OUT OF THE SHADOWS:

Starting the Conversation About Bowel Urgency in Patients with Crohn's Disease

This activity is supported by an educational grant from Lilly.

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Marla Dubinsky, MD

Professor of Pediatrics and Medicine
Co-Director, Susan and Leonard Feinstein
IBD Clinical Center
Director, Marie and Barry Lipman IBD
Preconception and Pregnancy Clinic
Icahn School of Medicine Mount Sinai New York
Chief, Division of Pediatric GI and Nutrition
Mount Sinai Kravis Children's Hospital
New York, NY



Tauseef Ali, MD, FACP, FACG, AGAF

Medical Director
SSM Health Crohn's and Colitis Center
Medical Executive Director
SSM Health Digestive Care
Clinical Associate Professor
University of Oklahoma Health Sciences Center
Oklahoma City, OK

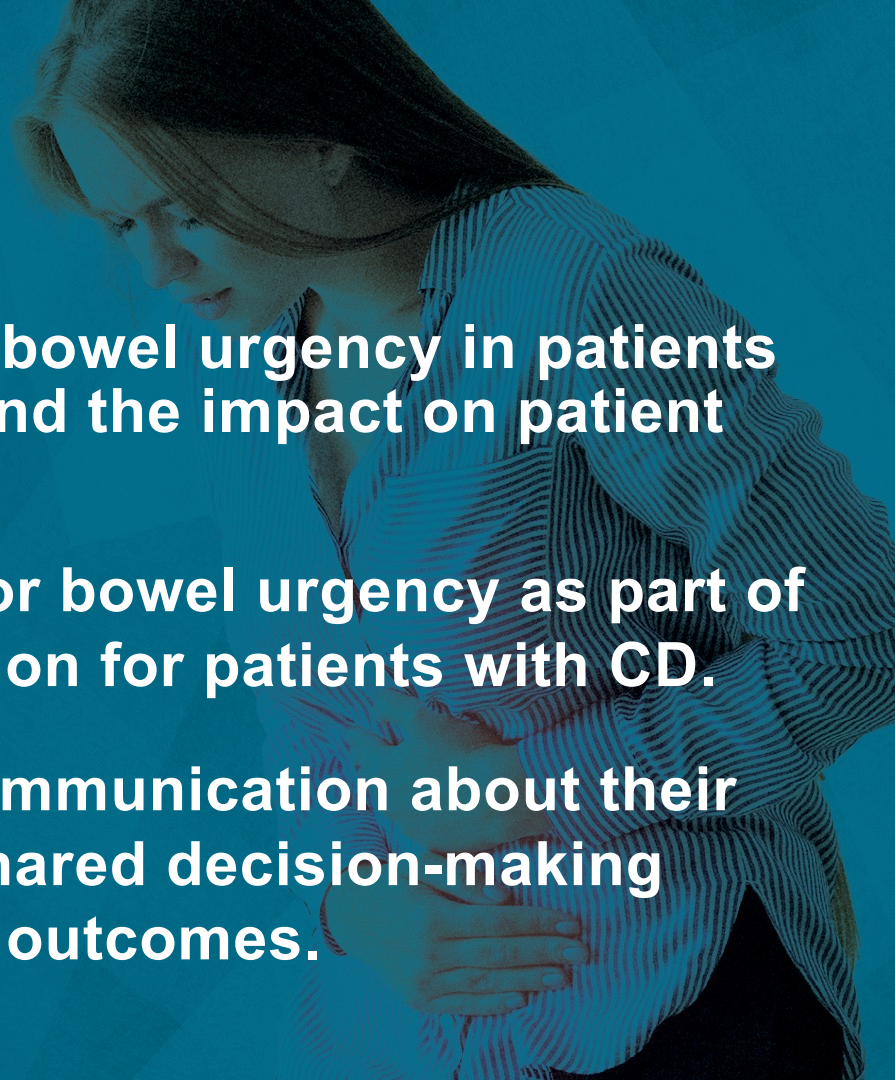


Millie D. Long, MD, MPH

Professor of Medicine
Vice-Chief for Education
Director, Gastroenterology and Hepatology Fellowship Program
Division of Gastroenterology and Hepatology
University of North Carolina
Chapel Hill, NC



LEARNING OBJECTIVES



1. Recognize the frequency of bowel urgency in patients with Crohn's disease (CD) and the impact on patient quality of life (QoL).
2. Incorporate assessments for bowel urgency as part of thorough symptom evaluation for patients with CD.
3. Engage patients in open communication about their bowel urgency as part of shared decision-making in order to improve clinical outcomes.

A patient journey: McCall M.



Patient Case: Susi M., 28 y/o woman



- **HPI:** 28-year-old woman diagnosed with CD 2 years ago; initial treatment with corticosteroids and 5-ASA; transitioned to infliximab 1 year ago
  - Severe Ileal disease at presentation
- **Current treatment:** Infliximab 5 mg/kg every 8 weeks

Patient Statements

"**I can't make it through a shift** at work without using the bathroom 2 or 3 times."

"**I feel exhausted** from having to wake up at night to run to the bathroom."

"I used to love going out with my friends, but it involves so much uncertainty. It's not safe to search for a bathroom when I need one. **It's better not to go out**."

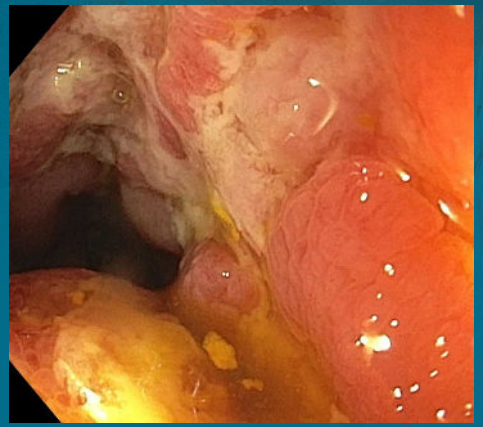
5-ASA = 5-aminosalicylic acid; HPI = history of present illness

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Patient Case: Susi M.



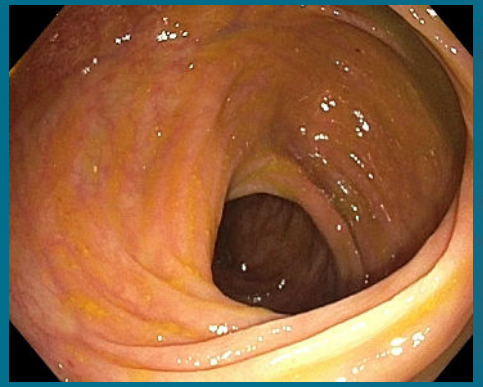
Ileum – severe longitudinal ulcerations





Rectum – normal, only mild hemorrhoids

Colon – normal





Follow up – normal ileum

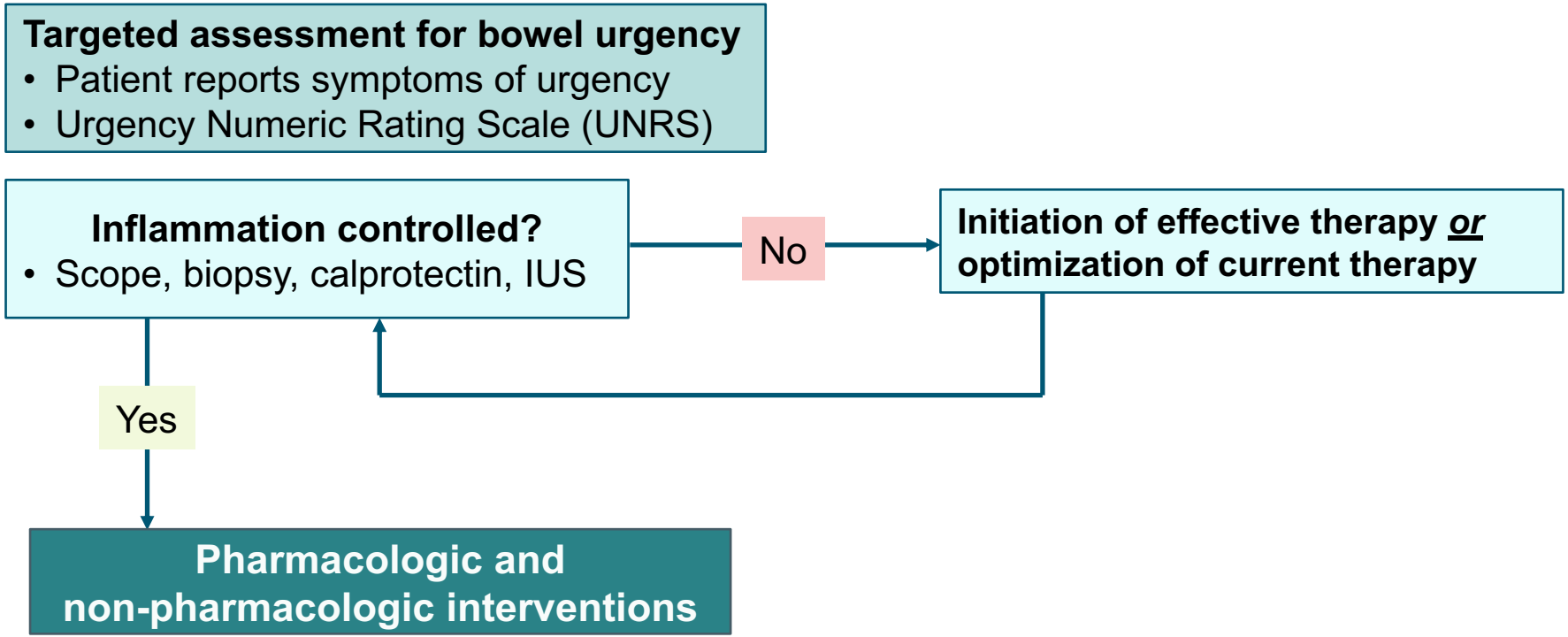
Audience Response

Which of the following is true regarding bowel urgency in patients with CD?

A. Patients reporting normal stool frequency are unlikely to have bowel urgency
B. Patients can expect bowel urgency to resolve with use of any advanced treatment
C. Bowel urgency can occur in both active and quiescent disease
D. Bowl urgency is most commonly due to bile acid malabsorption
E. I don’t know

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Approach to Bowel Urgency



IUS = intestinal ultrasound

Adapted from Caron B, et al. *Clin Gastroenterol Hepatol*. 2023;21(6):1403-1413.e27.

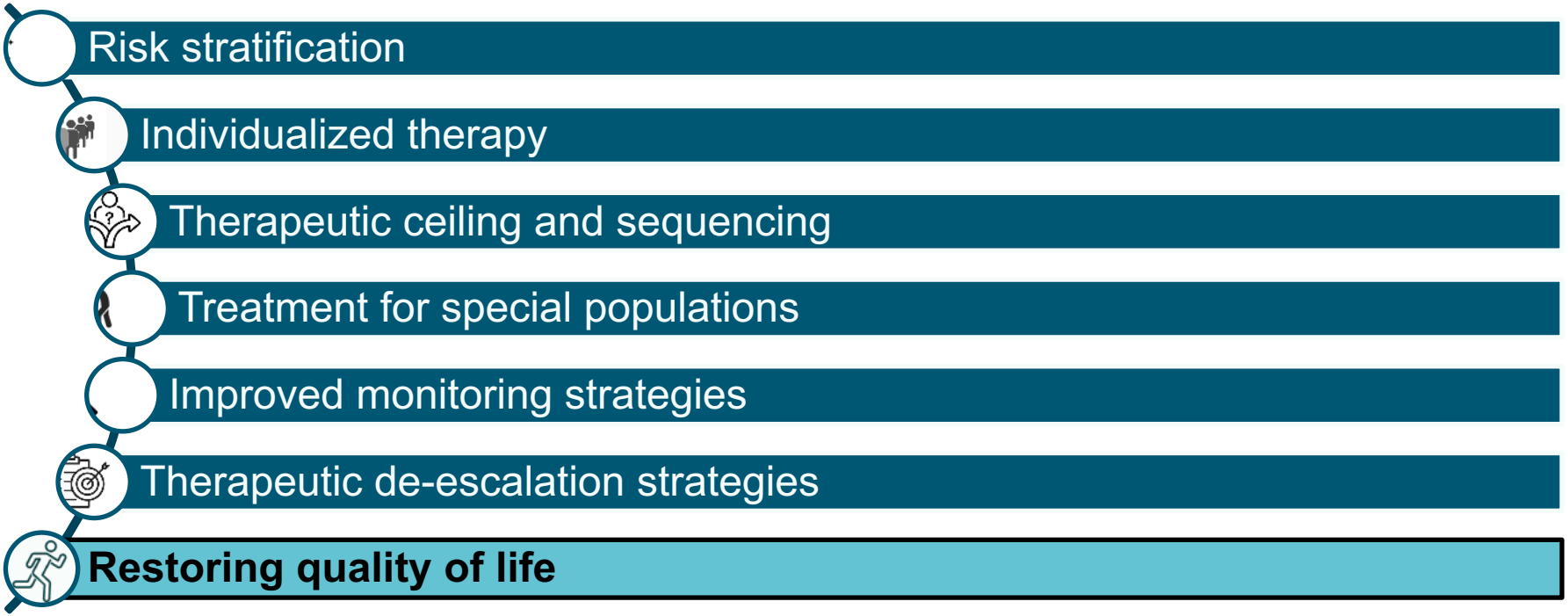
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Symptom Impact in CD



