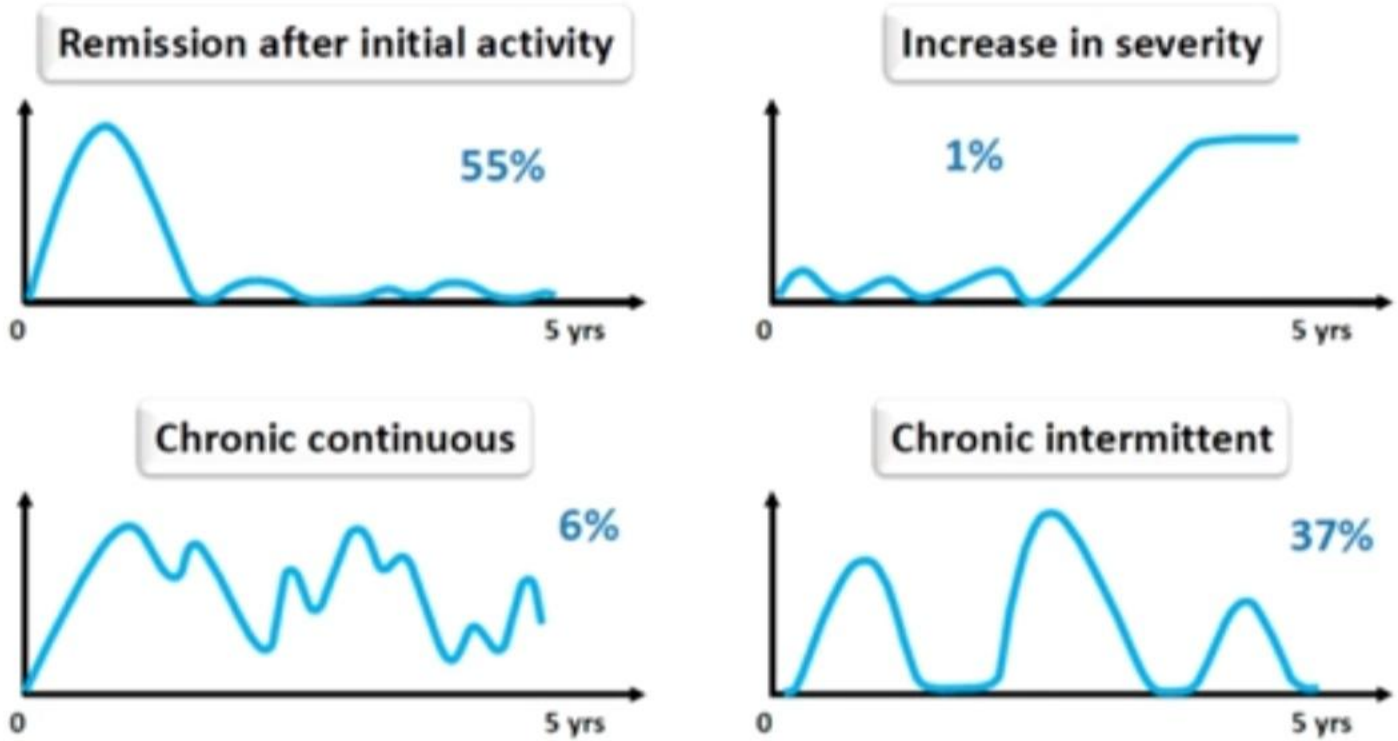
Management of Mild to Moderate Ulcerative Colitis

Shabnam Shahrokh, M.D

Shahid Beheshti medical university

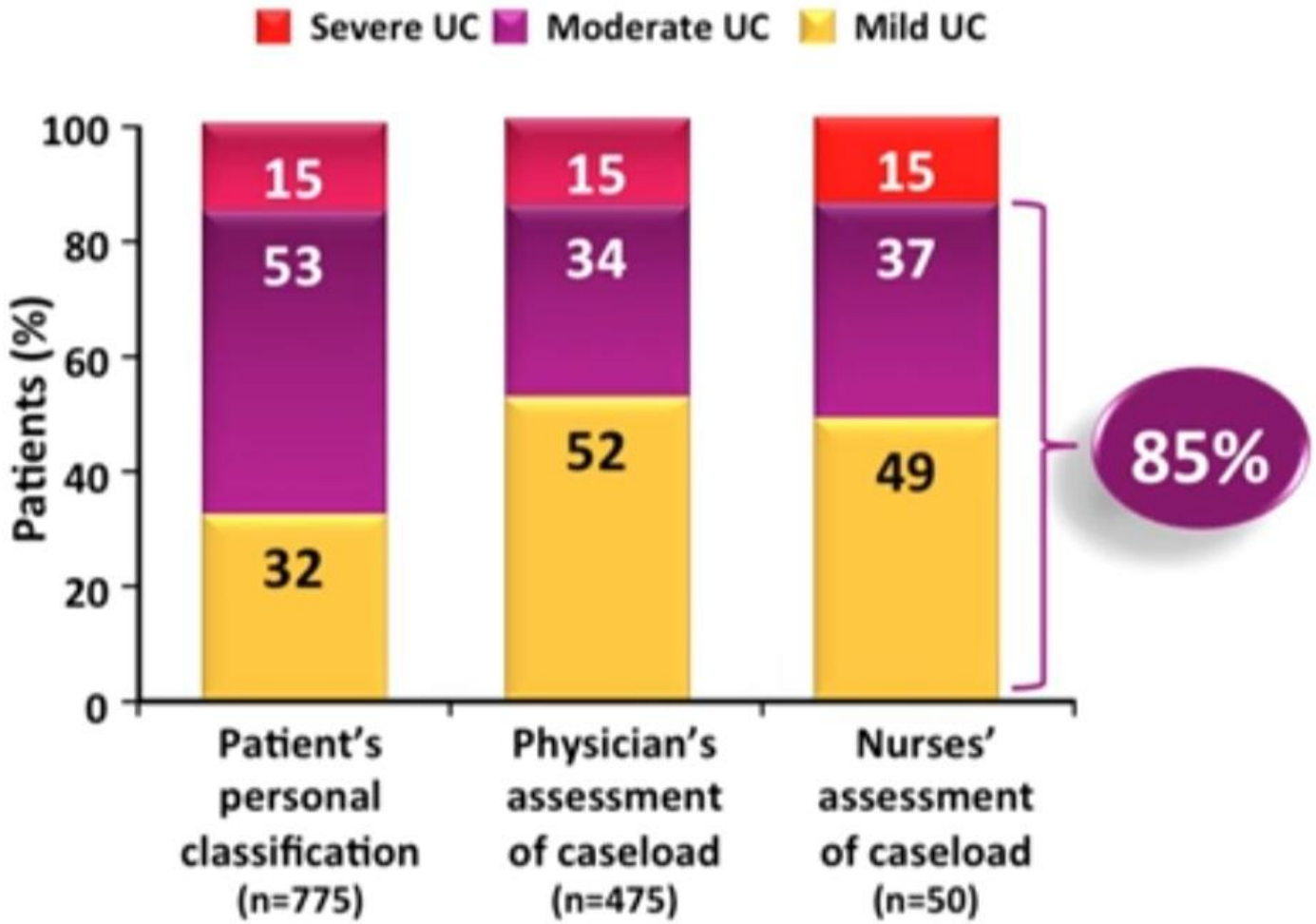
Disease course in UC



Imperial College

Solberg *et al.* 2009 Scand J Gastroenterol 44(4):431-40

Majority of patients have mild to moderate UC



Schreiber S *et al. BMC Gastroenterol* 2012;12(1):108

	AGA Living Guideline (2024)	ACG Clinical Guideline (2025)[2]
Focus	Pharmacologic management for moderate-to-severe UC	Comprehensive management of UC (diagnosis, monitoring, prevention, induction and maintenance of remission, and hospitalized care)
Scope of Patients	Adults with moderate-to-severe UC	Adults with UC of ALL severities, including hospitalized patients
Methodology	GRADE methodology, uses PICO questions	GRADE framework with recommendations and KEY CONCEPTS
Therapies Covered	Immunomodulators, advanced therapies with detailed comparative efficacy discussion	Conventional therapies, advanced therapies, detailed comparative efficacy discussion
Update Cycle	Living guideline designed for continuous updates every 6 months	Planned periodic updates
	***Gastroenterology*. 2024;167(7):1307-1343.**	***Am J Gastroenterol*. 2025;120(6):1187-1224.**

EXPERT REVIEW OF GASTROENTEROLOGY & HEPATOLOGY
2024, VOL. 18, NO. 8, 421–430
https://doi.org/10.1080/17474124.2024.2397650

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REVIEW

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Practical management of mild-to-moderate ulcerative colitis: an international expert consensus

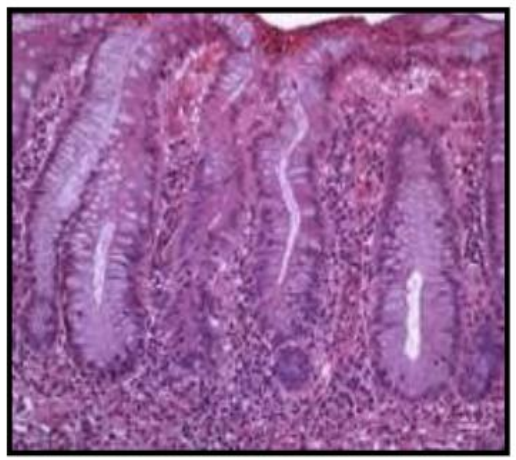
Ferdinando D'Amico[a], Fernando Magro[b], Axel Dignass[c], Sameer Al Awadhi[d], Ana Gutierrez Casbas[e,f], Natália Sousa Freitas Queiroz[g], Grażyna Rydzewska[h], Byong Duk Ye[i], Zhihua Ran[j], Ailsa Hart[k], Vipul Jairath[l], Gionata Fiorino [m], Laurent Peyrin-Biroulet[n,o,p,q,r,s] and Silvio Danese[a,t]

Diagnosis of UC

- Clinical suspicion
- Exclusion of infection
- Endoscopic assessment
- Histologic assessment showing chronicity
  - Histology of endoscopically normal mucosa
- Examination of terminal ileum
- Assessment of IC valve
- Upper GI not needed in adults unless other symptoms or unexplained findings



Endoscopically moderate colitis



Chronic inflammation with increase in plasma cells in the lamina propria and crypt architectural distortion

Images compliments David T. Rubin, MD

Am J Gastroenterol. 2025:120(6):1187-1224.

Updated Goals of Management of UC

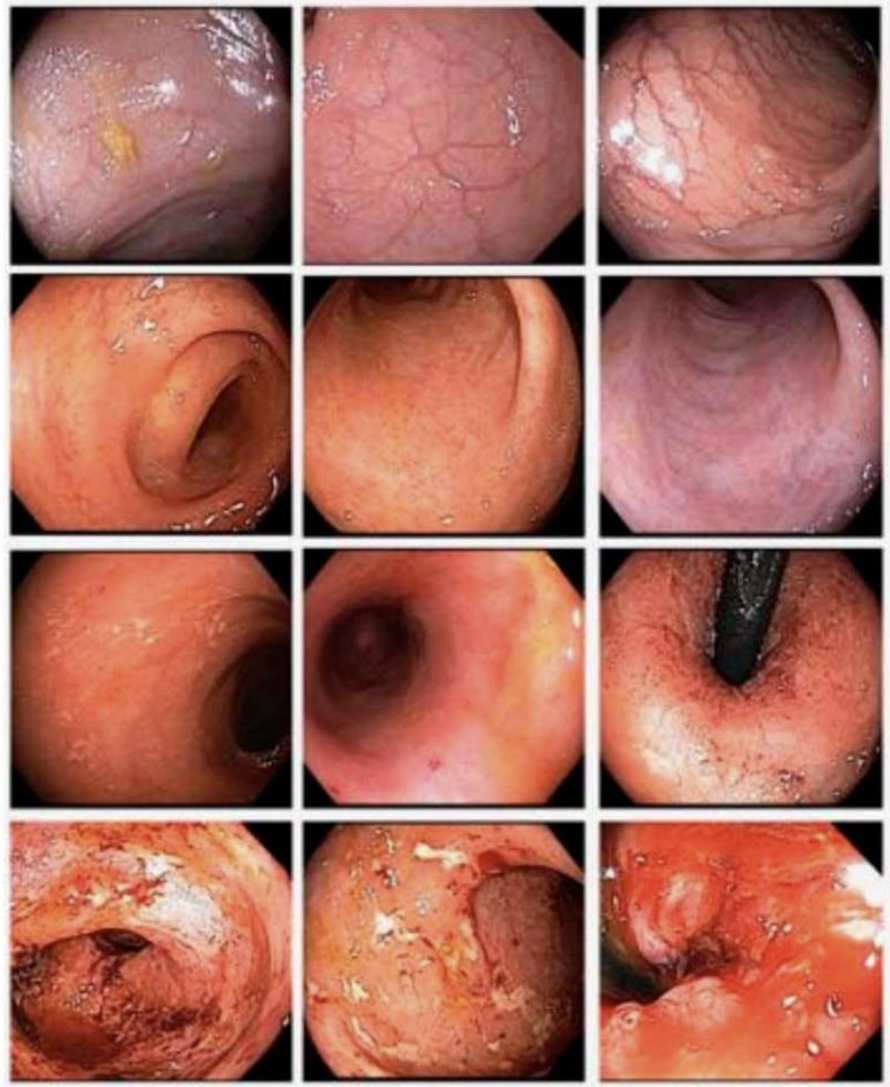
- Diagnosis including extent of disease and biopsy
- Movement to separate activity and severity
- Induction of clinical response/remission and mucosal healing
- Maintenance therapy identified based on induction therapy and prognosis
- Screen and treat for anxiety/depressive disorders
- Prevention of complications (cancer, hospitalization, infections, other drug-related)

Am J Gastroenterol. 2025;120(6):1187-1224.

