1200 mg/day) for Women >65 yo, male > 70 yo (regardless of clinical risk factors).
☐ Smoking	All	Refer current smokers for smoking cessation therapy.
☐ Latent infections Hepatitis B and tuberculosis	Patients with IBD starting on anti-TNF therapy.	Evaluate prior to starting anti-TNF therapy.
☐ Nutritional deficiencies	Patients with IBD annually.	Ferritin, Transferrin %, Vitamin D, Vitamin B12, and Vitamin B6.

https://www.crohnscolitisfoundation.org

Summary- IBD

- Colonoscopy is indicated for suspected IBD
- Treatment goal - clinical and endoscopic remission
- Avoid repeated or long-term steroid courses
- Biologic and small molecule therapies are evolving with improving safety profiles
- Multiple domains of health maintenance to consider