Dr. Long

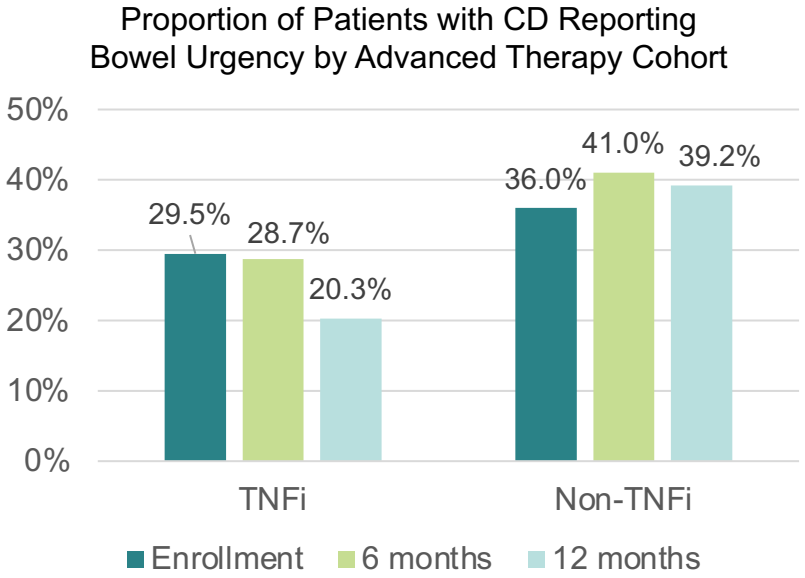
Unmet Needs in Crohn's Disease



Revés J, et al. *Curr Res Pharmacol Drug Discov*. 2021;2:100070.

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Patients with CD Experience Persistent Bowel Urgency Despite Use of Advanced Therapies



Worsening of Bowel Urgency Symptoms

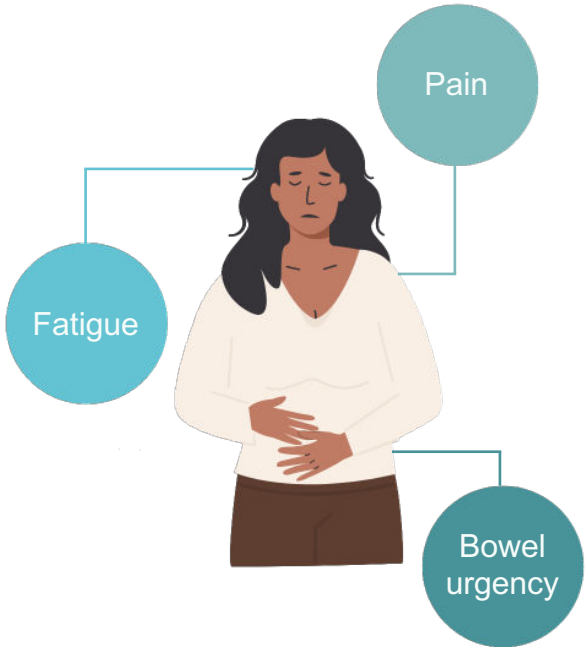
	TNFi N = 332	**Non-TNFi** N = 200
Enrollment to 6 months	21.3%	19.9%
Enrollment to 12 months	21.7%	19.4%

TNFi = tumor necrosis factor inhibitor

Lewis JD, et al. *Am J Gastroenterol*. 2023;118(12S):S7.

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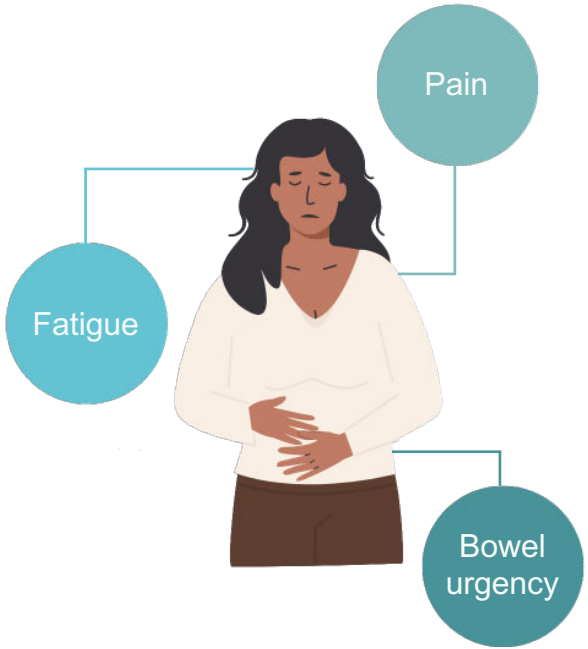
Symptoms Most Impacting QoL in CD



Adapted from Dibley L. et al. *Dig Dis Sci.* 2021; 66(10):3330-3342.

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Symptoms Most Impacting QoL in CD

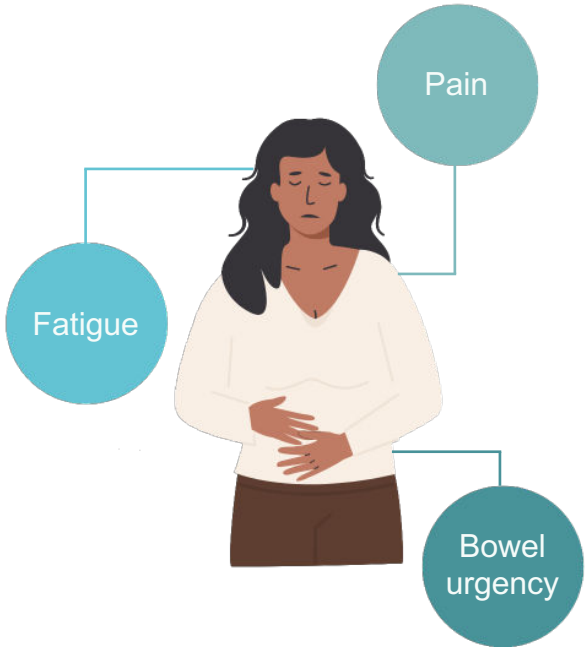


- Multiple aggravators
- Relentless and unpredictable symptoms
- Far-reaching negative impact

Adapted from Dibley L. et al. *Dig Dis Sci.* 2021; 66(10):3330-3342.

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Symptoms Most Impacting QoL in CD



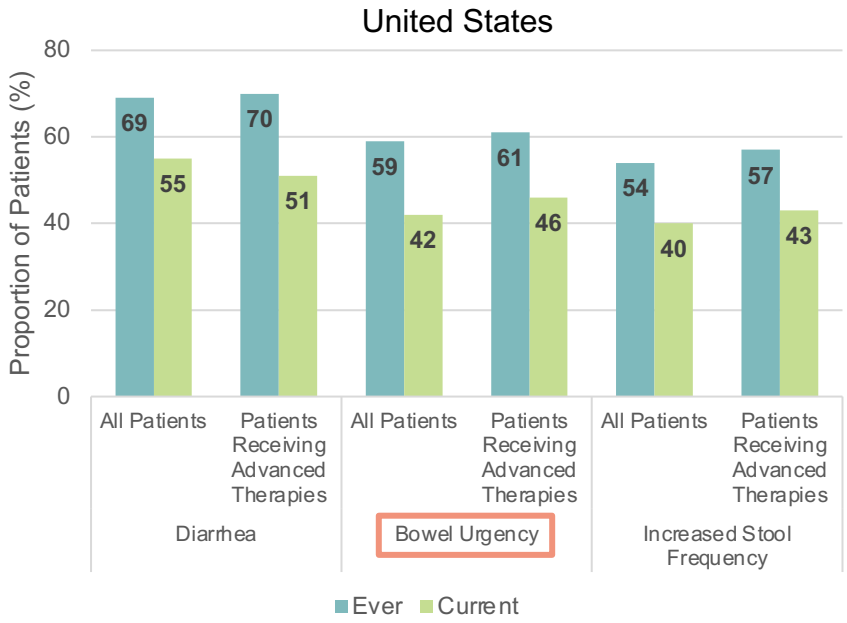
- Multiple aggravators
  - Requires constant planning and adaptation
- Relentless and unpredictable symptoms
  - Creates uncertainty/anxiety
- Far-reaching negative impact
  - Mental health
  - Relationship closeness and intimacy
  - Work or school performance
  - Social isolation and stigma

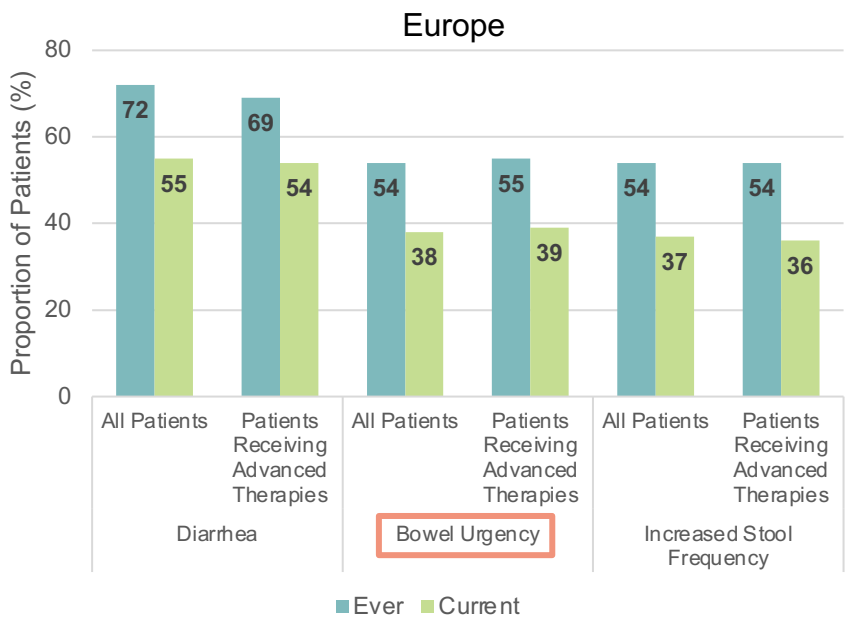
Adapted from Dibley L. et al. *Dig Dis Sci.* 2021; 66(10):3330-3342.

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CONFIDE Survey Results

Bowel urgency was among the top three most frequently reported CD symptoms





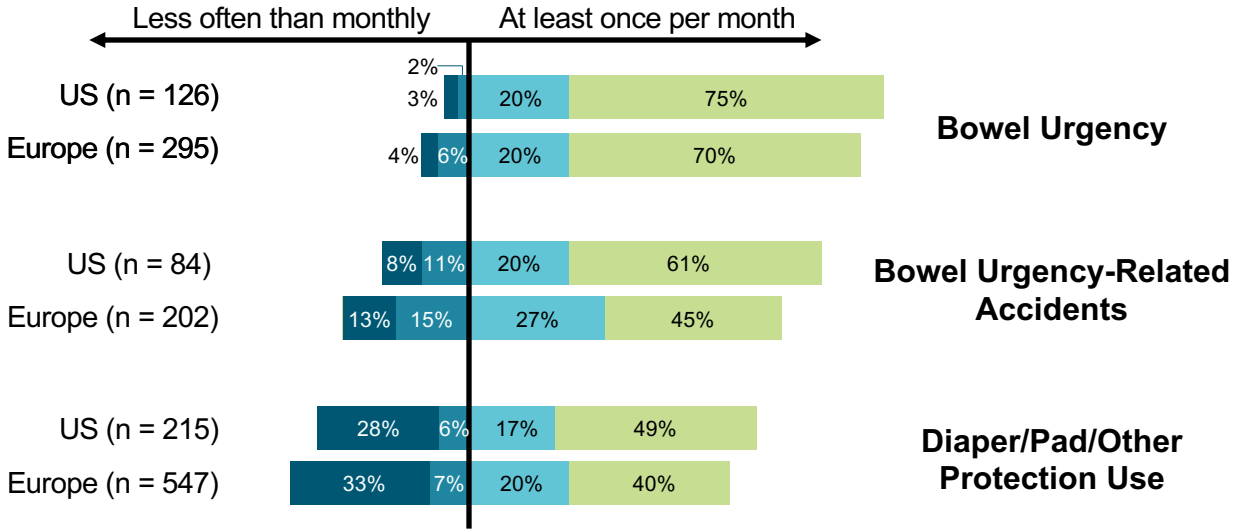
CONFIDE = Communicating Needs and Features of IBD Experiences

Schreiber S, Gibble TH, Dubinsky MC, et al. *Am J Gastroenterol*. 2023;118(10S):S815. https://journals.lww.com/ajg/fulltext/2023/10001/s1070_communication_gap_between_patients_and.1609.aspx.