Table 4. American College of Gastroenterology Ulcerative Colitis Activity Index (modified from Ref. 66)

	Remission	Mild	Moderate-severe	Fulminant
Stools (#/day)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
ESR	<30	<30	>30	>30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
Fecal calprotectin (μg/g)	<150–200	>150–200	>150–200	>150–200
Endoscopy (MES)	0–1	1	2–3	3
Endoscopy (UCEIS)	0–1	2–4	5–8	7–8
Intestinal ultrasound	Colonic BWT≤3 mm Rectal BWT ≤4 mm mLimberg = 0		Colonic BWT >3 mm Rectal BWT >4 mm mLimberg >0	

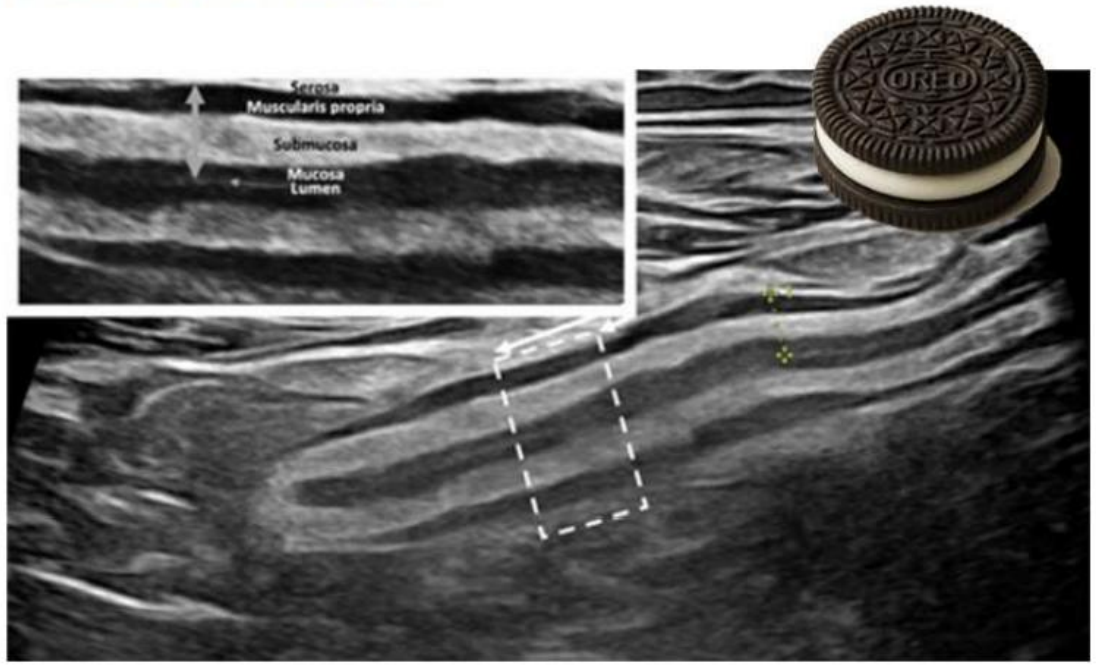
Endoscopic Assessment of Disease Activity

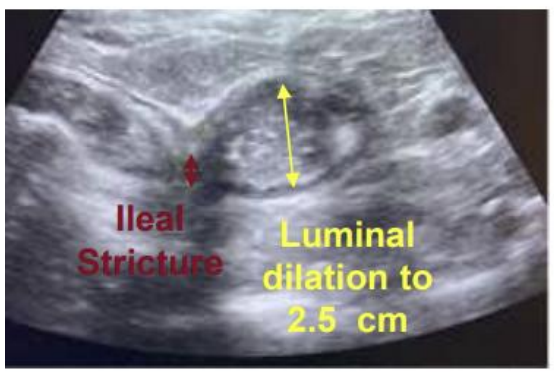


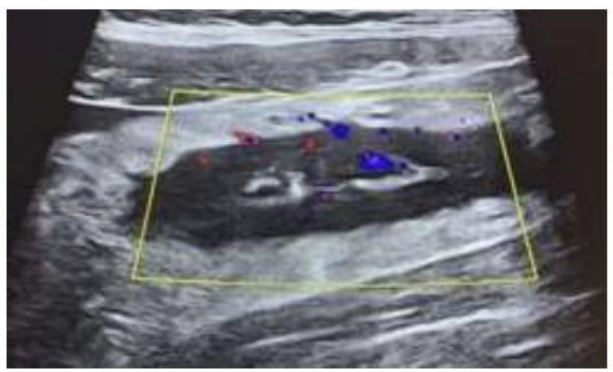
UCEIS Score	Mayo Score	Endoscopic Features
0	0	Normal
1-3	1	Erythema, decreased vascular pattern, mild friability
4-6	2	Marked erythema, absent vascular pattern, friability, erosions
7-8	3	Spontaneous bleeding, ulceration

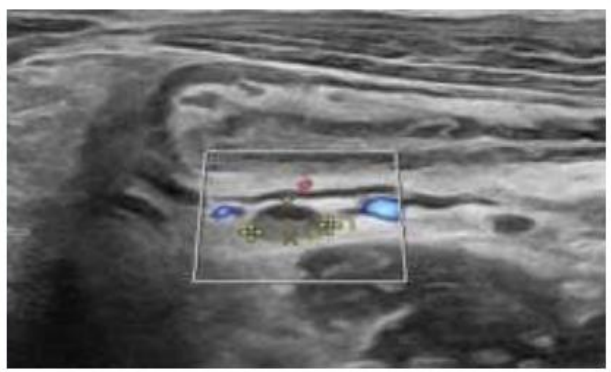
Standard Ultrasound Parameters

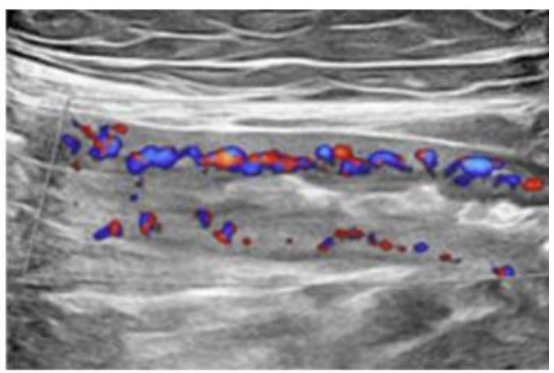
- Bowel wall thickness (normal ≤3 mm in TI and colon, ≤4 mm in rectum)
- Bowel wall hyperemia by color Doppler imaging
- Bowel wall layer stratification
- Presence of inflammatory/mesenteric fat
- Lymphadenopathy
- Complications (stricture, abscess, fistula)











IUS IN UC CORRELATES TO ENDOSCOPY

UC-IUS index

- EMS: r = 0.830; p <0.001
- UCEIS: r = 0.759; p <0.001
- Strong interobserver correlation of IUS scores ρ = 0.877

Parameters	Points [0–7]
Bowel wall thickness	
> 2 mm	1
> 3 mm	2
> 4 mm	3
Doppler signal	
Spots	1
Stretches	2
Abnormal haustrations	1
Fat wrapping	1

Milan Ultrasound Criteria

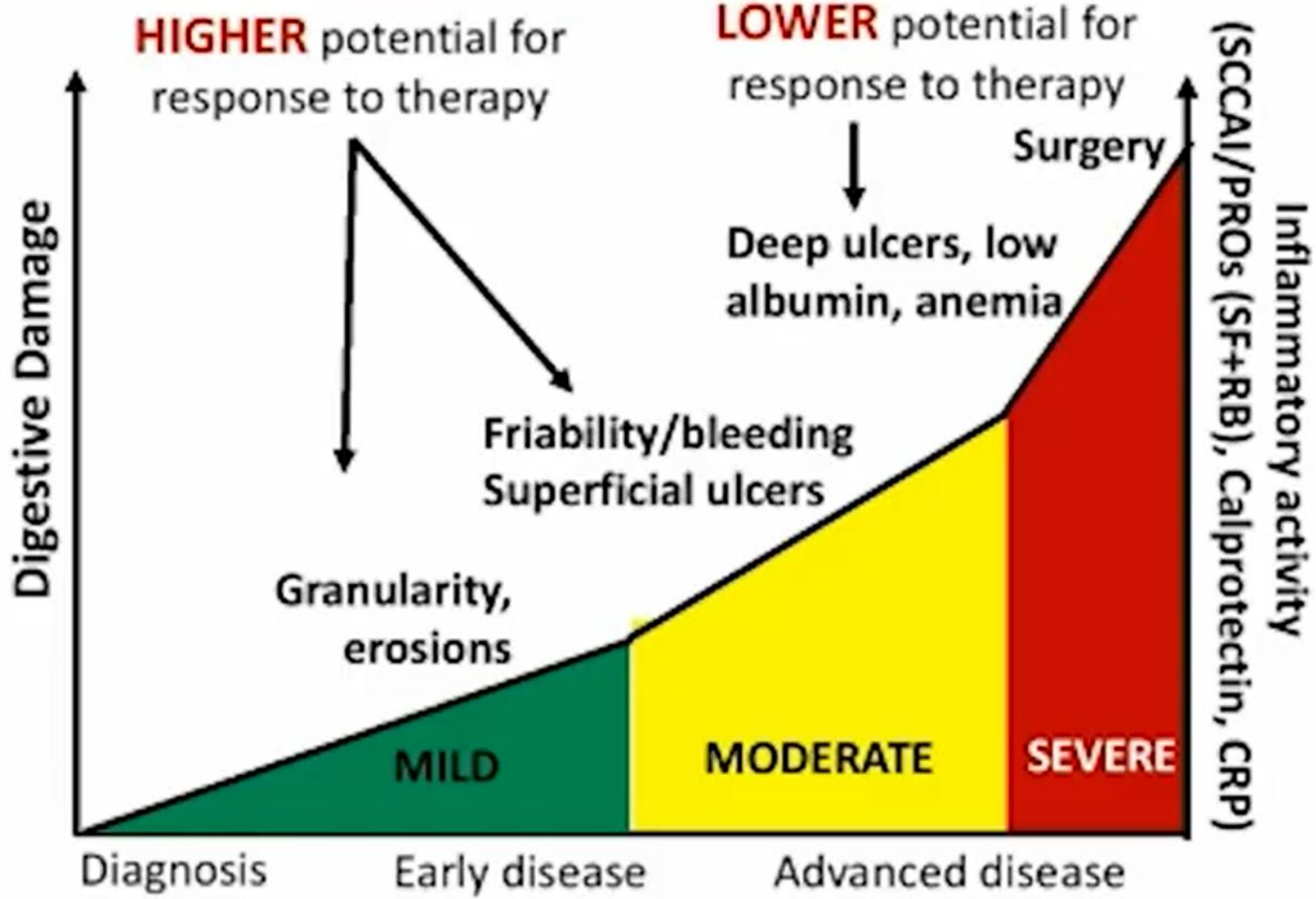
- EMS: ρ = 0.653; p <0.001
- Ultrasound remission: MUC >6.2 predicts endoscopic inflammation (Mayo endoscopic subscore >1)

MUC = 1.4 × BWT + 2 × BWF	
BWT	Bowel wall thickness in mm
BWF	Bowel wall flow (0 = absence; 1 = presence)

Bots S, et al. *J Crohns Colitis*. 2021;15(8):1264-1271.
Allocca M, et al. *United European Gastroenterol J*. 2022;10(2):190-197.

Defining UC disease **ACTIVITY** vs **SEVERITY**

Successful monitoring strategies begin with appropriate treatment selection at diagnosis



SCCAI: Simple Colitis Clinical Activity Index; PROs: patient reported outcomes, CRP: C-reactive protein

Assessment of Disease Risk "Severity" in UC

Ulcerative Colitis

Low Risk for Colectomy

- Limited anatomic extent
- Mild endoscopic disease

High Risk for Colectomy

- Extensive colitis
- Deep ulcers
- Age <40
- High CRP and ESR
- Steroid-requiring disease
- History of hospitalization
- *C. difficile* infection
- CMV infection

Rubin DT, et al. *Am J Gastroenterol.* 2025;120(6):1187-1224.
Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-45.