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CONFIDE Survey Results

Patients with CD



Bowel urgency is just as much of an issue in CD as it is in UC

UC = ulcerative colitis

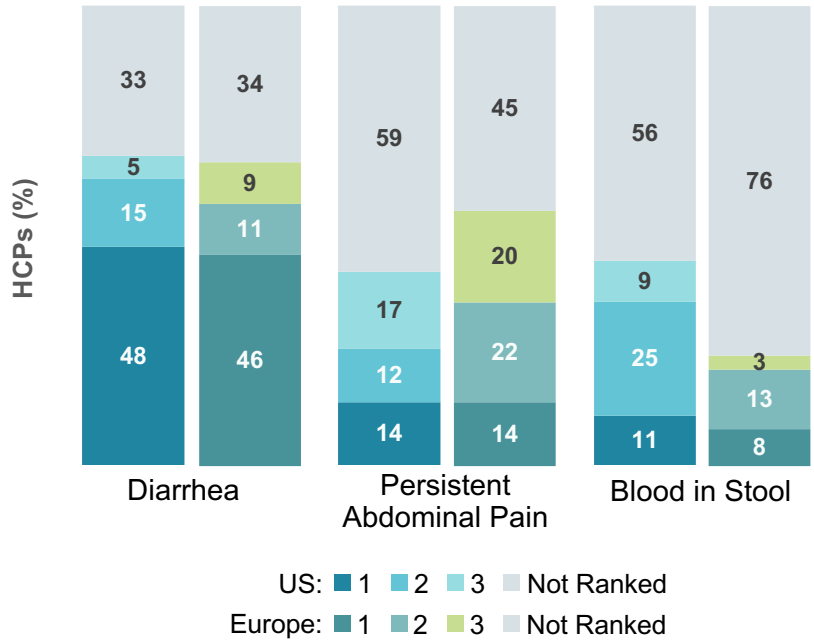
Schreiber S, Gibble TH, Dubinsky MC, et al. *Am J Gastroenterol*. 2023;118(10S):S815.
https://journals.lww.com/ajg/fulltext/2023/10001/s1070_communication_gap_between_patients_and.1609.aspx.

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CONFIDE Survey Results

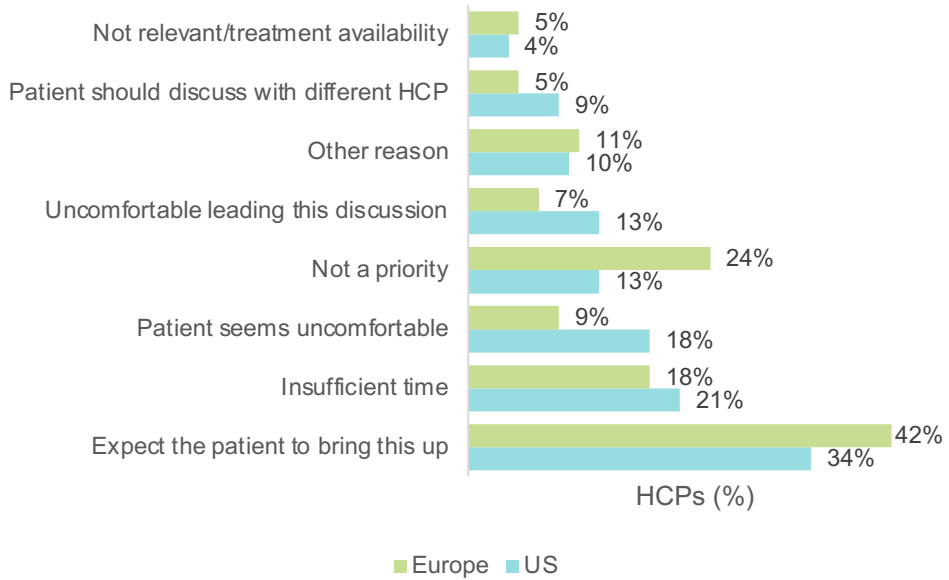
81% of US and 85% of European HCPs **did not rank bowel urgency** among the symptoms most reported by patients

Ranking of HCP-perceived top three CD symptoms reported by patients



HCPs **do not proactively discuss bowel urgency and bowel urgency-related accidents** with patients

HCP-reported reasons for not proactively discussing bowel urgency



HCPs = health care professionals

Schreiber S, Gibble TH, Dubinsky MC, et al. *Am J Gastroenterol*. 2023;118(10S):S815.
https://journals.lww.com/ajg/fulltext/2023/10001/s1070_communication_gap_between_patients_and.1609.aspx.

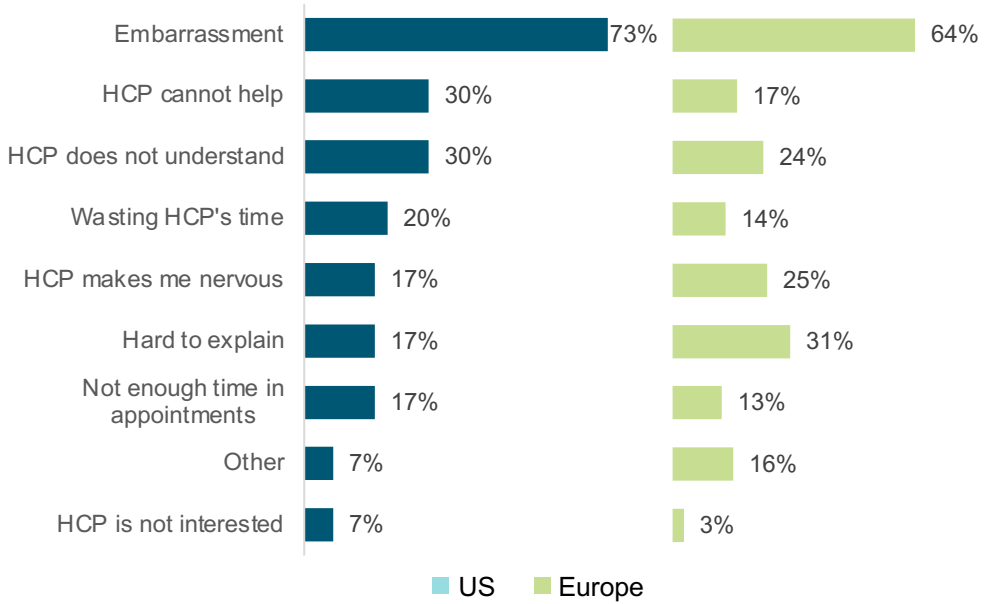
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CONFIDE Survey Results

- **Embarrassment was the most common reason** for patient discomfort in discussing bowel urgency and bowel urgency–related accidents with HCPs

- Only **40% of US** and **27% of European patients** were completely comfortable discussing bowel urgency with their HCPs

Patient-reported reasons for not feeling comfortable discussing bowel urgency



Schreiber S, Gibble TH, Dubinsky MC, et al. *Am J Gastroenterol*. 2023;118(10S):S815. https://journals.lww.com/ajg/fulltext/2023/10001/s1070_communication_gap_between_patients_and.1609.aspx.

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Impact of IBD on Daily Activity

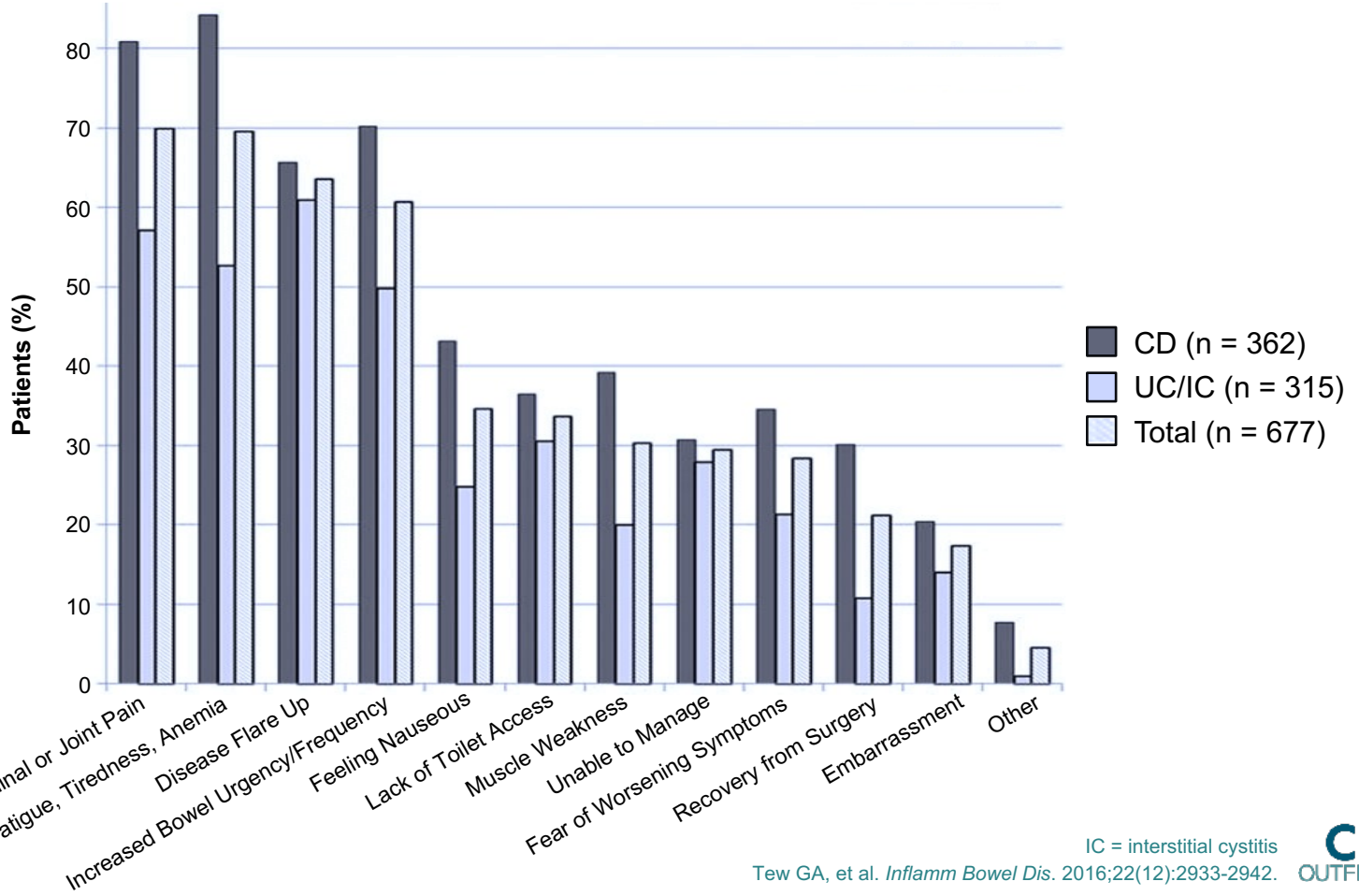
- 79% of patients limited physical activity
- 34% reported *avoiding* running or jogging
- Reasons for limited activity
  - 70% fatigue/tiredness
  - 69% disease flare-ups
  - 61% increased toilet urgency

IBD = inflammatory bowel disease

Tew GA, et al. *Inflamm Bowel Dis*. 2016;22(12):2933-2942.