Other Considerations

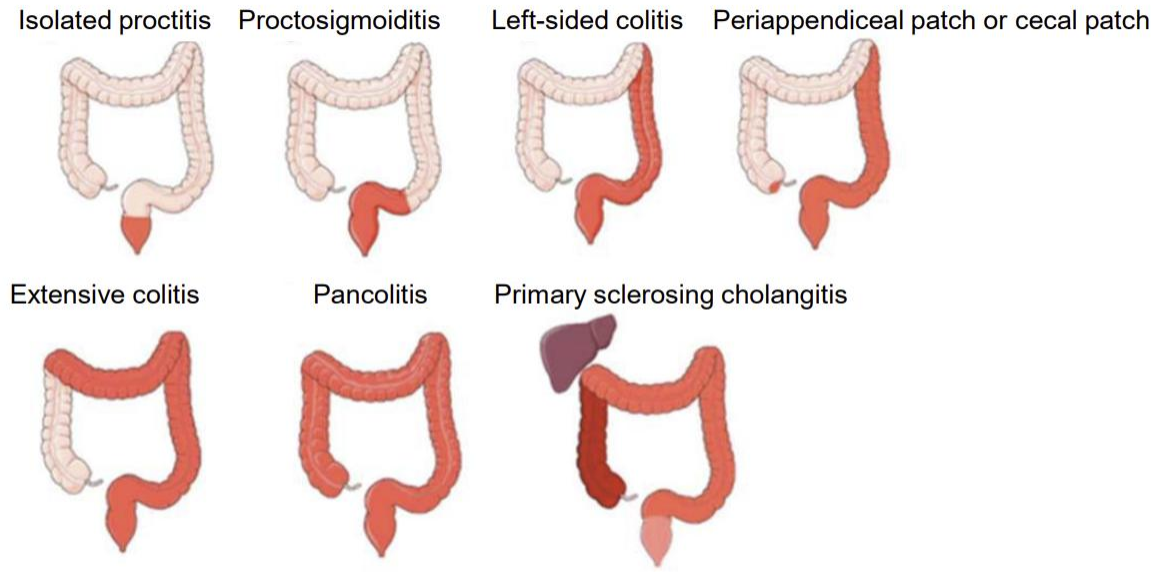
Moderate/High Risk for Complications

- Extra-intestinal manifestations (joints, skin, PSC)
- Steroid-dependence
- Delayed growth
- Mental health disorders
- Under/Un-insured

Jose FA, et al. *J Pediatr Gastroenterol Nutr*. 2008;46(2):124-33.
Waljee AK, et al. *PLoS One*. 2016;11(6):e0158017.
Amaro F, et al. *Biomedicines*. 2020;8(11):458.
Szigethy E, et al. *Clin Gastroenterol Hepatol.* 2017l;15(7):986-997.
Nguyen GC, et al. *Inflamm Bowel Dis*. 2009;15(5):726-33.

What are other factors for choosing medical options?

Different UC Clinical Phenotypes



Am J Gastroenterol. 2025;120(6):1187-1224

Other parameters

- Cost
- Safety
- Route of administration
- Patient preference

- Real world evidence +++

Choosing the Right 5-ASA

- **Release Location ➡ Location of disease**
- **Previous experience with 5-ASA**
- **Combination therapy (oral + topical)**
- **Adequate Dose**
- **Compliance**

Emphasis: Simplify Dosing Regimens:
↑compliance; better outcomes

Dosage of topical Tx

- No differences in efficacy were found between three different dosages of 5-ASA enemas (1 g, 2 g, and 4 g per day), suggesting that a 1-g enema is sufficient for managing symptom

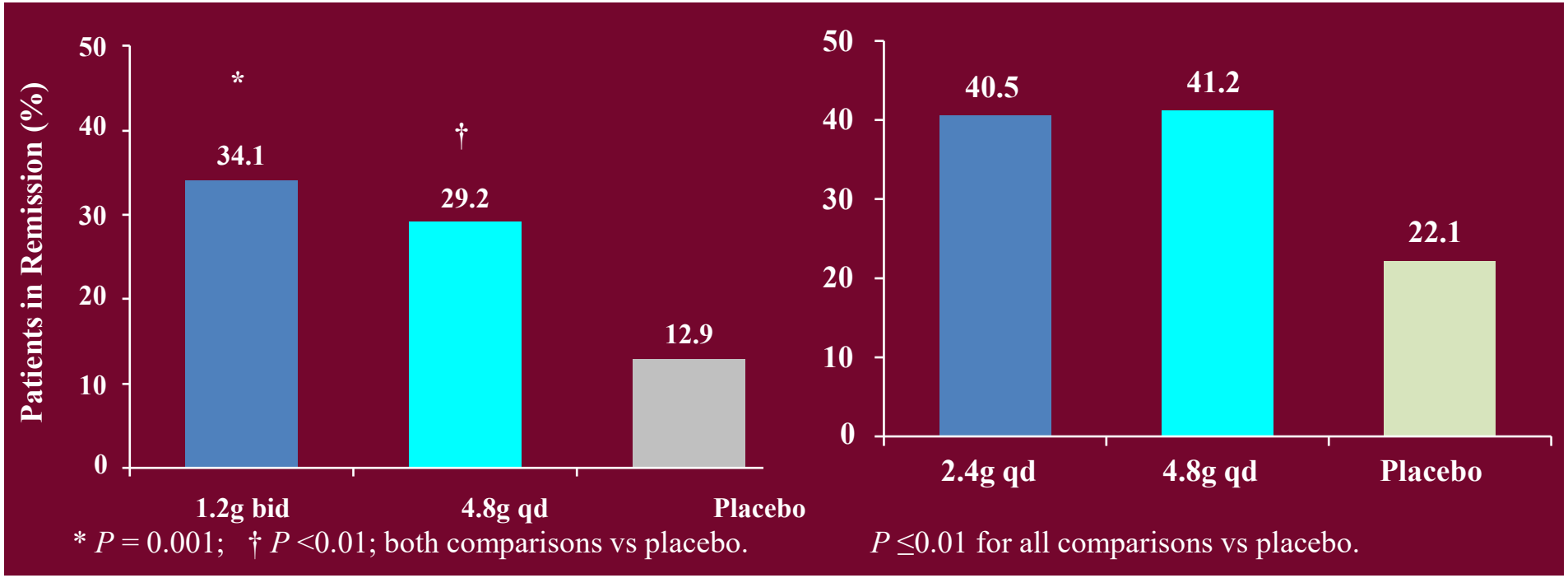
- For proctitis, 1g 5-ASA suppositories are effective and preferred by patients over the 500 mg formulations, which require more frequent administration

Topical steroid

- Rectal 5-ASA was also found to be superior to rectal corticosteroids for inducing symptomatic remission

- Steroids remain an important option for patients with mildly active left sided UC who cannot retain rectal 5-ASA, have hypersensitivity to 5-ASA, or who are not responding to 5-ASA

Little Evidence of 5-ASA Dose Response in Active UC Beyond 2.4 g/Day

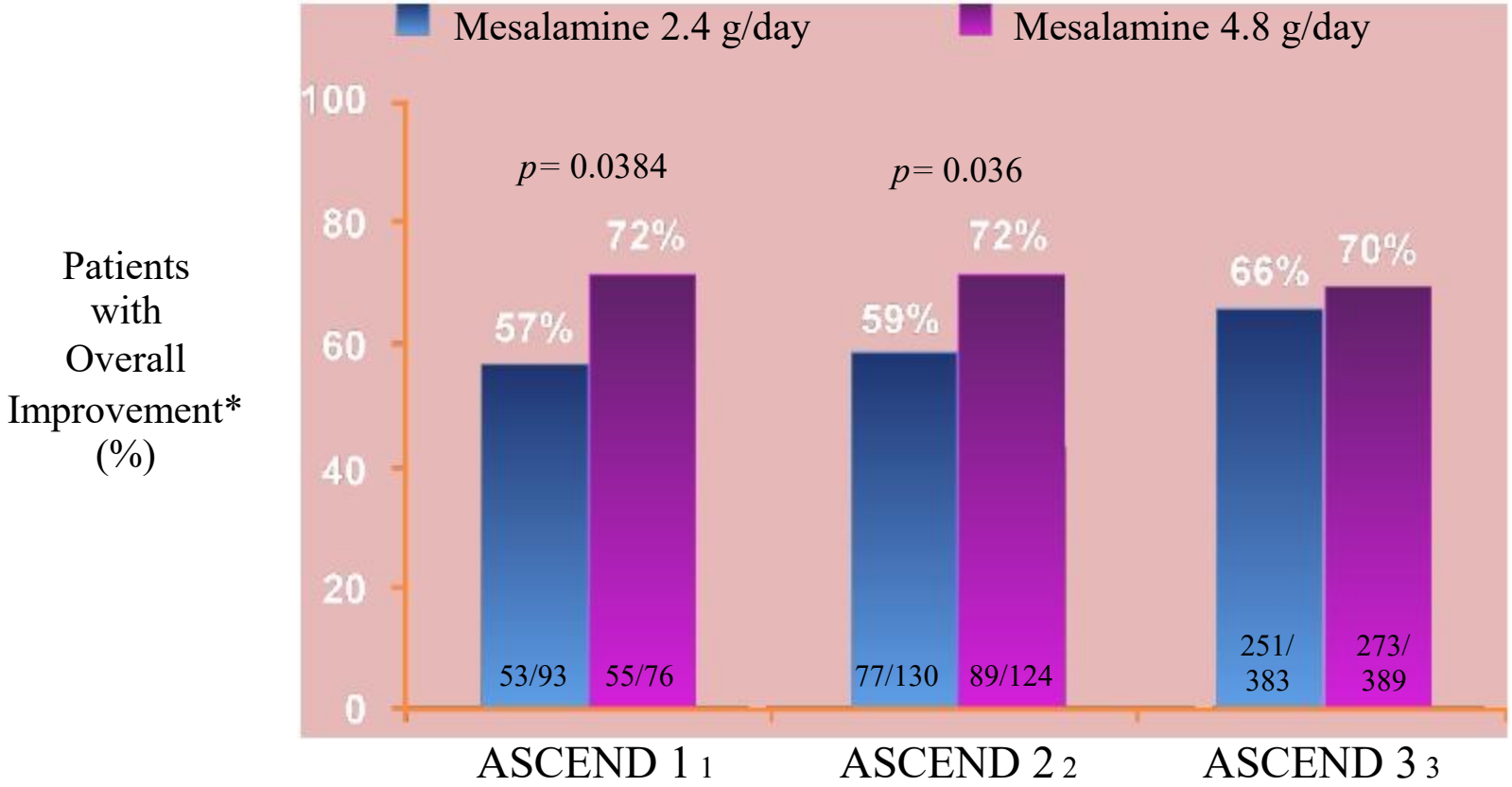


pH-Released Multimatrix Mesalamine Studies

Lichtenstein GR, et al. Clin Gastroenterol Hepatol. 2007; 5:95–102.

Kamm MA, et al. *Gastroenterology.* 2007;132:66–75.

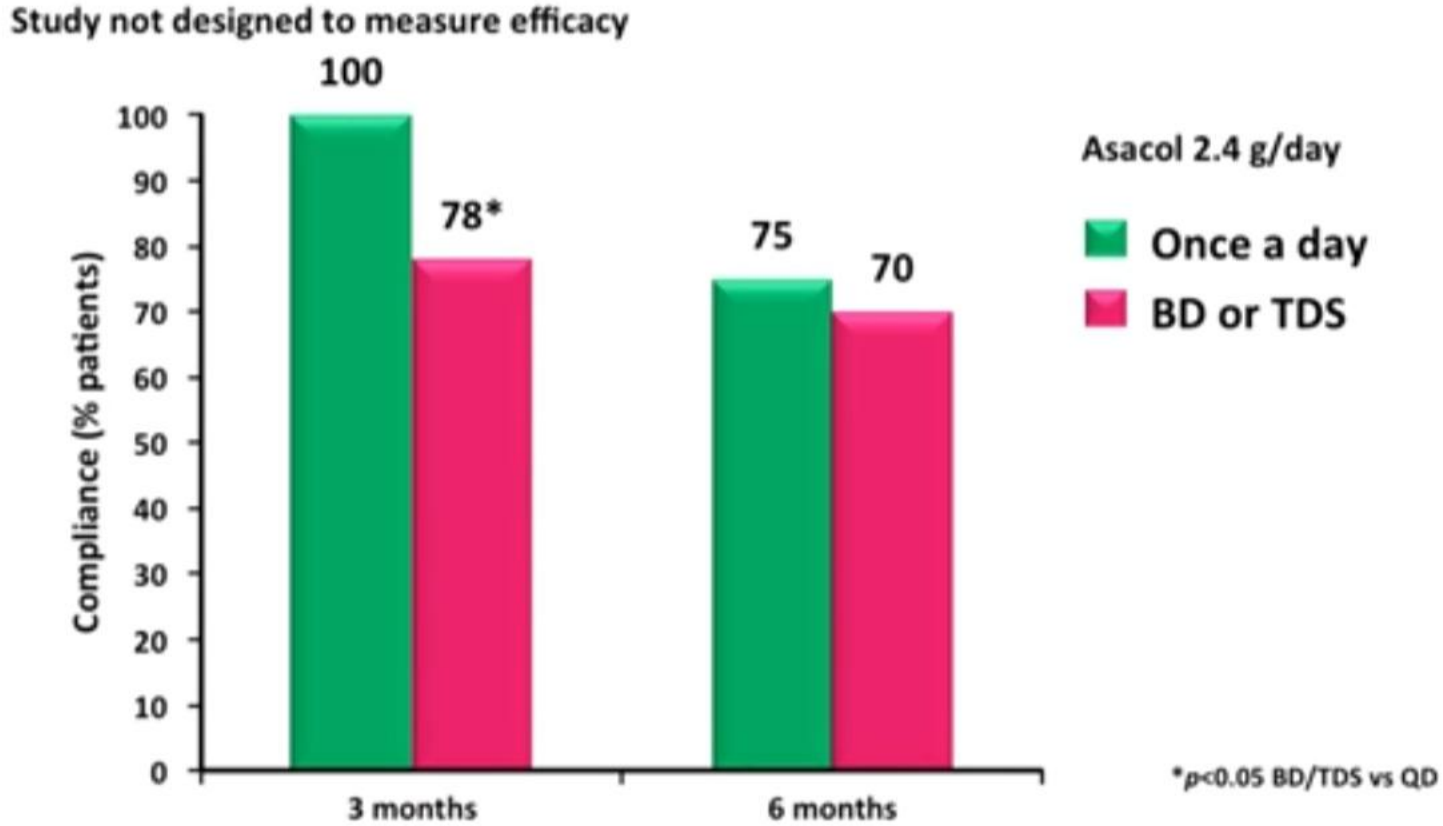
Probable Dose Response >2.4 g/Day in **Moderately Severe** Active UC



1 HanauerSB et al. Can J Gastroenterol 2007;21:827-834. 2) Hanauer SB et al. Am J Gastrenterol 2005;100:2478-2485.
3) Sandborn WJ et al. Gastroenterology 2009;137(6):1934-43..

In patients with mildly active UC of any extent, we suggest using a low dose (2.0–2.4 g) of 5-ASA, in comparison with a higher dose (4.8 g), because there is no difference in remission rate (Conditional recommendation, very low quality of evidence).

Once a day versus conventional dosing UC maintenance



Kane S *et al.* Clin Gastro Hepatol 2003;1:170–3

Statement 1: We recommend the combination of oral 5-ASA (from 2,0 to 4,8 g/day) and rectal 5-ASA (suppository 1 g/day for proctitis and enema ≥1 g/day for left-sided UC/pancolitis) for 8 weeks to induce remission.

Mild to mod proctitis

. In patients with mildly to moderately active ulcerative proctitis, we recommend rectal 5-aminosalicylate acid (5-ASA) therapies at a dose of 1 g/daily for induction of remission (Strong recommendation, moderate quality evidence).

For patients with mildly to moderately active proctitis not responsive to topical 5-ASA, we suggest tacrolimus suppository or beclomethasone suppository over no treatment (Conditional recommendation, low quality of evidence).

In patients with mildly to moderately active left-sided UC, we suggest rectal 5-ASA enemas at a dose of at least 1 g/daily combined with oral 5-ASA at a dose of at least 2.0 g/daily compared with oral 5-ASA therapy alone for induction of remission (Conditional recommendation, low quality of evidence).

In patients with mildly to moderately active extensive colitis, oral 5-ASA at a dose of at least 2.0 g daily is recommended to induce remission (Strong recommendation, moderate quality of evidence).

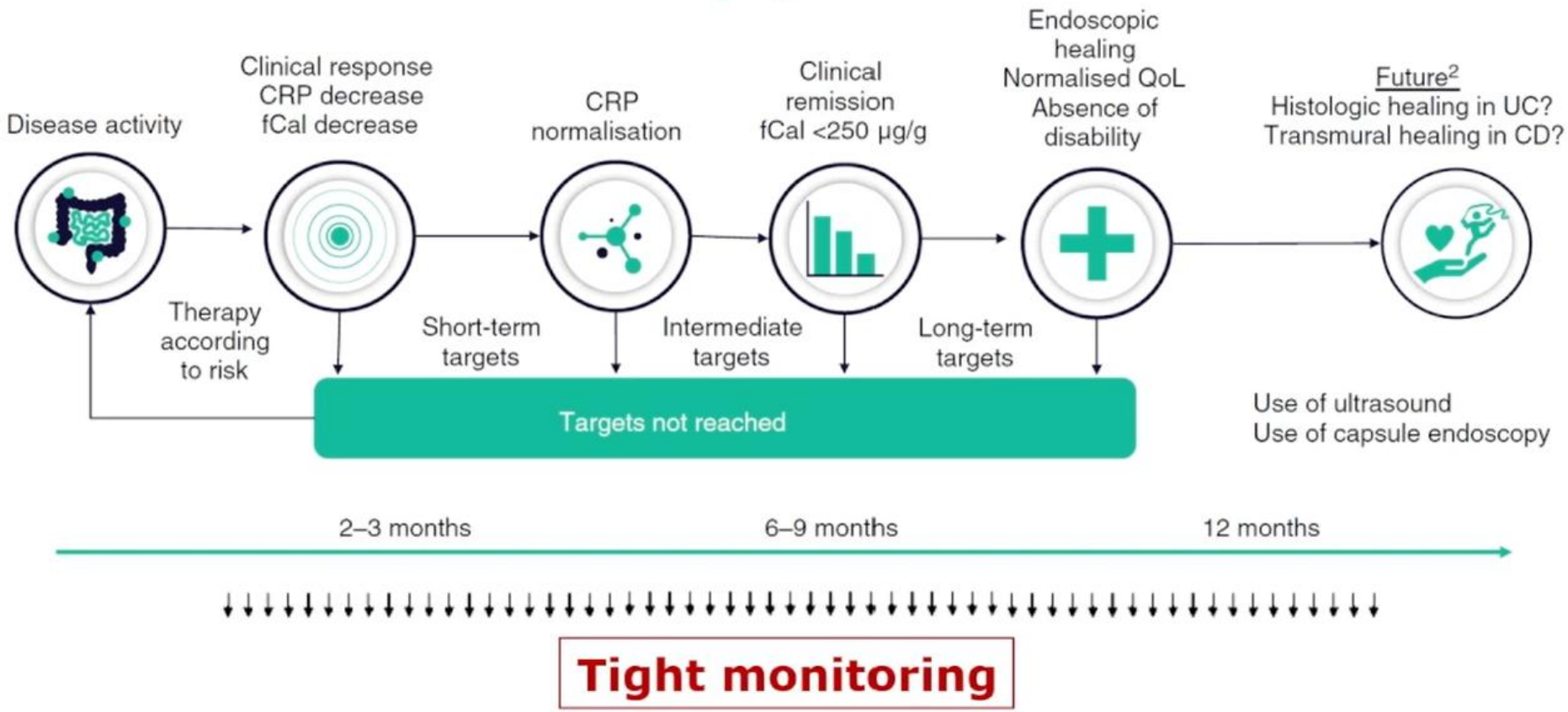
Management of Mildly-to-Moderately Active UC

Induction:

- Mild proctitis→ **rectal 5-ASA** recommended (1 g/day)[1,2,3,4,5]
- Mild proctitis not responsive to topical 5-ASA →suggest **tacrolimus suppository or beclomethasone suppository** over no treatment[6]
- Left-sided mild UC→ **rectal 5-ASA** (≥1 g/day) in combination with **oral 5-ASA** (≥ 2.0 g/day)[1,2,3,4,5,6]
- Mild extensive UC→ **oral 5-ASA** (≥ 2.0 g daily)[1,5]
- Mild UC (any extent)→ use a low dose (2.0-2.4 g) of **5-ASA**[2], in comparison with a higher dose (4.8 g)[1]

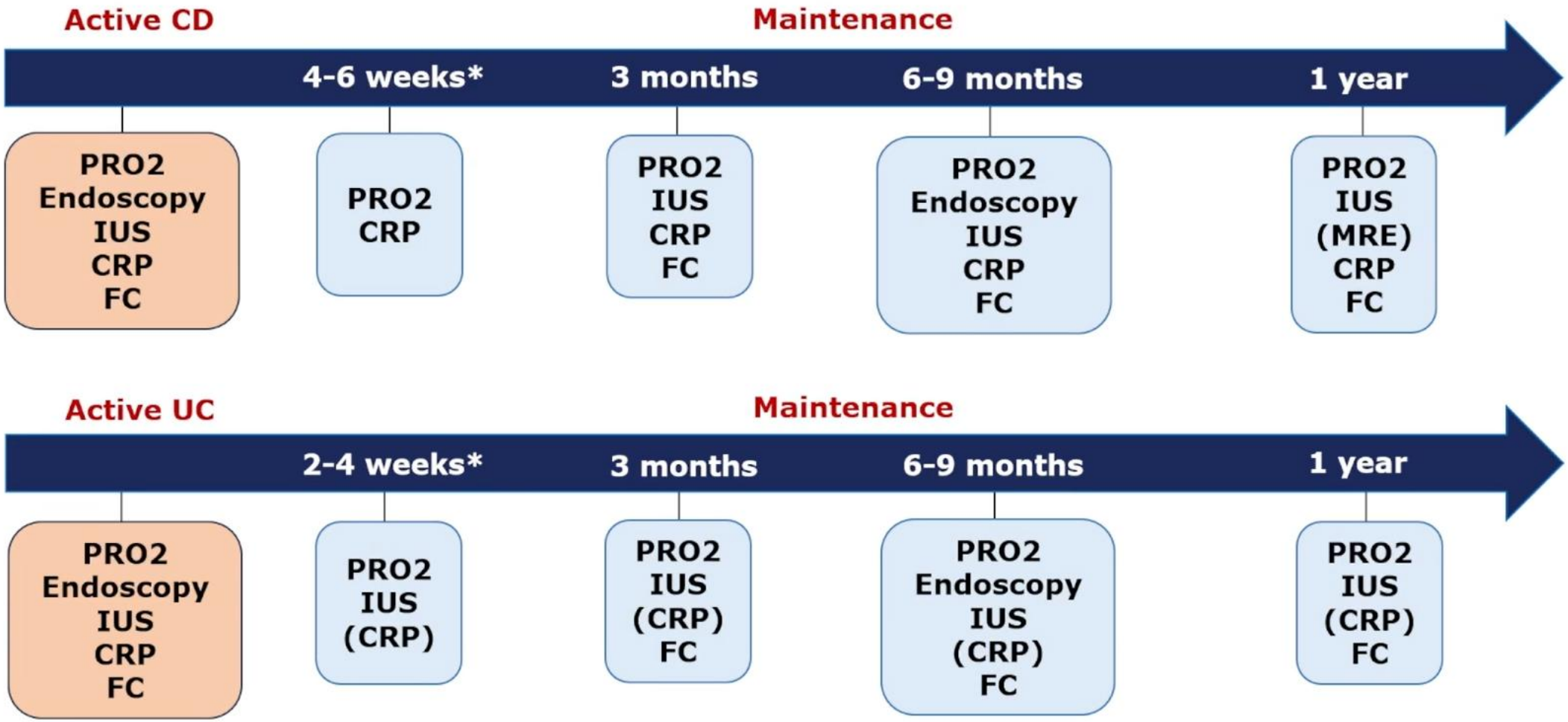
[1]Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.
[2]Hardbord M, et al. *J Crohns Colitis*. 2017;11(7):769-784.
[3]Bressler B, et al. *Gastroenterology*. 2015;148(5):1035-1058.
[4]Coi CH, et al. *Intest Res*. 2017;15(1):7-37.
[5]Ko CW, et al. *Gastroenterology*. 2019; 156(3):748-764.
[6]Lie M, et al. *Clin Gastroenterol Hepatol*. 2020;18(8):1777–84.
[7]Wei CS, et al. *Intest Res*. 2017;15(3):266-284.

Managing patients with IBD



Adapted from Dignass A, et al. Aliment Pharmacol Ther 2023

Monitoring algorithm with integration of monitoring tools



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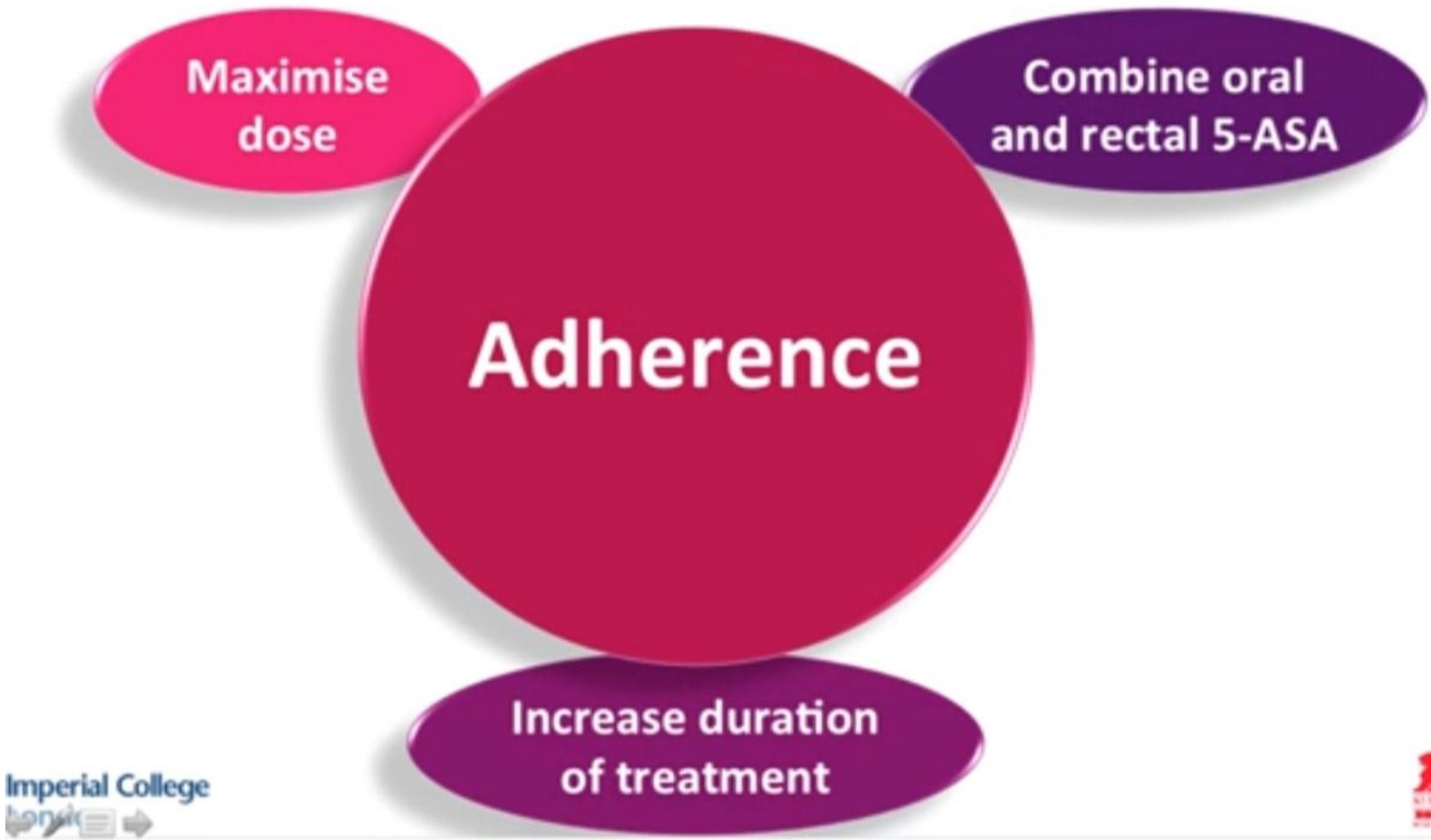
*Depending on disease activity