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Reasons for Avoiding Activity in IBD

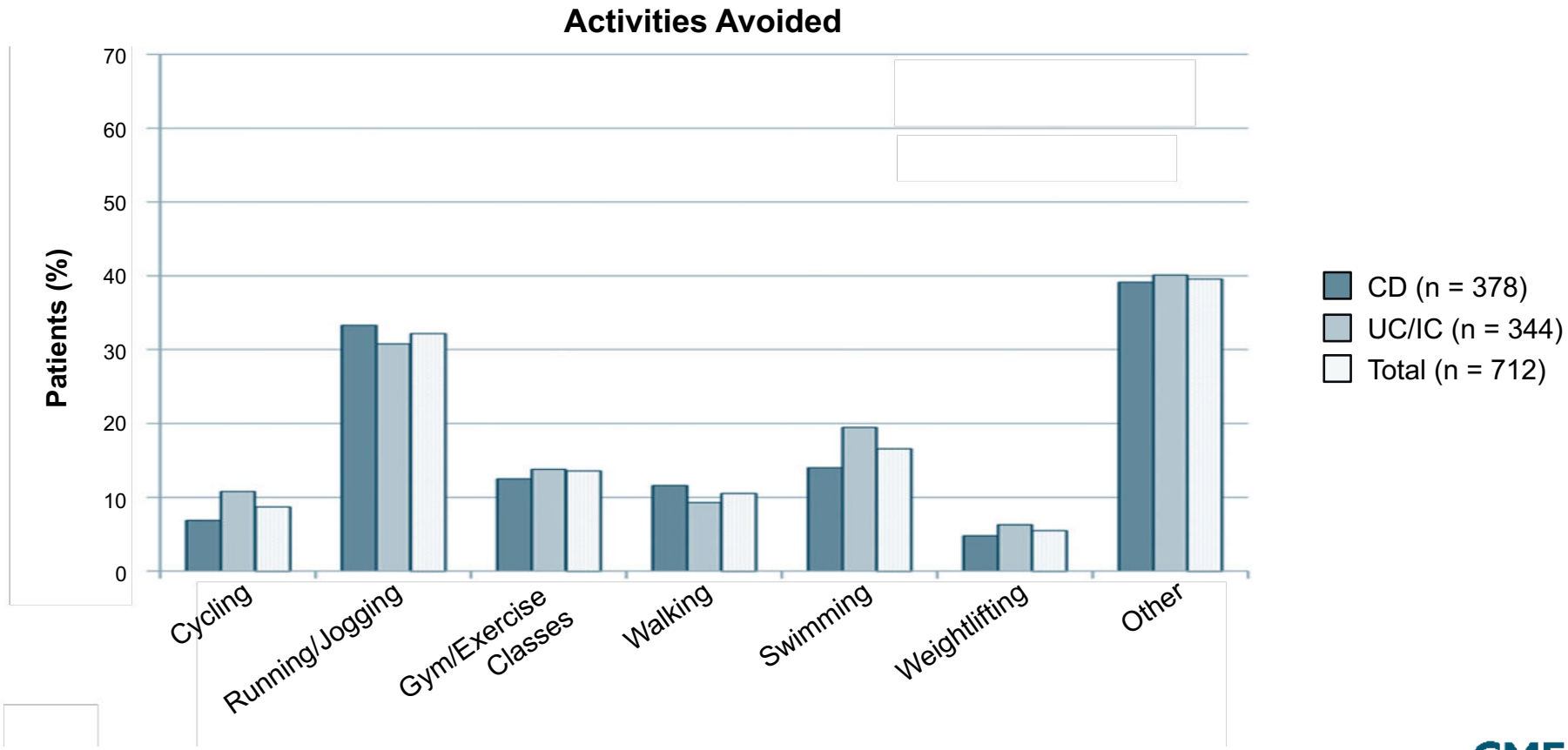


IC = interstitial cystitis

Tew GA, et al. *Inflamm Bowel Dis*. 2016;22(12):2933-2942.

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Activity Adaptation in IBD

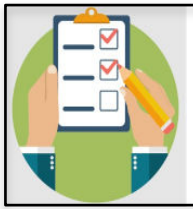


Tew GA, et al. *Inflamm Bowel Dis*. 2016;22(12):2933-2942.

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IBD and Sexual Health

- Sexual functioning, satisfaction, and sexual drive can be negatively impacted by IBD and can impact QoL



Survey of 426 gastroenterologists

70% never or rarely ask patients about sexual dysfunction

75% did not change treatment if a patient reported sexual dysfunction

Gastroenterology survey reported barriers to addressing sexual dysfunction during appointments

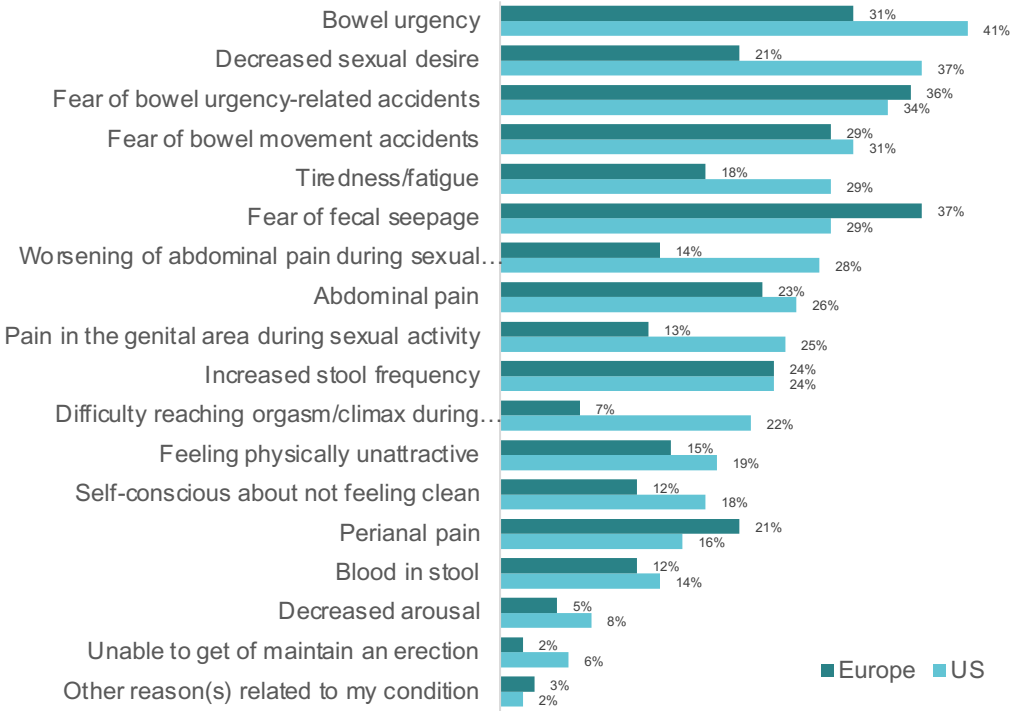
- Lack of knowledge (80%)
- Lack of experience (58%)
- Lack of time (44%)
- Embarrassment (30%)

Romano L, et al. *Dig Liver Dis*. 2022;54(11):1494-1501. Mantzouranis G. *J Crohns Colitis*. 2015;9(12):1160-1168.

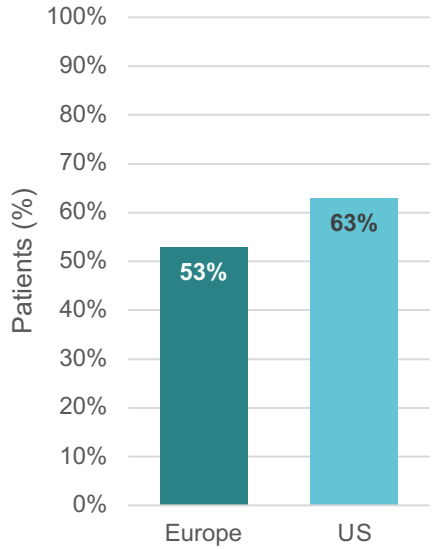
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Impact of Bowel Urgency on Sexual Activity

Patient-provided reasons for avoiding or decreasing sexual activity



Patients who avoided or decreased sexual activity in the last 3 months



Dubinsky MC, et al. United States and European patient perspectives on the impact of moderate-to-severe ulcerative colitis on sexual activity: Communicating Needs and Features of IBD Experiences (CONFIDE) survey. Abstract 1139. Presented at DDW; May 2023.

CME OUTFITTERS

MUSIC Study: Significant Proportion of Patients with CD Reported Bowel Urgency

Characteristic	Bowel Urgency (UNRS 2–10)* n = 883	No or Minimal Bowel Urgency (UNRS 0–1)* n = 650	*P* Value**
Age (years), mean (SD)	54.1 (15.5)	53.4 (16.1)	.320
Female gender, n (%)	632 (73)	452 (70)	.290
Education (> high school), n (%)	789 (89)	601 (92)	.039
Caucasian (White), n (%)	789 (89)	592 (91)	-
Current smoking (yes), n (%)	29 (3)	11 (2)	.053
Body mass index, mean (SD)	26.8 (6.3)	25.3 (4.9)	< .001
Disease duration (years), mean (SD)	25.7 (14.1)	23.7 (13.7)	.003
Ever GI surgery (yes), n (%)	540 (61)	311 (48)	< .001
Ever GI hospitalization (yes), n (%)	649 (73)	417 (64)	< .001
Number hospitalizations, mean (SD)	3.9 (2.6)	3.1 (2.3)	< .001
Remission (yes), n (%)	544 (62)	599 (92)	< .001

58% of patients reported bowel urgency

Bowel urgency was higher among patients with active disease as compared to those in remission

(87% vs 48%, $p < .001$)

*Urgency was measured using 11-point UNRS: 0-1 = no minimal bowel urgency, 2-10 = bowel urgency

**Chi-square test was used to compare no or minimal bowel urgency vs bowel urgency for each of the categorical variables and t-test was used for continuous variables

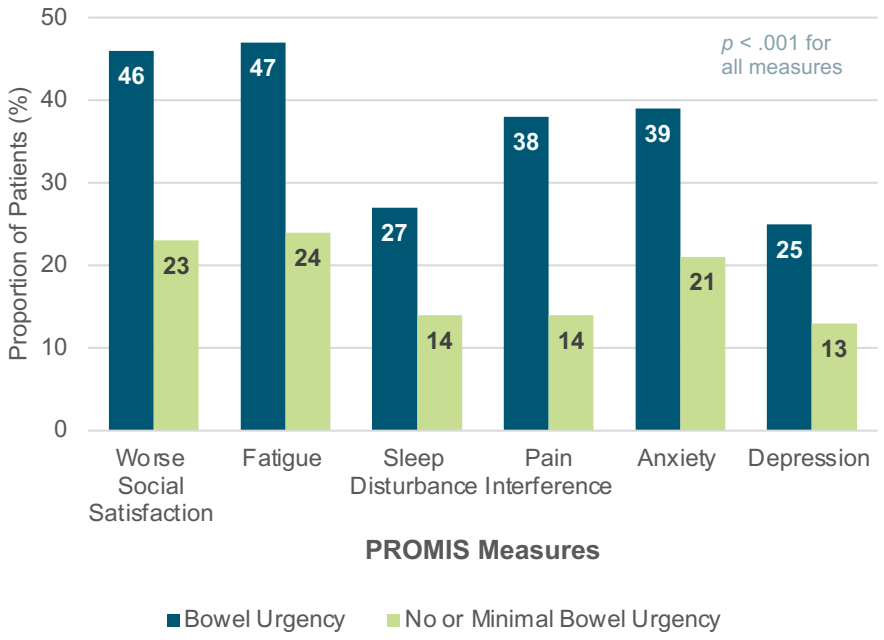
GI = gastrointestinal; SD = standard deviation

Long MD, et al. Prevalence of bowel urgency and its association with quality of life in a real-world Crohn's disease population: results from the Measuring Urgency Symptoms in Inflammatory Bowel Disease Collaboration (MUSIC) study. Poster presented at ACG; October 2023.

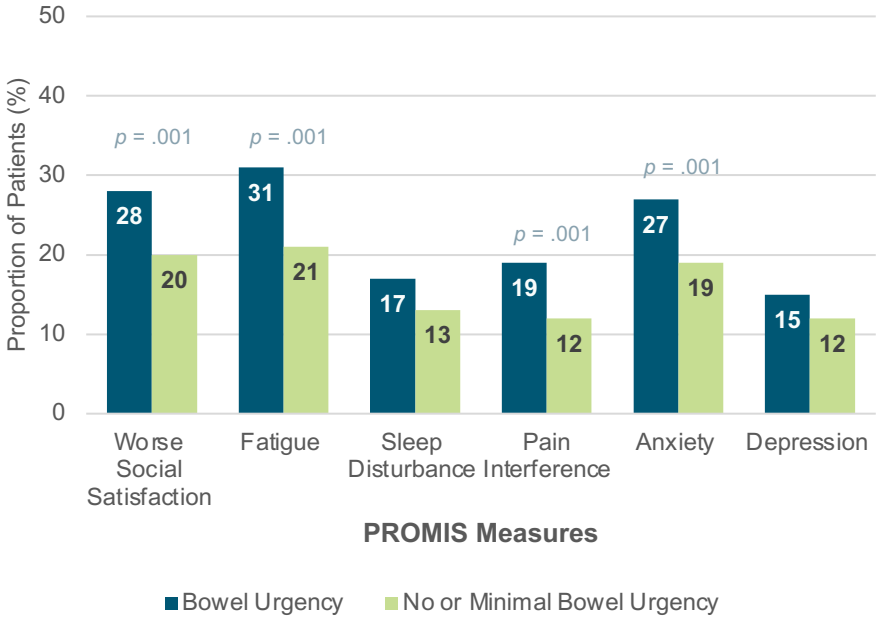
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MUSIC Study: Bowel Urgency Negatively Impacted Quality of Life in CD

Patients with bowel urgency had significantly worse quality of life



Of those in remission, bowel urgency was significantly associated with anxiety, pain, fatigue, and worse social satisfaction



Long MD, et al. Prevalence of bowel urgency and its association with quality of life in a real-world Crohn's disease population: results from the Measuring Urgency Symptoms in Inflammatory Bowel Disease Collaboration (MUSIC) study. Poster presented at ACG; October 2023.

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The impact of bowel urgency: McCall M.



Assessments for Bowel Urgency



Dr. Dubinsky

Audience Response

Which of the following assessments captures bowel urgency impact in patients with CD?

A. CDAI
B. HBI
C. UNRS
D. IBDQ
E. I don’t know

Defining Bowel Urgency

Definition Use in Study	N
Inability to defer defecation for more than 15 minutes	4
No definition	20
Not making it to the toilet in time	1
Immediate need to defecate	1
Hurry to/immediately go to the bathroom/unable to make it in time	1
Simple Clinical Colitis Activity Index (SCCAI) definition	2
Having to rush to the toilet to avoid an accident	1
Sudden and severe urge to defecate	1
Inability to defer defecation for more than 5 minutes after the first call to stool	2
Having to urgently visit the toilet to pass stool	1
Urgency to go to the bathroom	1
An irresistible and urgent desire to defecate	1

Caron B, et al. *Clin Gastroenterol Hepatol*. 2023;21(6):1403-1413.e27.

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Barriers to Identifying Bowel Urgency in Patients with CD

Does normal stool frequency mean no bowel urgency?



55% of patients report urgency symptoms with no change in stool frequency



Dibley L, Norton C. *Inflamm Bowel Dis*. 2013;19(7):1450-1462. Dubinsky MC, et al. *Qual Life Res*. 2023;32(12):3403-3415.

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Commonly Used CD Disease Activity Indices

- Clinical Disease Activity Index (CDAI)
- Harvey-Bradshaw Index (HBI)
- Inflammatory Bowel Disease Questionnaire (IBDQ)
- Patient reported outcome-2 (PRO- 2)

Di Palma JA, Farraye FA. *Gastroenterol Hepatol (N Y)*. 2011;7(3):163-169.

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Commonly Used CD Disease Activity Indices

- Clinical Disease Activity Index (CDAI)
- Harvey-Bradshaw Index (HBI)
- Inflammatory Bowel Disease Questionnaire (IBDQ)
- Patient reported outcome-2 (PRO- 2)

None of the commonly used scales capture bowel urgency severity

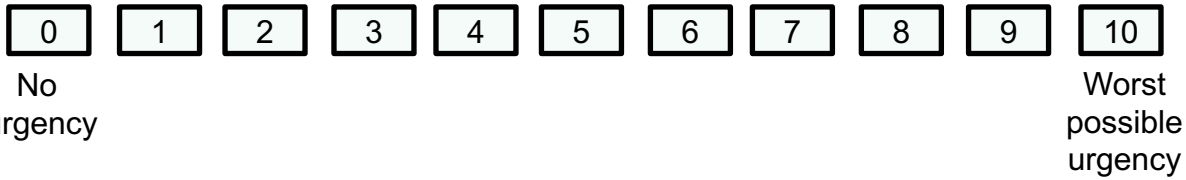
Di Palma JA, Farraye FA. *Gastroenterol Hepatol (N Y)*. 2011;7(3):163-169.

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The Urgency Numeric Rating Scale (UNRS)

Patients with UC have indicated that it is important to have a bowel urgency scale that distinguishes between different levels of severity instead of just a yes or no[1]

How severe was your urgency (sudden or immediate need) to have a bowel movement in the past 24 hours?



Patients report the severity of their bowel urgency symptoms over the past 24 hours

- Weekly average scores are calculated as mean score over a 7-day period
- Higher scores indicate worse urgency severity (e.g., immediacy of need to have a bowel movement)

The UNRS was used in the mirikizumab phase III studies to assess bowel urgency whereas the upadacitinib phase III studies used a yes/no binary scale[2,3]

1. Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6(1):31. 2. Danese S, et al. *Lancet*. 2022;399:2113-2128.
3. D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455.

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Urgency and Association with QoL and Clinical Outcomes in UC

Cross-sectional and Longitudinal Study

- Urgency is independently associated with a higher risk of depression, anxiety, and social impairment
- **Urgency is associated with a significant increase in risk of hospitalizations, corticosteroid use, and colectomy over 12-month follow-up**

Urgency responses*	OR for depression/anxiety vs no hurry (95% CI)
Hurry	Depression: 3.03 (1.82–5.15) Anxiety: 2.15 (1.40–3.30)
Immediately	Depression: 2.3 (0.84–5.99) Anxiety: 1.53 (0.63–3.62)
Incontinence	Depression: 13.7 (2.95–68.0) Anxiety: 5.45 (1.21–26.5)
Urgency responses*	**OR of social impairment vs no hurry (95% CI)**
Hurry	2.05 (1.24–3.40)
Immediately	2.76 (1.10–6.77)
Incontinence	7.7 (1.66–38.3)

*After adjusting for clinical variables

CI = confidence interval; OR = odds ratio

Sninsky JA, et al. *Am J Gastroenterol*. 2022;117:769-776.

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Second N-ECCO Consensus Statements in Caring for Patients With IBD

"A major life impact is the **need to be near a toilet**. **Urgency** can be severe, with some patients reporting less than 30 seconds between calls to stool and actual defecations. Fear of losing bowel control is so great that some patients always worry about where the nearest toilet is."

"Recent evidence suggests that, at some point of the disease course, between 31% and 74% of people with IBD experience fecal incontinence, not necessarily related to disease activity. **Despite it being a major concern, incontinence is rarely reported to or addressed by clinicians.**"

N-ECCO = Nurses European Crohn's and Colitis Organisation

Kemp K, et al. *J Crohns Colitis*. 2018;12:760-776.

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Third European Consensus on Diagnosis and Management of UC, ACG Guidelines, and FDA Guidance for Developing New Drugs

ECCO: Medical history statement 3C[1]

A full medical history should include detailed questioning about the onset of symptoms, rectal bleeding, stool consistency and frequency, **urgency**, tenesmus, abdominal pain, incontinence, nocturnal diarrhea, and extraintestinal manifestations. Recent travel, possible contact with enteric infectious illnesses, medication [including antibiotics and non-steroidal anti-inflammatory drugs], smoking habit, sexual behavior, family history of inflammatory bowel disease or colorectal cancer, and previous appendectomy should be recorded [EL5].

ACG: Goals for managing patients with UC[2]

Initial treatment of UC should focus on restoration of normal bowel frequency and control of the primary symptoms of bleeding and **urgency**. An endoscopically healed mucosa is associated with sustained remission and reduced risk of colectomy.

FDA: Draft Guidance for UC encourages the exploration of additional symptoms of UC identified by patients as important, but that are not currently captured by the modified Mayo Score, such as **bowel urgency**[3]

ACG = American College of Gastroenterology; ECCO = European Crohn's and Colitis Organisation; FDA = U.S. Food and Drug Administration

1. Magro F, et al. *J Crohns Colitis*. 2017;11:649-670. 2. Rubin DT, et al. *Am J Gastroenterol*. 2019;114:384-413.
3. UC: developing drugs for treatment. FDA.gov Website. 2022. www.fda.gov/media/158016/download.

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Assessment of Bowel Urgency: Patient-Reported Outcomes

FDA and EMA have recommended that clinical parameters, endoscopic findings, and patient-reported symptoms be separately quantified and reported in IBD trials



PRO tools developed per FDA guidance that include measures of urgency

- Symptoms and Impacts Questionnaire for UC (SIQ-UC)
- Ulcerative Colitis Patient-Reported Outcomes Signs and Symptoms (UC-PRO/SS) diary
- UNRS

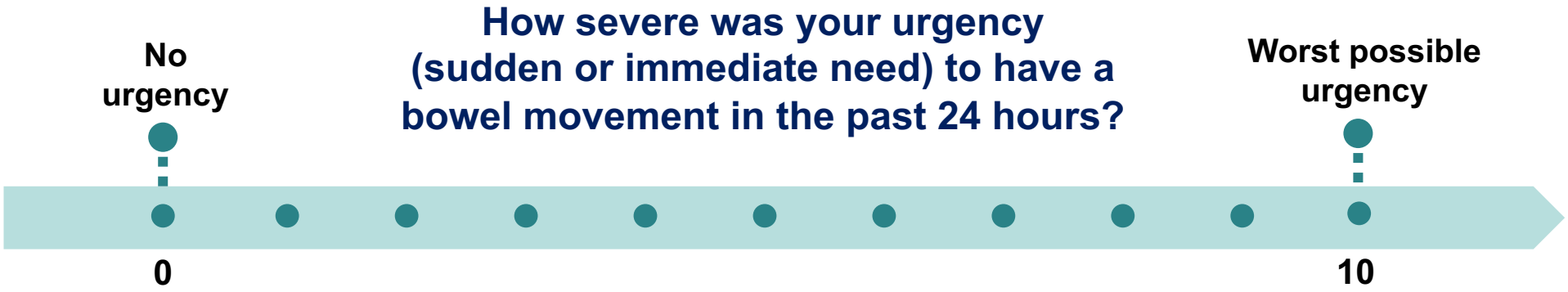
***Note:** Apart from the UNRS, the other PROs listed include multiple items and measure symptoms assessed by traditionally used scales (e.g., Mayo Score, SCCAI, pSCCAI) and therefore may be duplicative*

EMA = European Medicines Agency; PRO = patient-reported outcome; pSCCAI = Patient Simple Clinical Colitis Activity Index

Patient-reported outcome measures. FDA.gov Website. 2009. www.fda.gov/media/77832/download. Dulai PS, et al. *Aliment Pharmacol Ther.* 2020;51:1047-1066. Higgins PDR, et al. *J Patient Rep Outcomes*. 2017;2:26. Dubinsky MC, et al. *J Patient Rep Outcomes.* 2022;6:31. Ghosh S, et al. *J Crohns Co*litis. 2021;15:228-237.

CME OUTFITTERS

Recent Innovations: Urgency Score for Adults with UC



Urgency Score

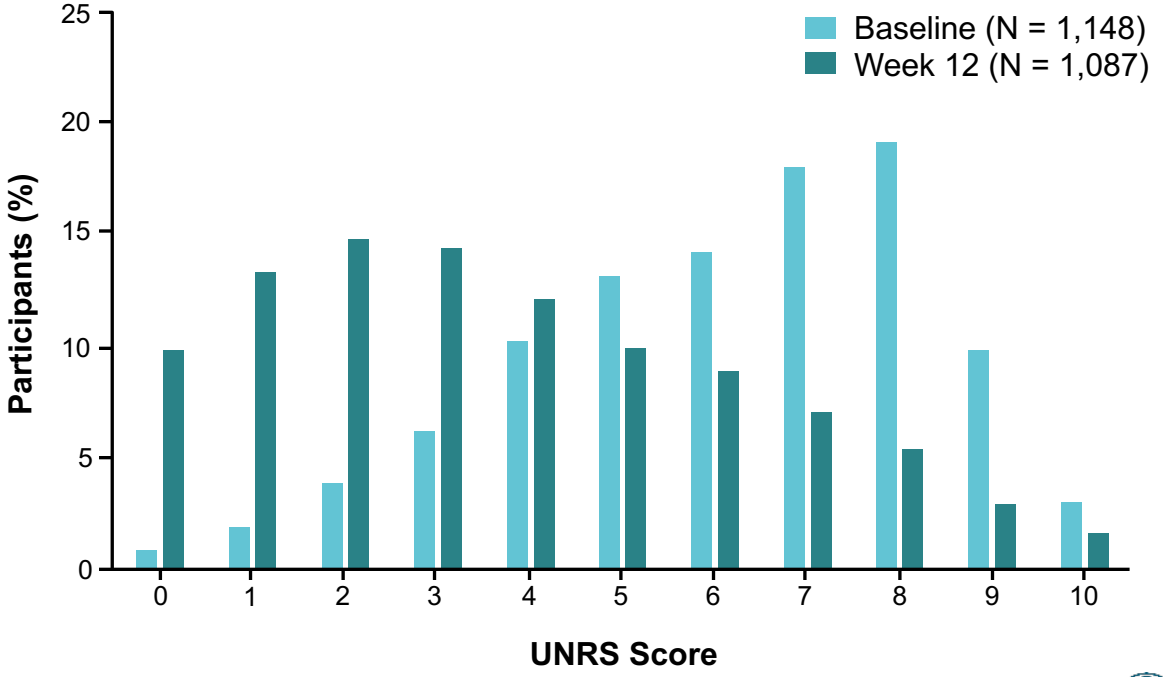
- Bowel urgency is a district symptom of UC
- Urgency score is correlated:
  - highly with patient global rating of severity scores
  - moderately with stool frequency

Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6:31.