Response to induction treatment should be monitored clinically and by fecal calprotectin

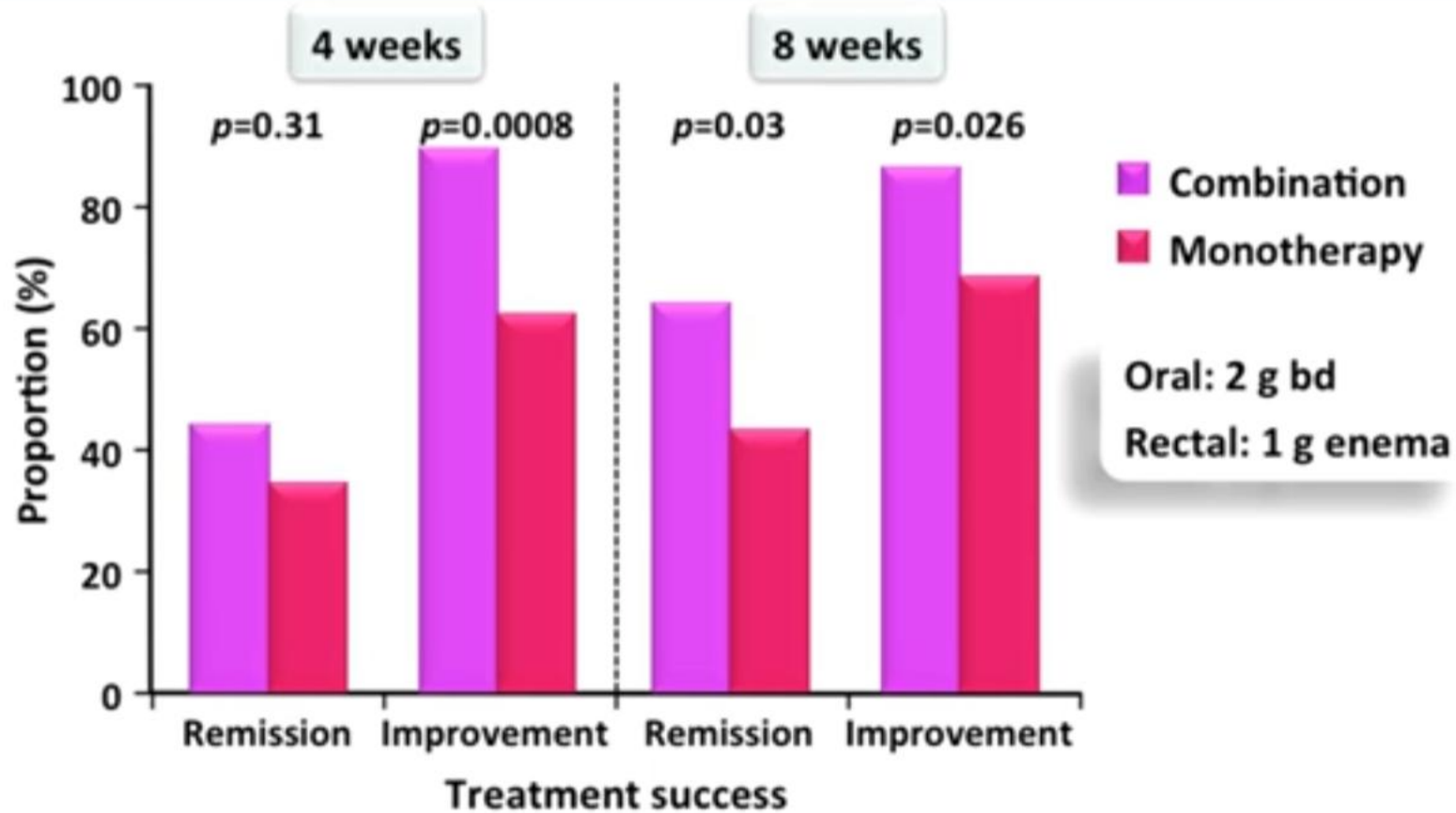
- Short term: 2-4 wk , clinical response, at least 50 % reduction in FC
- Fecal calprotectin measurement should be performed after 8-12 weeks of induction therapy with 5-ASA.
- 8-12 wk: clinical remission and normalized FC

In case of inadequate response after two to four weeks of treatment, we recommend optimizing medical therapy

How to optimise 5-ASA



Combination oral and rectal 5-ASA versus oral 5-ASA therapy alone in pancolitis



Imperial College

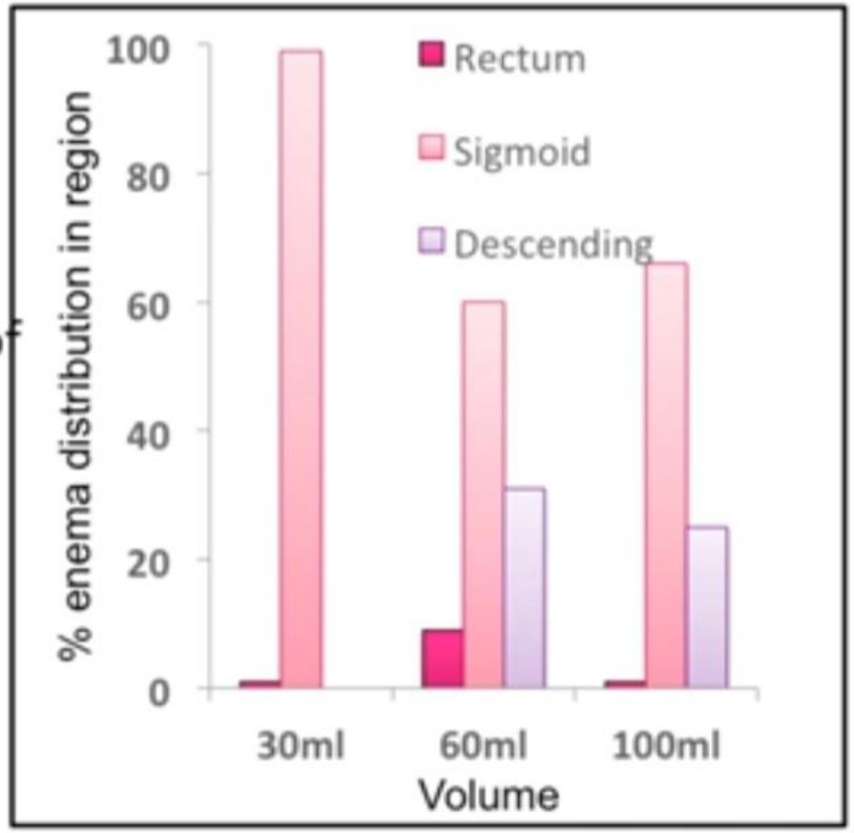
Marteau P *et al. Gut* 2005;54:960

Enemas may not provide good 5ASA delivery to rectum

31 patients with UC

Scintigraphy after administration of enemas of different volume

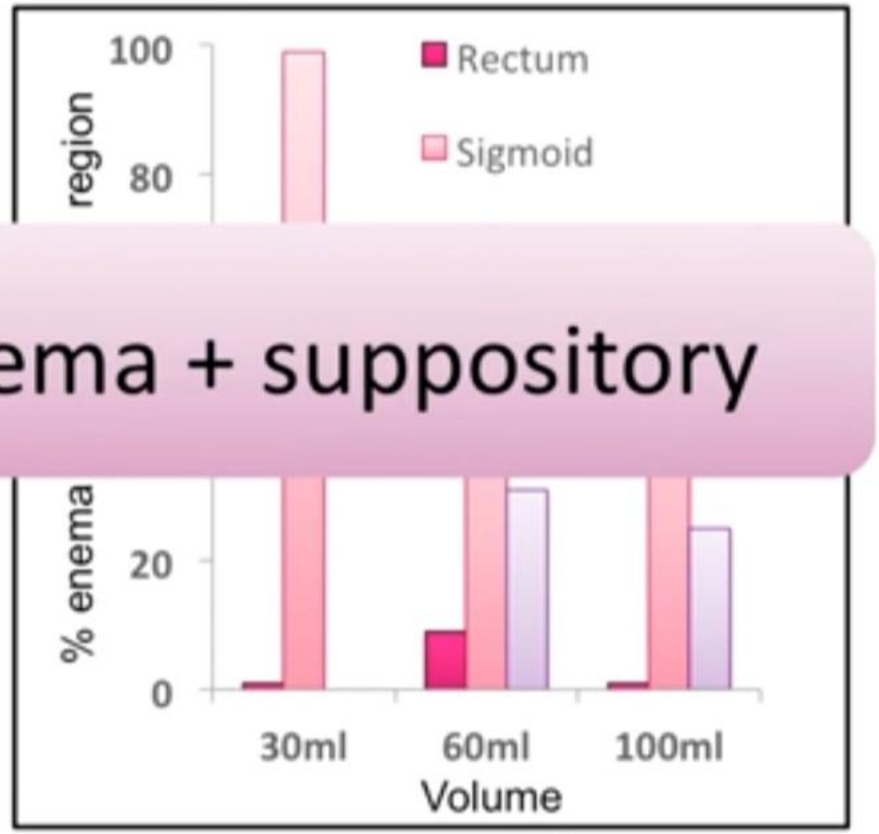
Median delivery to different areas of interest



Van Bodegraven *et al* Aliment Pharmacol Ther. 1996; 10, 327-332

Enemas may not provide good 5ASA delivery to rectum

31 patients with UC



Consider enema + suppository

Median delivery to different areas of interest

Imperial College

Van Bodegraven *et al* Aliment Pharmacol Ther. 1996; 10, 327-332

- It is not recommend to change to an alternate 5-ASA formulation in patients fail to reach remission with appropriate 5ASA dose

- Alternative therapeutic classes should be considered

In patients with mildly to moderately active UC of any extent not responding to oral 5-ASA, we recommend the addition of budesonide MMX 9 mg/d to induce remission (Strong recommendation, moderate quality of evidence).

Statement 7: In patients who do not respond to induction therapy we recommend budesonide MMX (9 mg/day) as an add-on therapy for 8 weeks.

Budesonide in UC

- 90% first pass effect in liver
- Low systemic effect
- High topical anti inflammatory activity
- Generally fast acting drug(clinical response in7-10 days)

Oral formulation:

- Ileal release (both may be used in crohn)
  - PH and time dependent release
  - PH dependent release
- Colonic release (Disolced in PH>7,multimatrix,used in UC)
- Rectal formulation

Which consideration is required

- Patient with cirrhosis
- Drug interaction(CYP3A inhibitor,ketoconazole,..)
- Grapefruit juice

Dosage recommendation

- Generally begin 9mg daily for 6-10 weeks.
- If symptoms improvd,reduce to 9mg every other day for 2 weeks
- Total :8-12 weeks

- If not responding in 10 weeks,change the drug
- Limit budesonide to a single course

- Limited effect on BMD
- Even better preservation of BMD in cs naïve
- Low risk in pregnancy
- Compatible with breast feeding

Management of Mildly-to-Moderately Active UC

Induction:

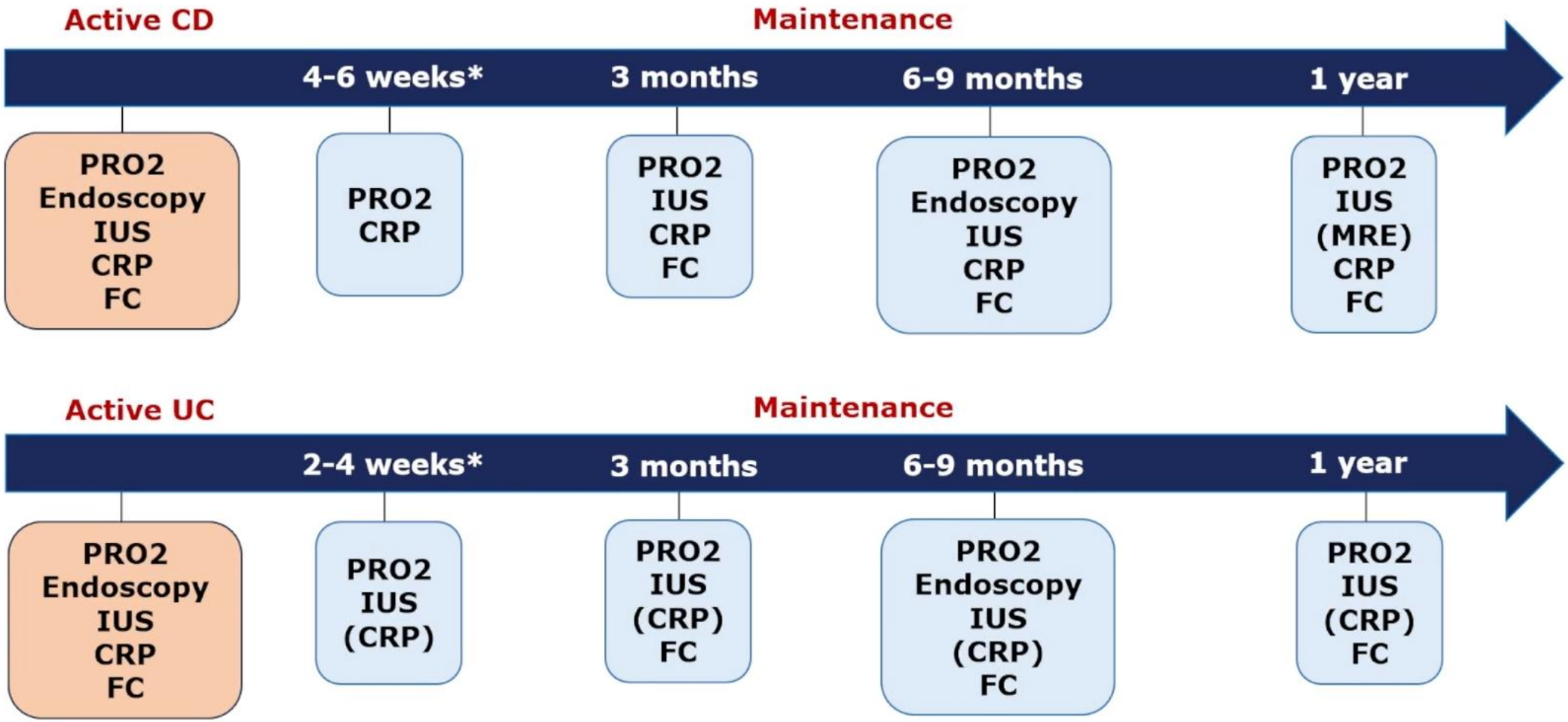
- Mild proctitis→ **rectal 5-ASA** recommended (1 g/day)[1,2,3,4,5]
- Mild proctitis not responsive to topical 5-ASA →suggest **tacrolimus suppository or beclomethasone suppository** over no treatment[6]
- Left-sided mild UC→ **rectal 5-ASA** (≥1 g/day) in combination with **oral 5-ASA** (≥ 2.0 g/day)[1,2,3,4,5,6]
- Mild extensive UC→ **oral 5-ASA** (≥ 2.0 g daily)[1,5]
- Mild UC (any extent)→ use a low dose (2.0-2.4 g) of **5-ASA**[2], in comparison with a higher dose (4.8 g)[1]
- Mild-moderate UC not responding to **oral 5-ASA**→ +**budesonide MMX** 9 mg/day[1,2,3,5]

Maintenance:

- Mildly active proctitis→ **rectal 5-ASA** (1 g daily)[1,2,7]
- Mildly active left-sided or extensive UC→ **oral 5-ASA** therapy (≥ 2 g/day)[1,2,3,4]
- **Recommend against** **systemic steroids**[1,3,6]

[1]Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.
[2]Hardbord M, et al. *J Crohns Colitis*. 2017;11(7):769-784.
[3]Bressler B, et al. *Gastroenterology*. 2015;148(5):1035-1058.
[4]Coi CH, et al. *Intest Res*. 2017;15(1):7-37.
[5]Ko CW, et al. *Gastroenterology*. 2019; 156(3):748-764.
[6]Lie M, et al. *Clin Gastroenterol Hepatol*. 2020;18(8):1777–84.
[7]Wei CS, et al. *Intest Res*. 2017;15(3):266-284.

Monitoring algorithm with integration of monitoring tools



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*Depending on disease activity

Patient under 5-ASA therapy(maintenance dosage <4 g/day) experiencing a disease flare

- Up to 70% of the patients experience disease recurrence during the first year of treatment with 5-ASA
- Tight monitoring is therefore necessary to optimize treatment
- A fecal calprotectin value >150 µg/g or a bowel wall thickness >3 mm could be indicators of disease activity

- Evaluate the compliance
- High doses of 5-ASA (≥4 g/day)
- Adding topical
- Adding short term Budesonide
- Rule out of infection
- Treat IBS!
- Rule out of drug induce colitis

Other Important aspects of management

Communication is Two Directions!

FROM PATIENT TO CLINICIAN

- "I don't feel well"
- "Something is wrong"
- Emotions
- Life events
- Patient reported outcomes (PROs)
  - Stool frequency
  - Abdominal pain
  - Rectal bleeding
  - Bowel urgency
  - Fatigue
- Extra-intestinal manifestations



FROM CLINICIAN TO PATIENT

- Focused questions
- Establishing disease
  - diagnosis
  - prognosis
- Explaining goals of management
  - short term
  - long term
  - disease monitoring
  - prevention
- Raising expectations for quality of life

Ulcerative Colitis is Burdensome: US UC NORMAL Study

Large majorities of UC patients report that living with UC is difficult and disruptive

	% of Patients
UC is disruptive to their lives generally (% very or somewhat)	77%
To their emotional state (% very or somewhat)	82%
Having sexual relations (% very or somewhat)	75%
Their relationship with a spouse or partner (% very or somewhat)	64%
Relationship with other family/friends (% very or somewhat)	59%
UC makes it difficult to lead a normal life (% somewhat or strongly agree)	62%
Living with UC is a daily struggle (% somewhat or strongly agree)	61%
Having UC has wrecked important moments in their lives (% somewhat or strongly agree)	60%
Feel UC controls them, rather than them controlling UC (% somewhat or strongly agree)	53%

Patients Q17. Overall, how disruptive has having UC been to your life? How disruptive, if at all, is UC when it comes to: Your emotional state, Having sexual relations, Your relationship with your spouse or partner, Your relationship with other family and friends. 24e. UC makes it difficult to lead a normal life. 24b. Living with UC is a daily struggle . 24c. I feel like UC has wrecked important moments in my life . 24a. I feel like UC controls my life, rather than me controlling it.

Rubin DT, et al. *Inflamm Bowel Dis*. 2009;15(4):581-588.

UC is Worse Than Other Chronic Conditions

Migraine patients and asthma patients are somewhat less likely to report their suffering has become "normal" and they are less likely to feel like it is controlling their lives

	UC patients	RA patients	Asthma patients	Migraine patients
Not feeling well has become normal	73%	77%	43% ▼	64% ▼
Difficult to lead a normal life	62%	61%	33% ▼	59% ▼
Has wrecked important moments in life	60%	48% ▼	25% ▼	53%
Daily struggle	61%	66%	33% ▼	45%
Controls me, rather than me controlling it	53%	44% ▼	19% ▼	37% ▼
Not much can do	70%	73%	56% ▼	60% ▼

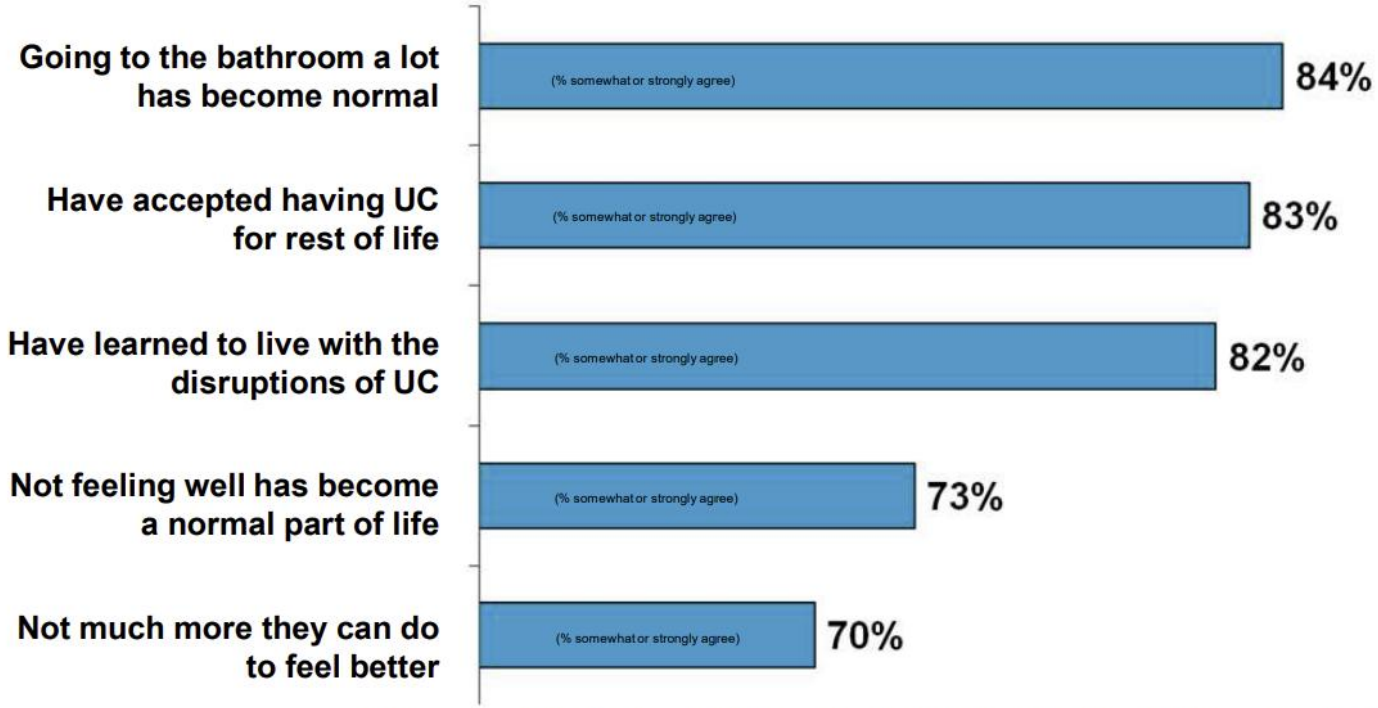
Patients Q24g. I worry about the long-term health effects of having <>. Q23. When your <> is not active, how often do you think about when you will experience your next <>? Q24d. <> makes my life more stressful. Q25. How often do you feel: (b) Helpless to do much about <>. (e) Depressed about having <>.

▼ Lower: statistically significant

Rubin DT, et al. *Dig Dis Sci*. 2010;55(4):1044-1052.

Patients "Normalize" Living with UC: UC NORMAL Study

Despite not feeling well and having their lives disrupted, patients have "normalized" aspects of their experience, just as they believe that flare-ups are now a normal part of life



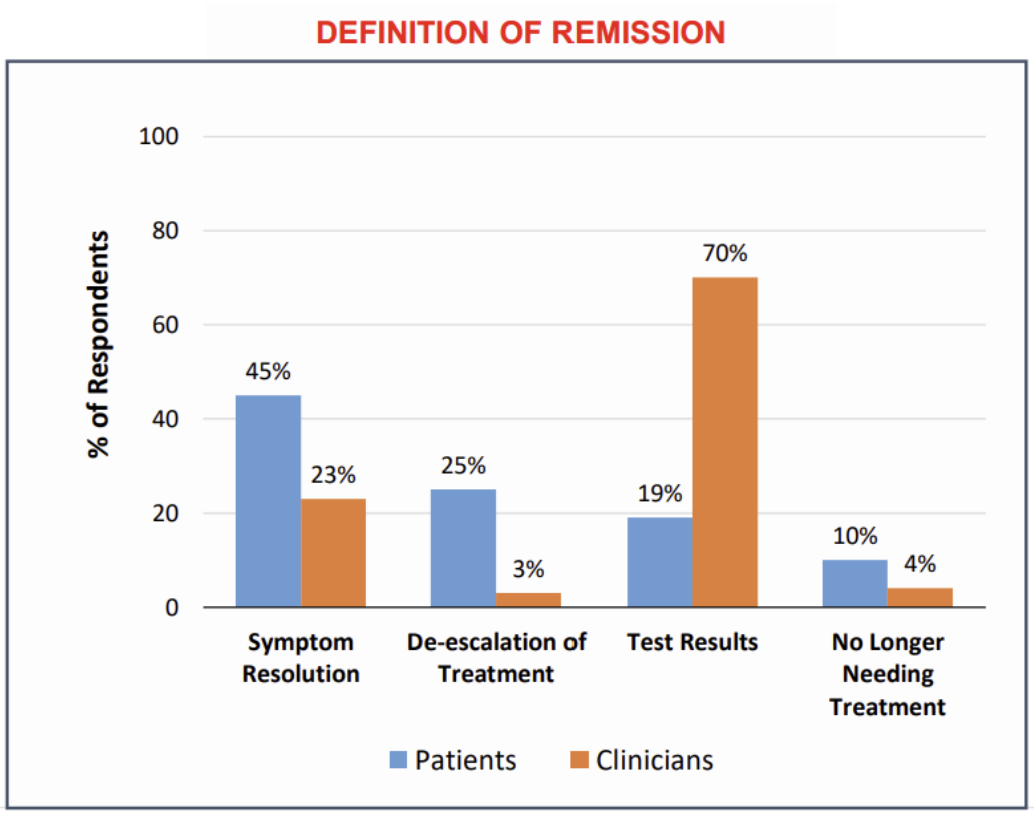
Patients Q35f. I've accepted that I will have to take medication for UC for the rest of my life. Q24i. Going to the bathroom a lot has become a normal part of my life. Q24k. I have accepted that I will have UC fo the rest of my life. Q24h. I have learned to live with the disruptions to my life that UC causes. Q24j. Not feeling well from UC has become a normal part of my life. Q35c. Beyond what I'm doing already, there is not much I can do about my UC.