CME OUTFITTERS

Psychometric Evaluation of UNRS: UNRS Score Distributions

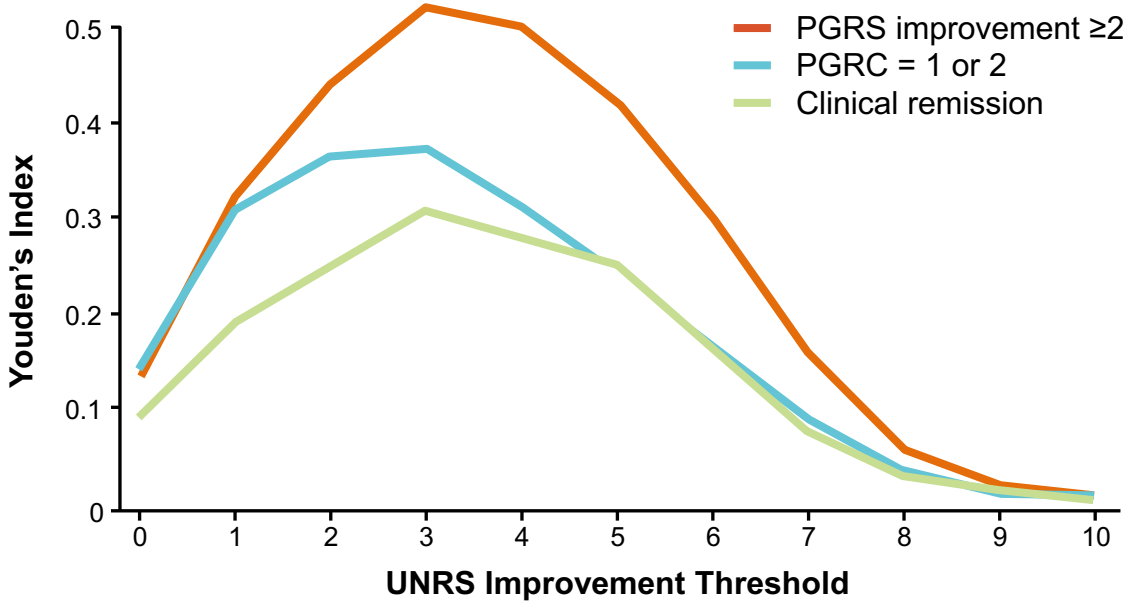
- Participants registered full range of weekly average UNRS scores (0 to 10) at baseline and at Week 12
- Mean UNRS score was higher (worse) at baseline than at Week 12 (6.2 vs 3.7)
- Weekly averages were appropriate to summarize daily UNRS scores



Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6:114.

CME OUTFITTERS

Psychometric Evaluation of UNRS Meaningful Within: Patient Improvement from Baseline



≥3-point improvement on UNRS yields best balance between sensitivity and specificity of any UNRS threshold at identifying large improvement in overall symptom severity

Youden's Index from an anchor-based analysis of improvement in UNRS from baseline to week 12
Clinical remission was defined as Mayo stool frequency subscore of 0, or 1 with a ≥1-point decrease from baseline; a Mayo rectal bleeding subscore of 0; and a Mayo endoscopic subscore of 0 or 1 (excluding friability)

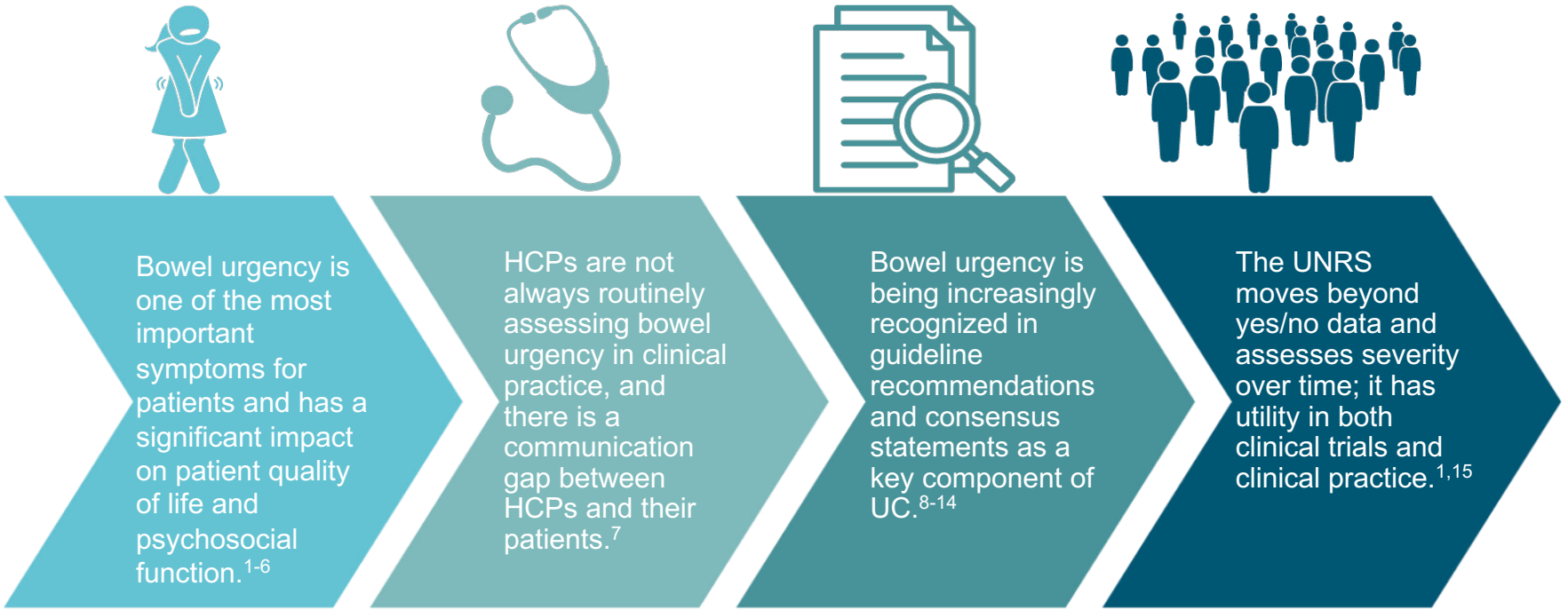
≥3-point improvement on UNRS yields best balance between sensitivity and specificity of any UNRS threshold at identifying large improvement in overall symptom severity

PGRC = Patient Global Rating of Change; PGRS = Patient Global Rating of Severity

Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6:114.

CME OUTFITTERS

Why Bowel Urgency Matters: Summary



1. Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6:31. 2. Petryszyn PW, Paradowski L. *Adv Clin Exp Med*. 2018;27:813-818. 3. Ghosh S, et al. *J Crohns Colitis*, 2019;13(suppl 1):S240-S241 (Abstract P283). 4. Rasmussen B, et al. *Scand J Gastroenterol*. 2020;55:656-663. 5. Rubin DT, et al. *Inflamm Bowel Dis*. 2021;27:1942-1953. 6. Ueno F, et al. *J Gastroenterol*. 2017;52:555-567. 7. Rubin D, et al. *Am J Gastroenterol*. 2021;116(suppl 7);S7 (Abstract P028). 8. Rubin DT, et al. *Am J Gastroenterol*. 2019;114:384-413. 9. Ananthakrishnan AN, et al. *Gastroenterology*. 2021;160:445-451. 10. Bernstein CN, et al. *J Clin Gastroenterol*. 2016;50:803-818. 11. Magro F, et al. *J Crohns Colitis*. 2017;11:649-670. 12. Kemp K, et al. *J Crohns Colitis*. 2018;12:760-776. 13. NICE Guideline NG130 ulcerative colitis. National Institutes for Health and Care Excellence (NICE) Website. 2019. https://www.nice.org.uk/guidance/ng130. 14. Lamb CA, et al. *Gut*. 2019;68(suppl 3):s1-s106. 15. Surti B, et al. *Dig Dis Sci*. 2013;58:1313-1321.

CME OUTFITTERS

Treatment Planning



Dr. Ali

What success means to me:

McCall M.



Patient Case: Susi M. (continued)



Urgency-Related Symptoms

"**I can't make it through a shift** at work without using the bathroom 2 or 3 times."

"**I feel exhausted** from having to wake up at night to run to the bathroom."

"I used to love going out with my friends, but it involves so much uncertainty. It's not safe to search for a bathroom when I need one. **It's better not to go out**."

Patient Treatment Goals

Work an 8-hour shift with a maximum of **1 or 2 *planned*** restroom breaks

Wake up to use the restroom **less than 1x** per week

Attend social events with friends. Start with a **goal of 1 hour** without disruptive symptoms

CME OUTFITTERS

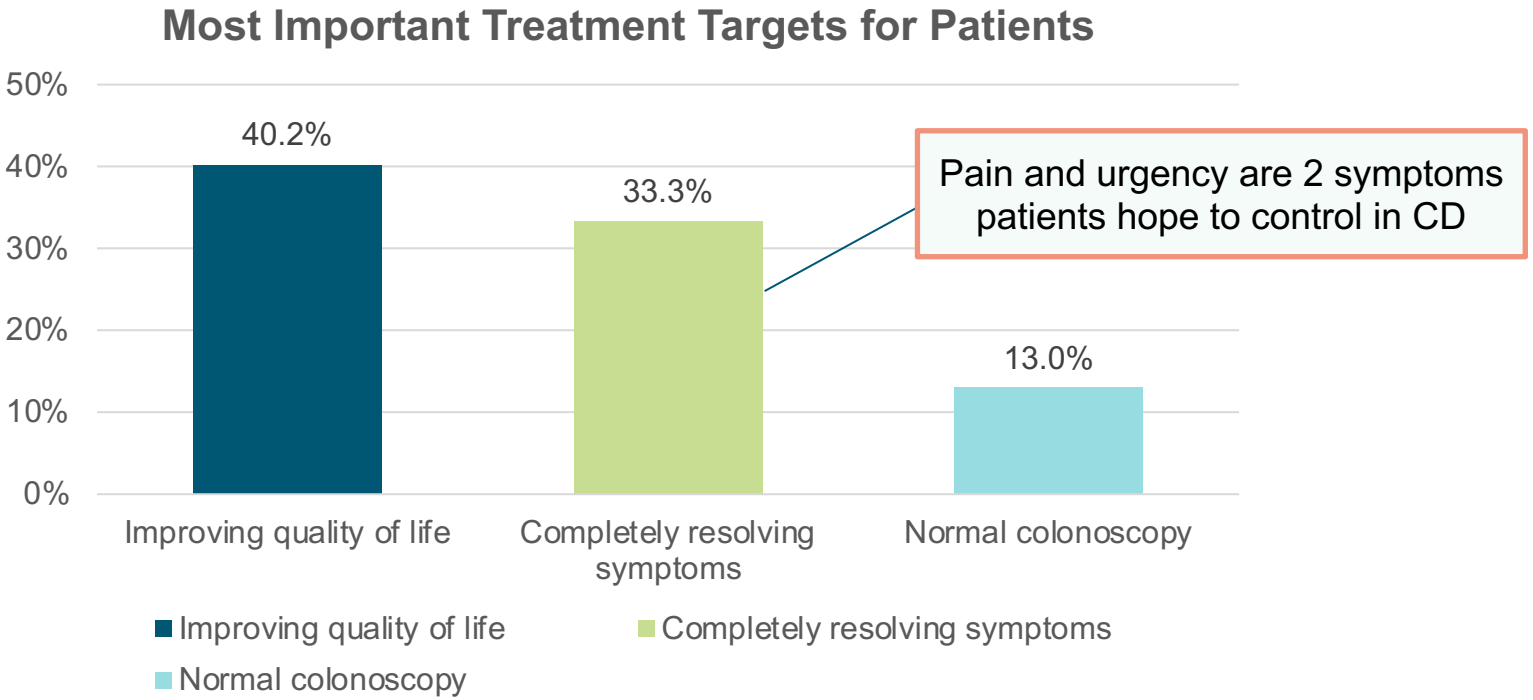
Audience Response

Abnormal anorectal physiology has been seen in which patient populations with CD?