Rubin DT, et al. *Inflamm Bowel Dis*. 2009;15(4):581-588.

Patients Do Not View Remission the Same Way We Do
CONFIDE Study

In a 2019 survey that included UC patients* (n=1030) and clinicians (N=654)

The COmmunicating Needs and Features of IBD Experiences





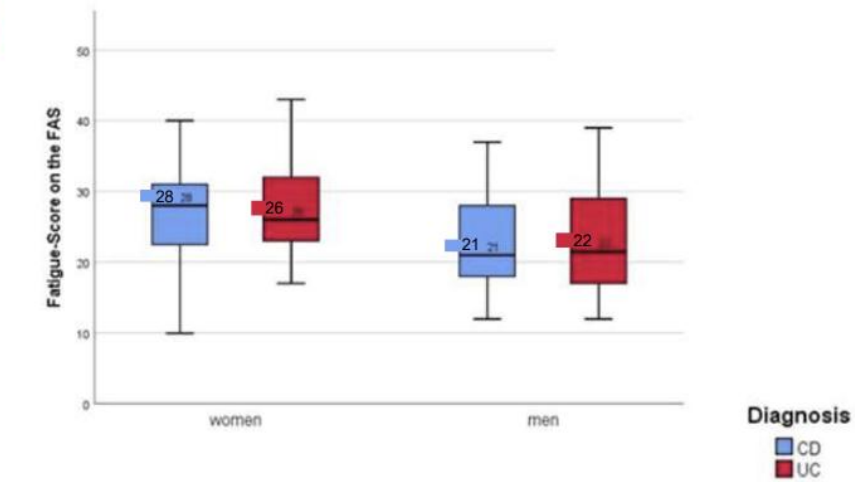
Rubin DT, et al. *Inflamm Bowel Dis*. 2021;27(12):1942-1953.

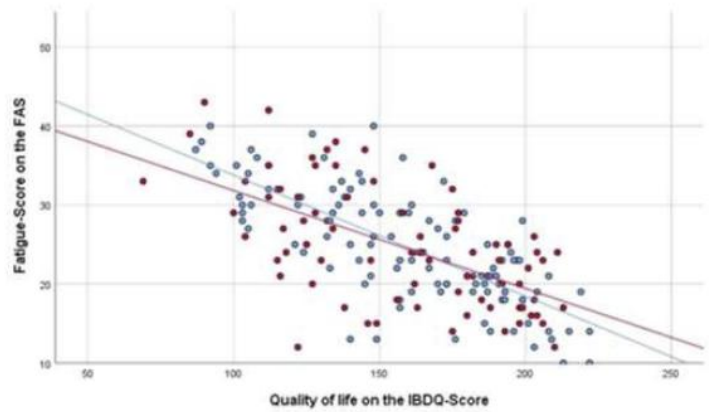
Fatigue is Prevalent in IBD

- n=189
- HADS, Fatigue Assessment Scale, McGill Pain Questionnaire, IBDQ and general well-being

- 2/3 of patients were either fatigued (CD: 53.1%, UC: 48.7%) or extremely fatigued (CD: 10.7%, UC: 14.5%)
- women (80.9%) > men (48.0%)
- Strong association between fatigue and depression

- Fatigue should be assessed: simple fatigue survey (FAS)



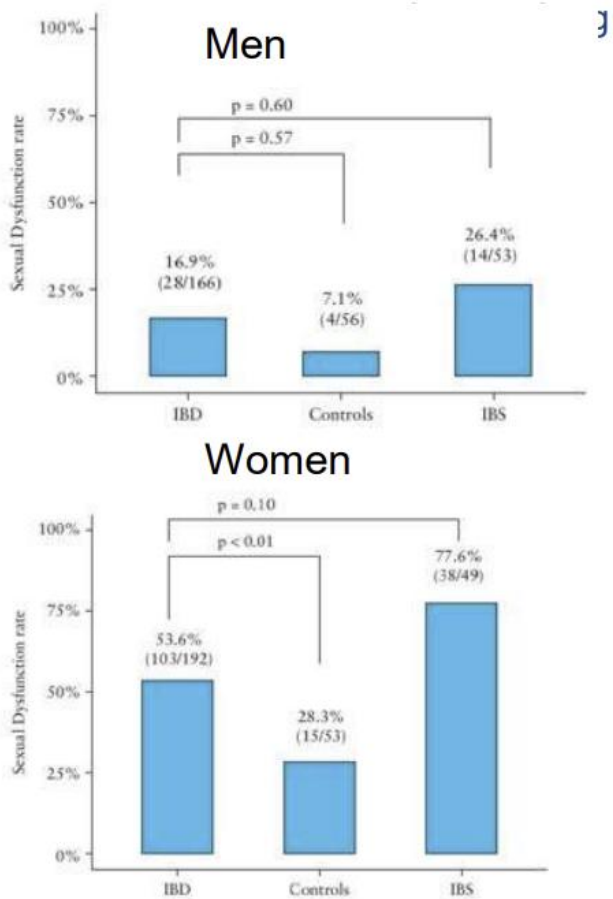


Uhlir V, et al. *BMC Gastroenterol*. 2023;23(1):288.

Sexual Dysfunction is Prevalent in IBD … and under-identified

- **Definition:** Problems that occur during the sexual response cycle that decrease satisfaction with sexual activity
- **Common Symptoms:** Painful intercourse, low libido, difficulty with erections, inability to have an orgasm

- **In IBD:**
  - In women, rates of SD range from 49%-97%
  - In men, rates of SD range from 14%-39.1%

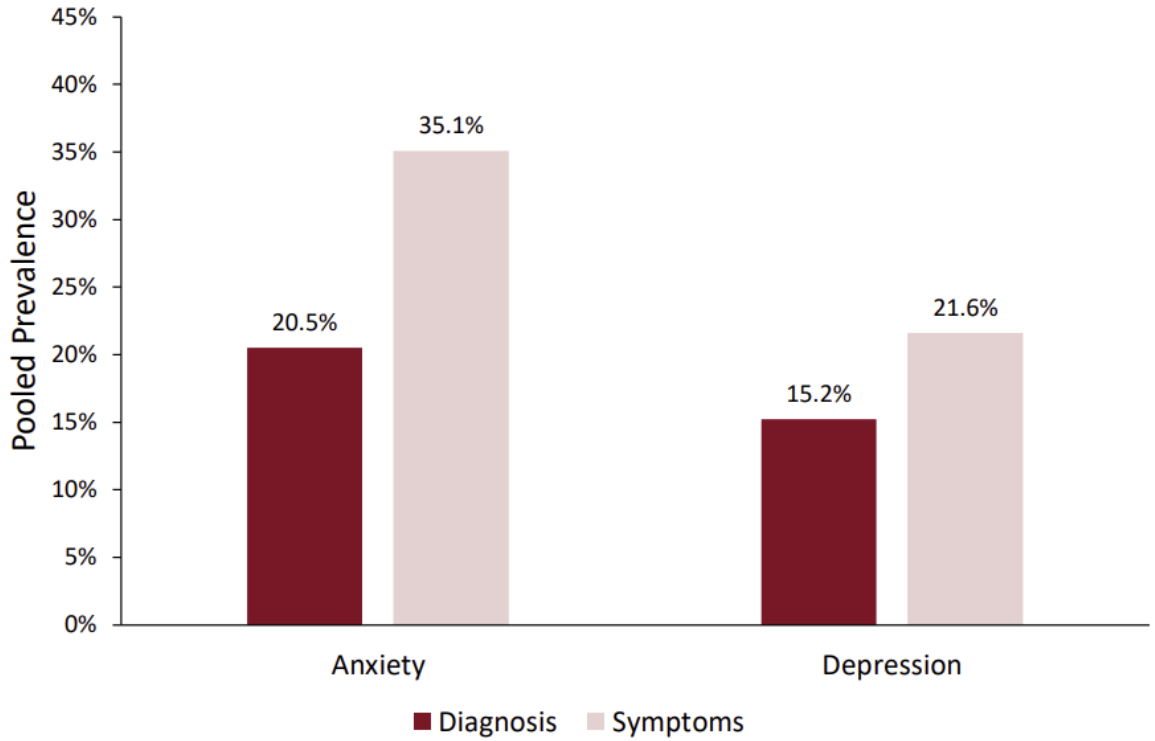


METHODS
- Postal survey (Marin)
- Female sexual function index and International Index of Erectile Function during clinic (Schmidt)
- Anonymous validated questionnaires on sexual function(FSIF and IIEF) (Riviere)

Marín L, et al. *J Gastroenterol*. 2013;48(6):713-20.
Shmidt E, et al. *Inflamm Bowel Dis*. 2019;25(7):1262-1270.
Shmidt E, et al. *Inflamm Bowel Dis*. 2019;25(8):1408-1416.
Riviere P, et al. *J Crohns Colitis*. 2017;11(11):1347-52.

Anxiety and Depression are Prevalent in IBD … and often undiagnosed

- **Systematic Review of 171 studies**
- **N= 158,371**



Neuendorf R, *et al. J Psychosom Res.* 2016;87:70-80.

Irritable Bowel Syndrome in Inflammatory Bowel Disease: Systematic Review and Meta-Analysis

Table 2. Prevalence of IBS in IBD according to disease activity and disease type

	Number of studies	Total number of subjects	Number meeting criteria for IBS	Pooled prevalence of IBS (%)	95% confidence interval	I^2	*P* value for I^2
All IBD patients	13	1703	583	39.0	30.0–48.0	92.6%	<0.001
IBD in remission	11	1197	363	35.0	25.0–46.0	63.5%	<0.001
Active IBD	3	299	115	44.0	24.0–64.0	NA[a]	NA[a]
All UC patients	10	772	251	36.0	25.0–47.0	89.9%	<0.001
UC in remission	9						<0.001
Active UC	2						NA[a]
All CD patients	9						<0.001
CD in remission	8						<0.001
Active CD	2						NA[a]

CD, Crohn's disease; IBD, inflam
[a]NA; not applicable, too few stud

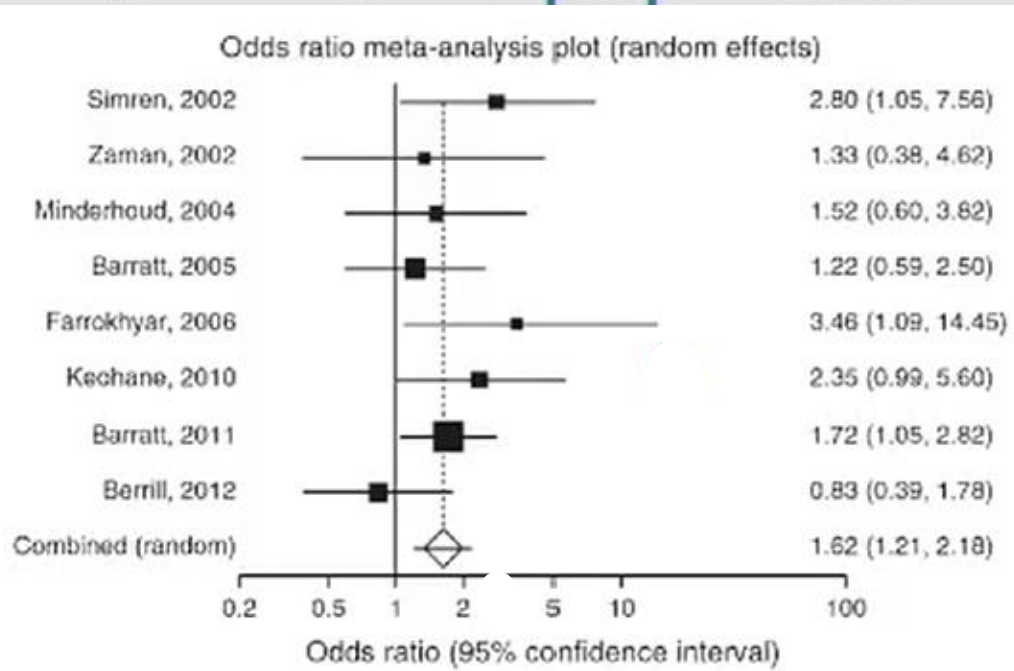
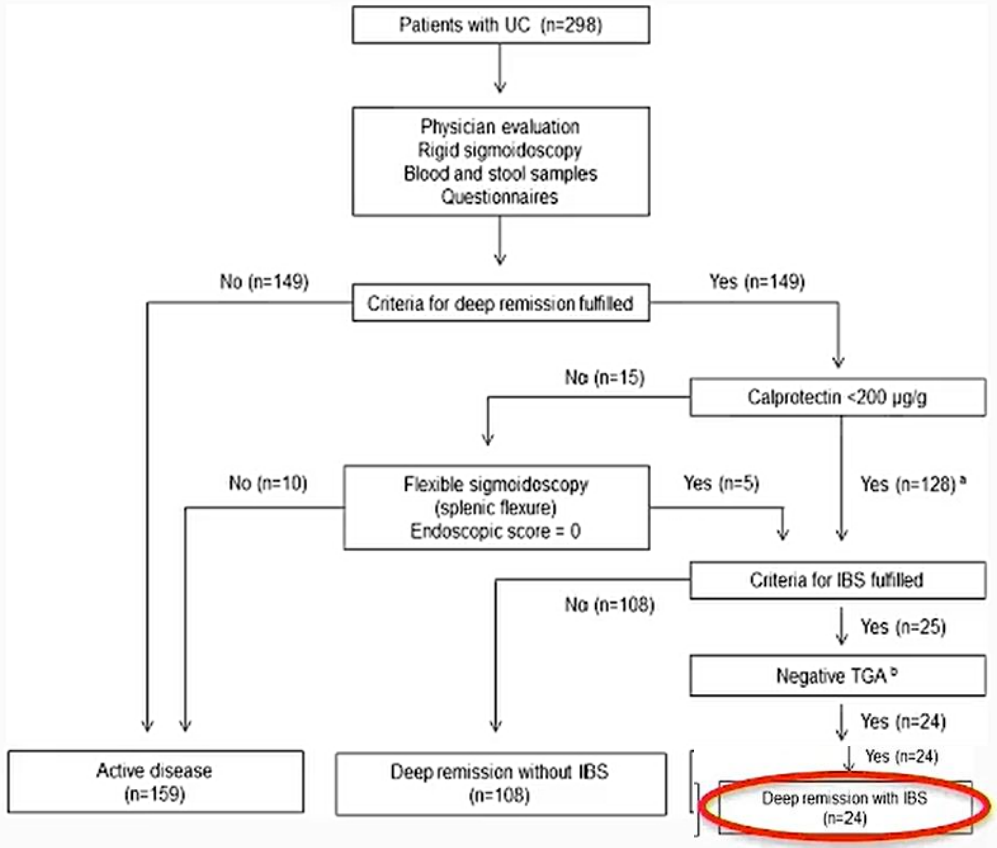


Figure 3. Odds ratio for symptoms meeting criteria for irritable bowel syndrome in Crohn's disease patients vs. ulcerative colitis patients.

Am J Gastroenterol 2012; 107:1474– 1482; doi: 10.1038/ajg.2012.260

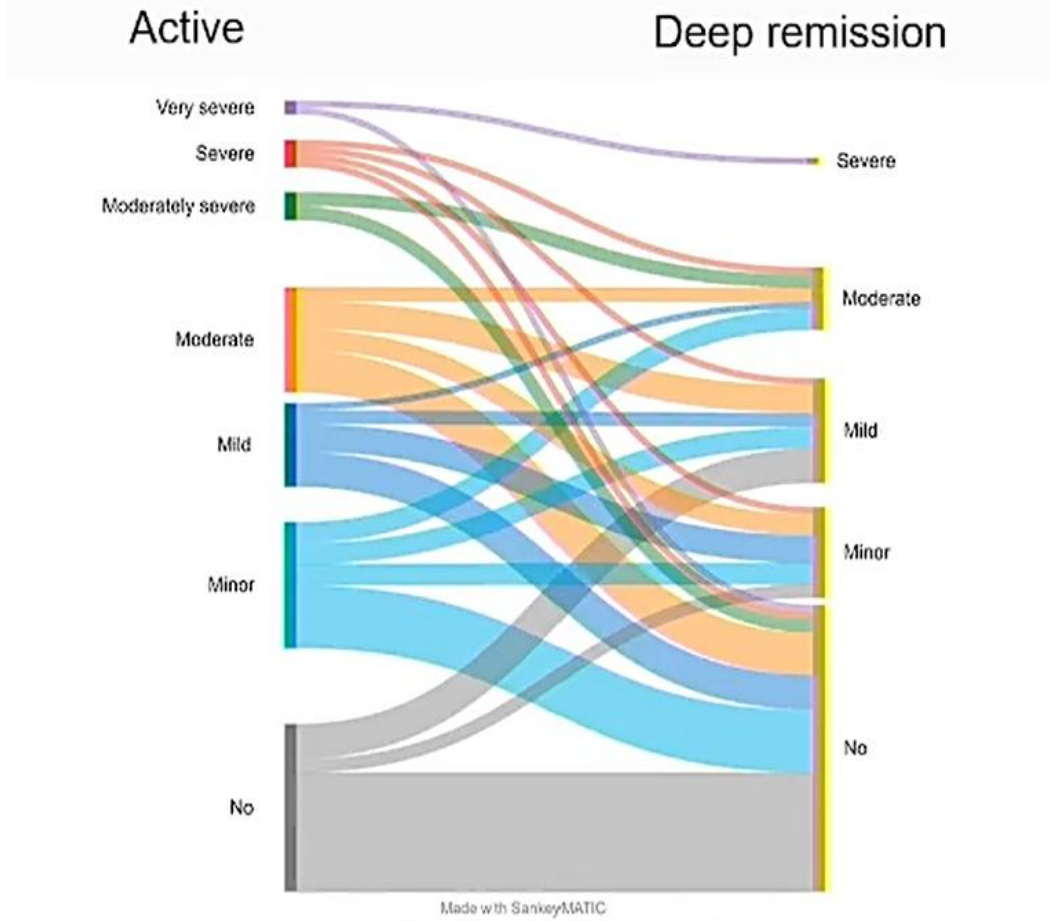
Ulcerative colitis in remission



Jonefjäll et al Inflamm Bowel Dis 2016

18%

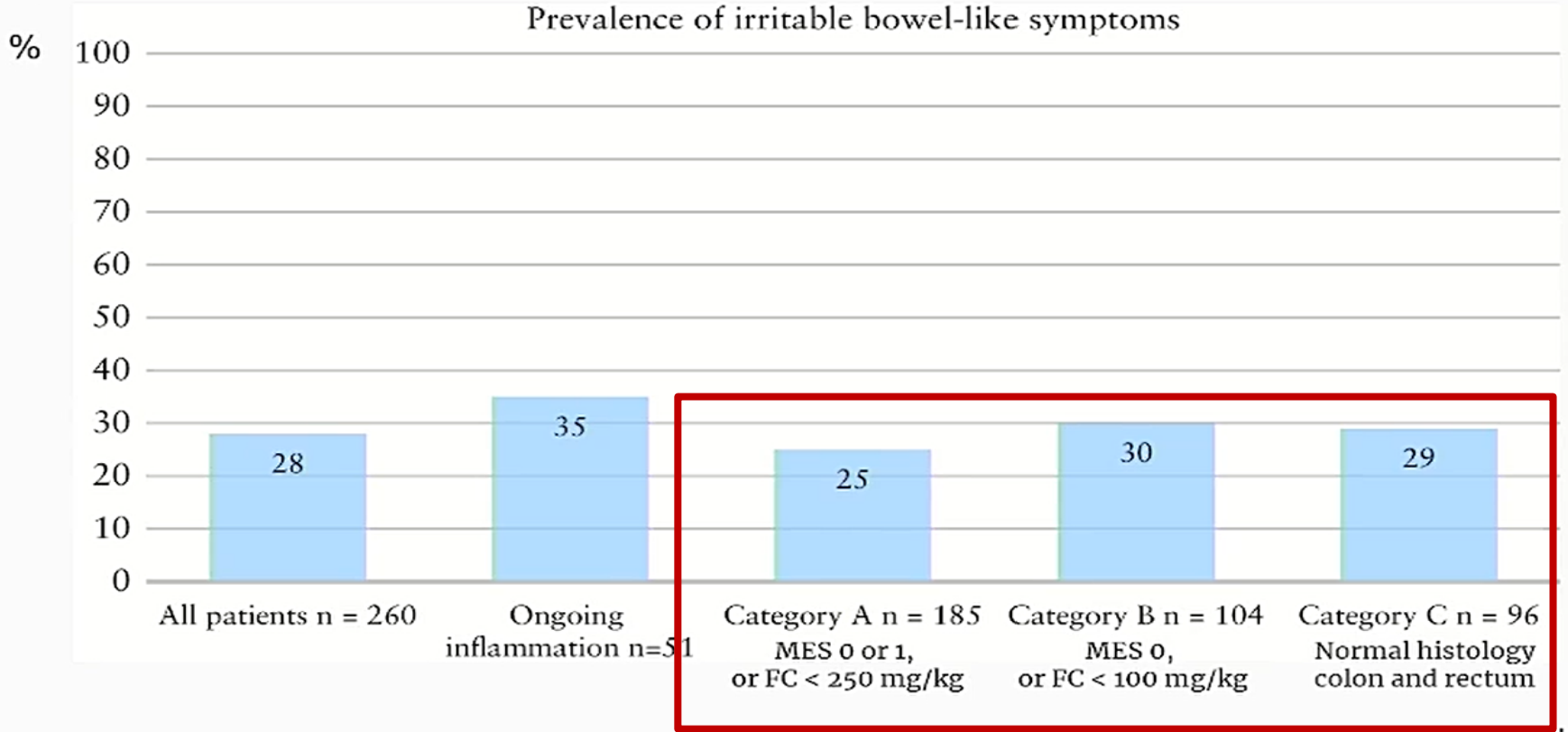
Abdominal pain or discomfort during the last week?



Unpublished data

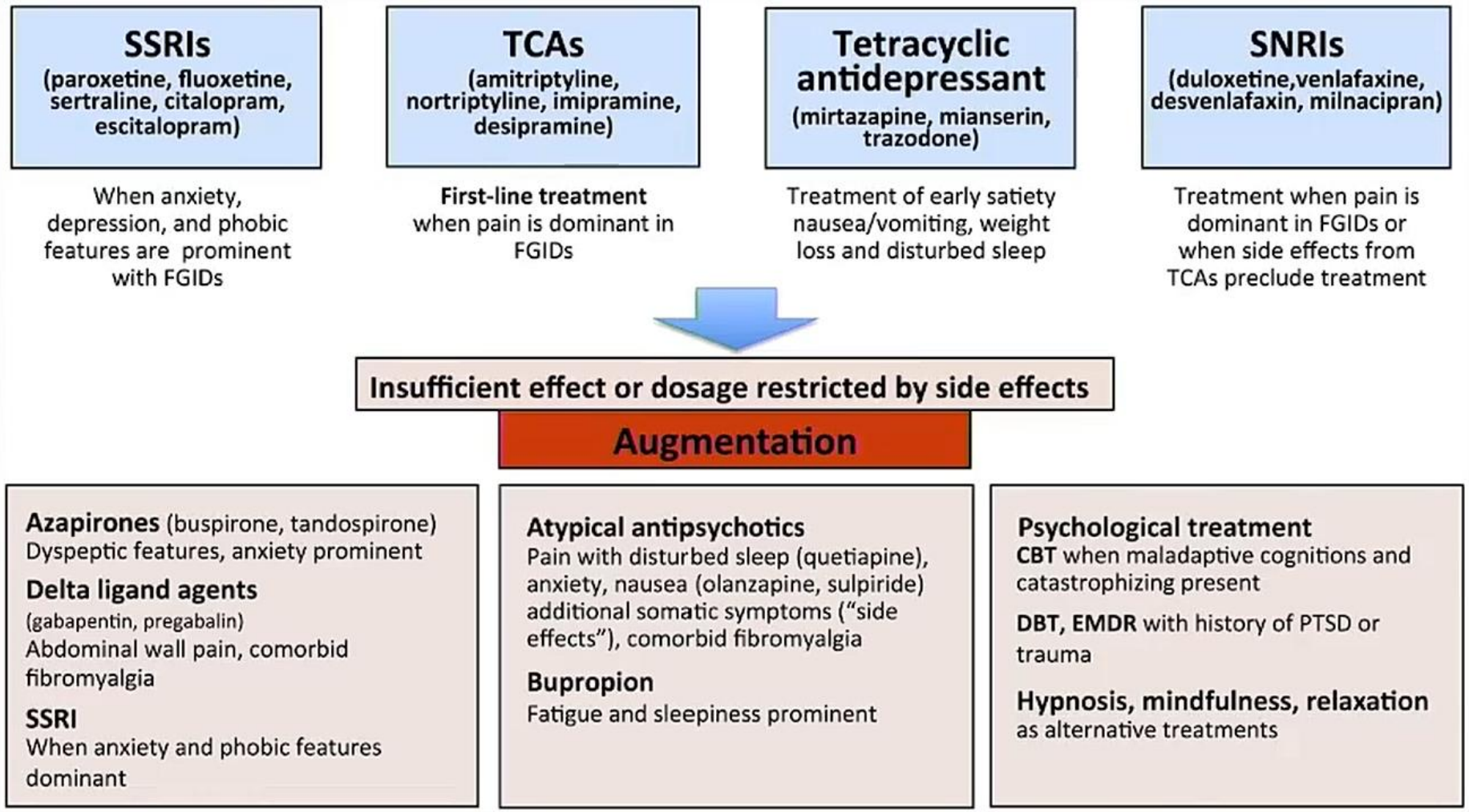
IBS-like symptoms, ulcerative colitis

20-year follow-up (IBSEN cohort)



Henriksen et al J Crohns Colitis 2018

Neuromodulators for disorders of gut-brain interaction



Drossman et al Gastroenterology 2018

Take home massege

- **Diagnosis including extent of disease and biopsy**
- **Movement to separate activity and severity**
- **Induction of clinical response/remission and mucosal healing**
- **Maintenance therapy identified based on induction therapy and prognosis**
- **Screen and treat for anxiety/depressive disorders**
- **Prevention of complications (cancer, hospitalization, infections, other drug-related)**