A. Patients with an IPAA
B. All patients with CD
C. Patients with bile acid malabsorption
D. Patients with active inflammation
E. I don’t know

CME OUTFITTERS

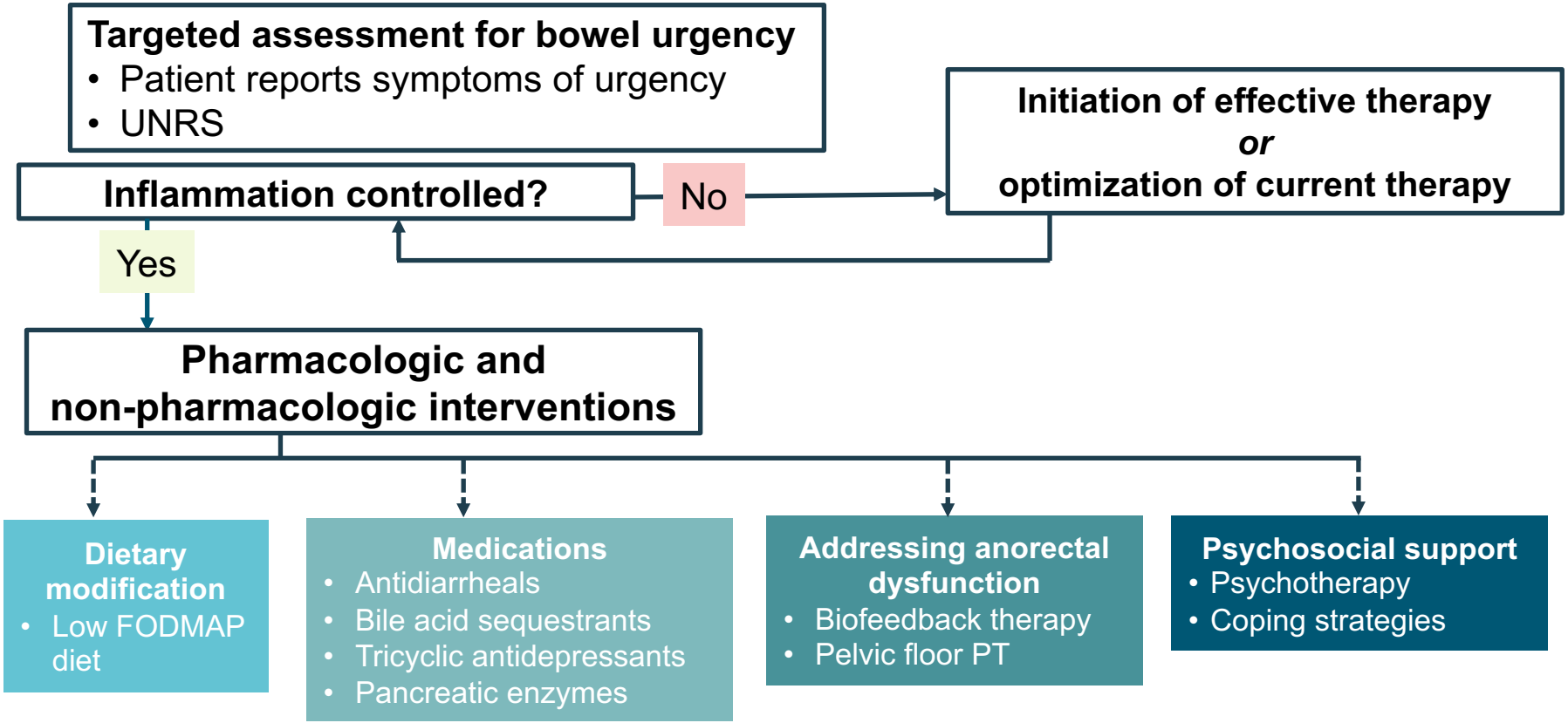
Patients with CD Most Want Pain and Urgency to Improve with Treatment



Casellas F, et al. *Dig Liver Dis*. 2017;49(2):152-156.

CME OUTFITTERS

Approach to Bowel Urgency



FODMAP = fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; PT = physical therapy

Adapted from Caron B, et al. *Clin Gastroenterol Hepatol*. 2023;21(6):1403-1413.e27.

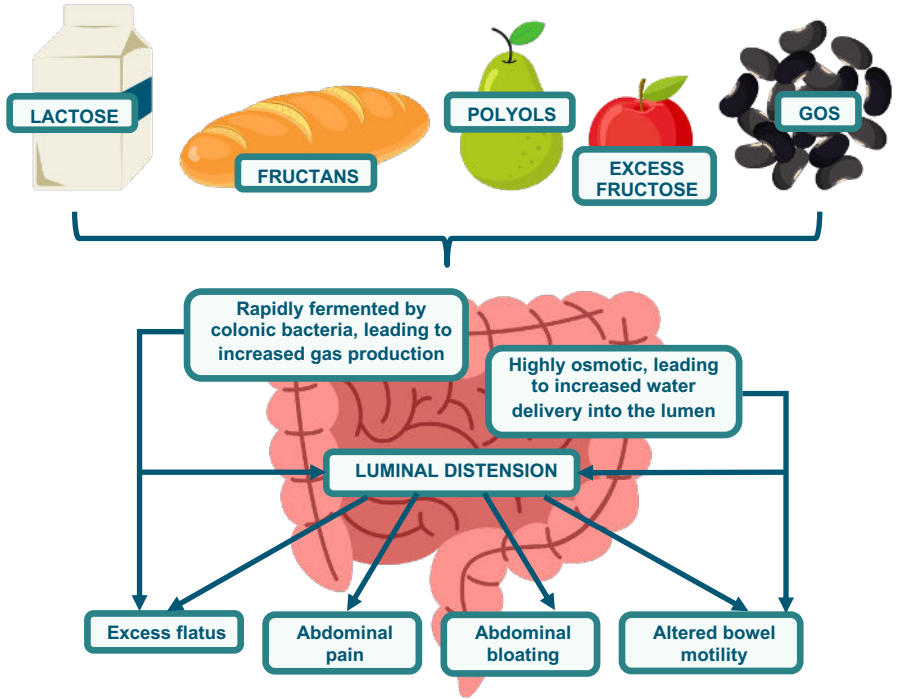
CME OUTFITTERS

When Inflammation Is Under Control

Dietary Modification

Low FODMAP Diet (LFD)

Limits highly-fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) to reduce bowel water and gas that can lead to distension and symptoms



GOS = galacto-oligosaccharides

Cox SR, et al. *Gastroenterology*. 2020;158(1):176-188.e7. Manski S, et al. *Crohns Colitis 360*. 2023;6(1):otad077. Mullin GE, et al. *JPEN J Parenter Enteral Nutr*. 2014;38(7):781-799.

CME OUTFITTERS

When Inflammation Is Under Control

Dietary Modification

Low FODMAP Diet (LFD)



Quiescent IBD
Ongoing gut symptoms
n = 26 UC, 26 CD



4-week low FODMAP diet vs sham dietary advice

	Low FODMAP	Control	*P* Value
Baseline Total IBS-SSS, mean (SD)	222 (76)	227 (81)	.847
End of Trial IBS-SSS, mean (SD)	158 (12)	190 (13)	.75
Relief of gut symptoms	**52%**	**16%**	**.007**

IBS-SSS = Irritable Bowel Severity Scoring System

Cox SR, et al. *Gastroenterology*. 2020;158(1):176-188.e7. Manski S, et al. *Crohns Colitis 360*. 2023;6(1):otad077.
Mullin GE, et al. *JPEN J Parenter Enteral Nutr*. 2014;38(7):781-799.

CME OUTFITTERS

When Inflammation Is Under Control

Dietary Modification

Low FODMAP Diet (LFD)



Patients with quiescent IBD
and FGS who
are responsive
to a low FODMAP diet



n = 12 CD
n = 17 UC
3-day FODMAP
challenges with washout

Incidence [number of days] of Moderate or Severe Symptoms During the 3-Day Challenges, Mean [SD]					
	Fructan	GOS	Sorbitol	Glucose	*P* Value**
Abdominal pain	1.1 [0.8]*	0.8 [0.9]	0.7 [0.9]	0.5 [0.6]	.006
Bloating	1.3 [0.9]*	0.6 [0.7]	0.8 [0.8]	0.6 [0.7]	<.001
Flatulence	1.5 [0.8]*	0.9 [1.0]	0.7 [0.6]	0.7 [0.7]	<.001
Borborygmi	0.7 [0.9]	0.4 [0.8]	0.3 [0.5]	0.3 [0.5]	.036
Fecal urgency	0.9 [1.1]*	0.7 [1.0]	0.5 [0.7]	0.4 [0.6]	.011
Overall	1.1 [0.9]	0.7 [0.8]	0.6 [0.7]	0.7 [0.6]	.006

*Significantly different from placebo [glucose] on post hoc analysis with Bonferroni correction for multiple comparisons
**Repeated-measures ANOVA across four challenges

Cox SR. *J Crohn's Colitis*. 2017;11:1420-1429.

CME OUTFITTERS

When Inflammation Is Under Control
Pharmacotherapy

Antidiarrheals

- Antidiarrheal agents (e.g., loperamide) can improve bowel urgency caused by both inflammatory and non-inflammatory mechanisms
- Normalizes colon transit time and is thought to increase internal anal sphincter (IAS) tone

Dubinsky M, et al. *Am J Gastroenterol*. 2023;118(11):1940-1953. Read M, et al. *Dig Dis Sci*. 1982;27(9):807-814. Sun WM, et al. *Scand J Gastroenterol*. 1997;32(1):34-38.

CME OUTFITTERS

When Inflammation Is Under Control

Pharmacotherapy

Antidiarrheals

Studies have indicated that loperamide decreases several functional gastrointestinal symptoms, such as **fecal urgency and stool frequency**, and can **improve stool consistency** and resting anal sphincter function in individuals with **diarrhea-predominant IBS and inactive IBD**[1,2]

Patients with CD[3] *Loperamide vs placebo over 1 week (van Outryve and Toussaint)*
After first week (1 mg after each unformed stool): • Both investigator's and patients' evaluations of global efficacy* were significantly in favor of loperamide (p = .025 and p = .020) • Patient-reported severity of diarrhea was improved with loperamide compared to placebo (p = .046) • Change in abdominal pain was significant for loperamide oxide (p = .020) but not for placebo
After second week (responders to first week continued to 1 mg twice daily) • Both the investigator's and the patients' assessments of global efficacy and symptom improvement continued to favor loperamide (difference was not significant)

*Improved stool consistency, **decreased fecal urgency** and stool frequency

1. Pezzone MA, Wald A. *Gastroenterol Clin North Am*. 2002;31(1):347-357. 2. Efskind PS, et al. *Scand J Gastroenterol*. 1996;31(5):463-468.
3. van Outryve M, Toussaint J. *J Int Med Res.* 1995;23:335-341.

CME OUTFITTERS

When Inflammation Is Under Control

Pharmacotherapy

Tricyclic Antidepressants

Idiopathic fecal incontinence (IFI)
n = 18 with IFI
- 8 (44%) complained of urgency of defecation

n = 24 controls

Amitriptyline 20 mg daily x 4 weeks

Evaluated before and after four weeks of therapy:
- Idiopathic fecal incontinence scores
- Number of bowel movements
- Computerized ambulatory anorectal pressures
- Pudendal nerve terminal motor latencies

After 4-weeks, n = 13 (72%) of patients with IFI experienced a ”satisfactory result” (no soiling episodes or **urgency of defecation** at all and full continence to fluid and solid stool)

Incontinence		
Median pretreatment score	16	$p < .001$
Median posttreatment score	3	

Bowel Frequency (BM/day)		
Median pretreatment	3	$p < .001$
Median posttreatment	1	

BM = bowel movement; NS = not significant

Santoro GA, et al. *Dis Colon Rectum*. 2000;43(12):1676-1681.

CME OUTFITTERS

When Inflammation Is Under Control

Pharmacotherapy

Tricyclic Antidepressants

Results of Pretreatment and Posttreatment Anorectal Physiology Measurements in Patients with Idiopathic Fecal Incontinence

	Pretreatment	Posttreatment	*P* Value
Median resting and pressure			
Daytime	64	68	NS
Nocturnal	26	16	NS
Median resting rectal pressure			
Daytime	32	32	NS
Nocturnal	12	12	NS
Median maximum and squeeze pressure	108	123	NS
Internal sphincter relaxations			
Median no. per hour	3.1	3.3	NS
Median anal pressure	38	34	NS
Median rectal pressure	30	32	NS
Rectal motor complexes			
Median no. per hour	4.5	1.2	< .05
Median anal pressure	49	66	< .001
Median rectal pressure	94	58	< .05

NS = not significant

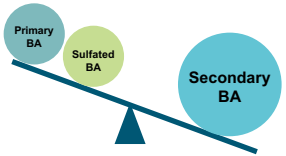
Pressures are in centimeters of water

Santoro GA, et al. *Dis Colon Rectum*. 2000;43(12):1676-1681.

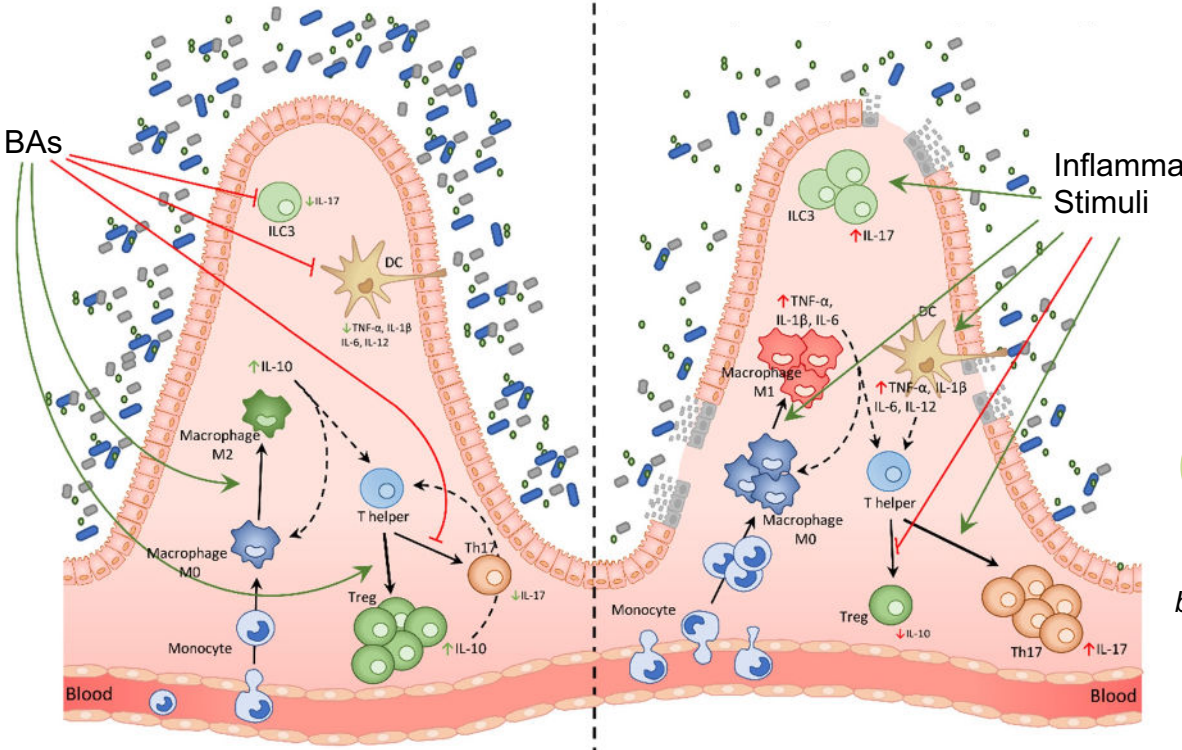
CME OUTFITTERS

Bile Acid Malabsorption (BAM) in IBD

Normal Bile Acid Pool



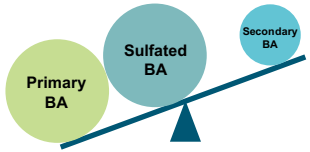
Eubiosis



Tolerogenic Immune Response

Pro-Inflammatory Immune Response

Altered Bile Acid Pool



Dysbiosis in IBD with ↓ bacterial species diversity

BA = bile acid

Adapted from Biagioli M, et al. *Cells.* 2021;10(6):1281.

Bile Acid Malabsorption (BAM) in IBD



SeHCAT scan of patients with CD (n = 22);
76% had longstanding diarrhea

Abnormal SeHCAT retention seen in:

90% of patients *with* bowel resections

28% of patients who had *not* undergone resection

BAM Diagnosis

- SeHCAT scan (nuclear medicine test)
- Fecal bile acid measurement (not widely available)
- Serum 7-alpha-hydroxy-4-cholesten-3-one
- Trial of bile acid sequestrant (lack of response does not exclude BAM)

Nyhlin H, et al. *Gut*. 1994;35(1):90-3. Farrugia A, et al. *Frontline Gastroenterol*. 2020;12(6):500-507.

CME OUTFITTERS

When Inflammation Is Under Control

Pharmacotherapy

Pancreatic Enzymes

- Exocrine pancreatic insufficiency
- Risks in IBD-related loose stools, larger number of bowel movements per day, and previous surgery
- Persistent EPI not associated with clinically active disease
- Reduced fecal elastase levels in up to 18% of patients with IBD

2023 AGA Clinical Practice Update on EPI

EPI should be considered in patients with moderate-risk clinical conditions such as CD

Testing: Fecal elastase test

Response to a therapeutic trial of pancreatic enzymes is unreliable for EPI diagnosis

If testing positive, initiate PERT:

- Adults typical starting dose is 500 units of lipase per kg per meal and 250 units of lipase per kg per snack
- Titrate dose up as needed to reduce steatorrhea or gastrointestinal symptoms of maldigestion
- Initiate vitamin supplementation (fat-soluble vitamins)

EPI = exocrine pancreatic insufficiency; PERT = pancreatic enzyme replacement therapy

Antonini F, et al. *World J Gastrointest Pathophysiol*. 2016;7(3):276-282. Massironi S, et al. *Aliment Pharmacol Ther*. 2022;55(12):1478-1491. Whitcomb DC, et al. *Gastroenterology*. 2023;165(5):1292-1301.

CME OUTFITTERS

Addressing Anorectal Dysfunction

Rectal inflammation is the main cause of bowel urgency in IBD

Other potential causes:

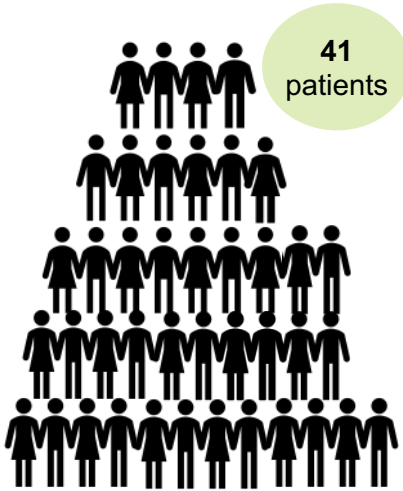
- IBS
- Bile acid malabsorption
- Small intestinal bacterial overgrowth
- Poor rectal compliance
- Neurologic
- Anal sphincter dysfunction

Nigam GB, et al. *Therap Adv Gastroenterol*. 2018;11:1756284818816956.

CME OUTFITTERS

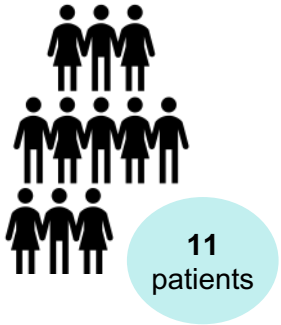
Effect of Microscopic Presence of CD in Rectal Tissue

Confirmed CD



No endoscopic rectal lesions

Positive rectal biopsy for CD



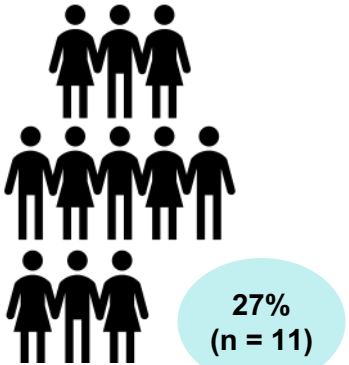
Chrysos E, et al. *Dis Colon Rectum*. 2001;44:1509-1513.

CME OUTFITTERS

Microscopic Presence of CD in Rectal Tissue Causes Motility Disorders

No endoscopic rectal lesions

Positive rectal biopsy for CD



Compared to Negative Rectal Pathology
Lower anal resting and squeeze pressure
Lower sphincter and high-pressure zone length
Rectal sensation more affected
Ultra slow wave amplitude and ultra slow wave frequency significantly lower
Rectal compliance significantly reduced

Chrysos E, et al. *Dis Colon Rectum*. 2001;44:1509-1513.

CME OUTFITTERS

When Inflammation Is Under Control

Biofeedback Therapy

Components of Biofeedback Therapy for fecal incontinence and Bowel Urgency

Phase 1: Assessment and Education

- Evaluation of defecation behavior with manometry or electromyography (EMG) probe

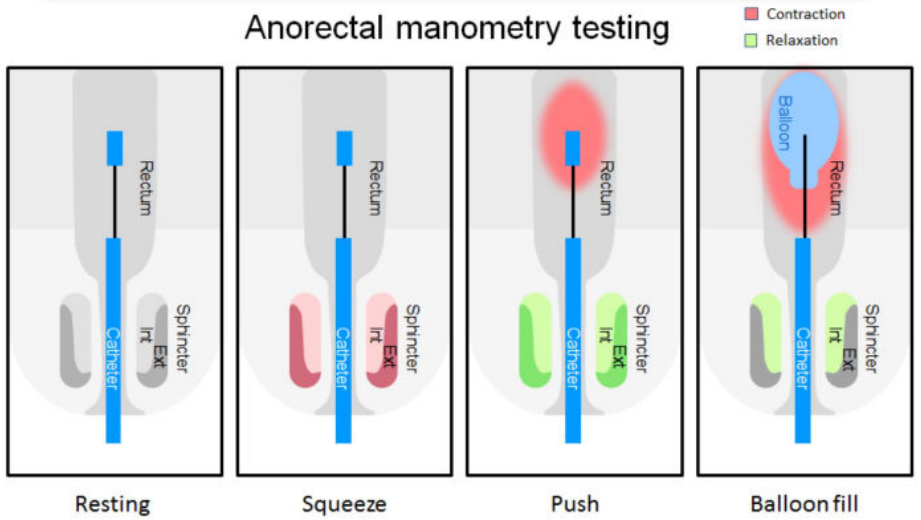
Phase 2: Active Exercise and Training

- Strength Training—improve speed, duration, and timing of voluntary contractions of the external anal sphincter
- Rectal sensory training—**Tolerate larger volumes until a normal level of urge sensation is achieved**
- Coordination training—increase voluntary anal contraction in response to rectal filling **to increase threshold for urgency**

Phase 3: Weaning and Reinforcement

- As patient gains confidence in muscle control, the frequency of therapy is reduced
- Number, frequency, intensity, and duration of sessions highly individualized for each patient

Biofeedback is a self-regulation technique that attempts to teach patients with defecatory defects to strengthen pelvic floor muscles, retain rectal sensation, and coordinate pelvic floor muscles during evacuation



Lee HJ, et al. *J Neurogastroenterol Motil.* 2013;19(4):532-537.
Western Sydney University: GI Motility Disorders Unit. 2018.

CME OUTFITTERS

When Inflammation Is Under Control

Biofeedback Therapy

Frequency of dyssynergic defecation in IBD	45-97% patients w/out IPAA
	25-75% of patients with IPAA
Pooled response rate to biofeedback therapy	70% (95% CI 55%-84%) w/out IPAA
	86% (95% CI 67%-98%) with IPAA

IPAA = ileal pouch-anal anastomoses

Rezaie A, *Inflamm Bowel Dis*. 2018 ;24(5):1065-1073.

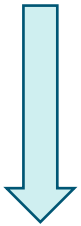
CME OUTFITTERS

When Inflammation Is Under Control

Pelvic Floor Training

- Pelvic floor muscle training, with or without biofeedback therapy, improved fecal incontinence in 20/25 (80%) of patients with quiescent IBD
- Patients with IBD completing treatment (n = 29) demonstrated improved symptom scores ($p < .001$), IBD-specific QoL ($p = .008$) and illness perception scores ($p = .0030$)
- Those who are most likely to benefit are **individuals experiencing fecal incontinence or impaired evacuation** and **exhibit dysfunction in pelvic floor or anal sphincter muscles**
  - Pelvic floor dysfunction diagnosis: anal manometry, balloon expulsion testing, EMG, defecography, or ultrasound

Pelvic muscle contraction strength can be diminished in shortened, tight, or tense muscles



Affects continence and the ability to evacuate effectively

Khera AJ, et al. *JGH Open*. 2019;3(6):494-507. Khera AJ, et al. *Scand J Gastroenterol*. 2022;57(7):807-813. Wald A, et al. *Am J Gastroenterol*. 2021;116(10):1987-2008.

CME OUTFITTERS

When Inflammation Is Under Control

Pelvic Floor Training

- Pelvic floor muscle training does not solely include strength training. Incorporates exercises to:
  - Improve the awareness of muscle contraction and relaxation
  - Coordinate with abdominal and diaphragm muscles for the normal functions of continence and effective defecation

Behavioral Treatments Tailored to Individual Patient Symptoms

- ***Pelvic floor muscle training, with or without biofeedback***
- Toileting behavior modifications
- Urge resistance or deferral techniques
- Lifestyle changes
- Emotional support

Khera AJ, et al. *JGH Open*. 2019;3(6):494-507. Khera AJ, et al. *Scand J Gastroenterol*. 2022;57(7):807-813.

CME OUTFITTERS

Holistic Approach to Management of Urgency

Treatment Consideration	Example
Recognition of the presence and impact of urgency	• Explicit, empathetic inquiry of patients about urgency and its consequences (eg, via the UNRS)
Emotional support	• Access to counseling • IBD specialist nurses • Community continence advisory team
Social support	• Dedicated social support networks • Clinician liaison with employers/schools
Physical support	• Diagnostic investigations • Medical management of urgency • Pelvic floor PT or biofeedback therapy • Complementary medical therapy

Adapted from Pakpoor J. *Gastroenterol Hepatol (N Y)*. 2023;19(2):95-100.

CME OUTFITTERS

Patient Case: Susi M. (continued)



Patient Treatment Goals

Work an 8-hour shift with a maximum of **1 or 2 *planned*** restroom breaks

Wake up to use the restroom **less than 1x** per week

Attend social events with friends. Start with a **goal of 1 hour** without disruptive symptoms

Bowel Urgency Treatment Plan

- Referral for anorectal manometry testing
- SeHCAT to evaluate for BAM
- Discuss trial of amitriptyline 10 mg daily vs low FODMAP diet to manage symptoms
- Assess for depression/anxiety; consider treatment or referral to mental health services
- Trial loperamide 1 mg prior to outing, additional 1 mg as needed for urgency symptoms

CME OUTFITTERS

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely



- Proactively screen patients with CD for bowel urgency symptoms, using a meaningful assessment tool such as the UNRS.
- Increase the percentage of patients with CD who have an individualized treatment plan to address bowel urgency during periods when inflammation is controlled.
- Improve the proportion of patients with CD who identify personalized treatment goals for addressing the impact of bowel urgency and other CD symptoms on daily life.

CME OUTFITTERS

To Ask a Question

To submit a question,
please go to the *Ask Question* tab
at the bottom of the screen.

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