
GI ON DEMAND
Access GI Expertise, Educational Resources and Support for You and Your Patients
Registered Dietitians
GI Psychologists
GI Sub-Specialists
APP
Patient
GI
Genetic Testing
Telehealth Features
Education Resources
A Free ACG Member Benefit Designed to Help You and Your Patients!
Learn More and Join Today at
GIONDEMAND.COM

1


Virtual Grand Rounds
universe.gi.org
2023
ACG IBD SCHOOL & SOUTHERN REGIONAL
POSTGRADUATE COURSE
DECEMBER 1-3, 2023 | RENAISSANCE NASHVILLE HOTEL
NASHVILLE, TENNESSEE
Register online: meetings.gi.org

2

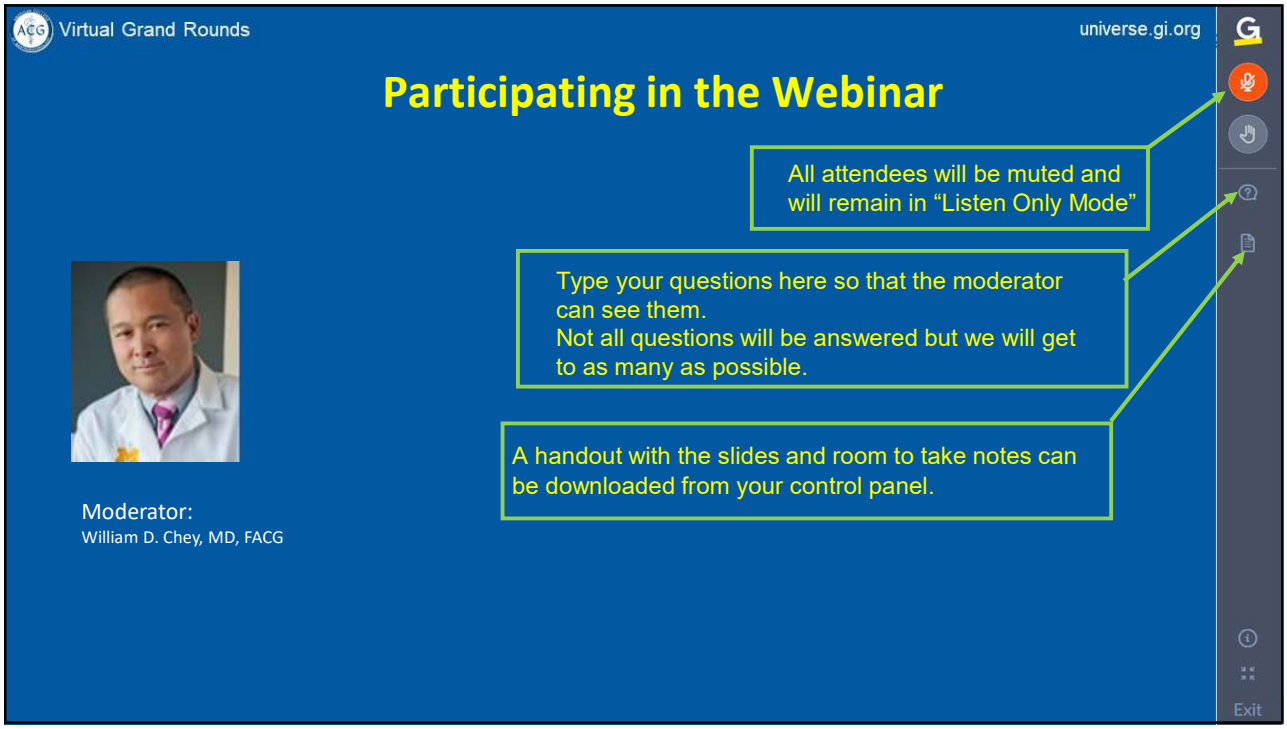
Those selected will be required to participate and complete the International Guideline Development Credentialing & Certification Program through McMaster University. The onsite training will be in Spring 2024 and is sponsored by the ACG. Applicants must agree to a 5-year term as a GRADE Methodologist.

Want to Learn More?

GRADE INFORMATION SESSION IN VANCOUVER:

Sunday October 22 3:30-4pm Room 111-112

3



4

Virtual Grand Rounds universe.gi.org

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 39 – Thursday, September 28, 2023
Identification & Management of Hereditary Pancreatic Cancer Risk
Faculty: Bryson Katona, MD, PhD, CGAF
Faculty: Beth Dudley Yurkovich, MS, MPH, CGC, CGAF
Moderator: Thomas Slavin Jr., MD, FACMGG, DABCC
Moderator: Veroushka Ballester, MD, MS
At Noon and 8pm Eastern

Week 40 – Thursday, October, 5, 2023
Private Equity
Faculty: Scott Fraser, MBA
Moderator: Daniel J. Pambianco, MD, FACG
At Noon and 8pm Eastern

Visit **gi.org/ACGVGR** to Register

5

6

ACG Standard Slide Decks

Colorectal Cancer Screening and Surveillance Slide Deck

Ulcerative Colitis Slide Deck

ACG has created presentation-ready, semi-customizable MS PowerPoint clinical slide decks for your unique teaching and learning needs.

Visit gi.org/ACGSlideDecks to learn more and request access to the standard slide decks!

7

Virtual Grand Rounds

universe.gi.org

Disclosures

Lin Chang, MD, FACG:

AbbVie: Organized educational symposium (Terminated); AnX Robotica: Grant/Research Support; Arena: Advisory Committee/Board Member (Terminated), Grant/Research Support (Terminated); Bausche Health: Developed an educational lecture slide set; Ironwood Pharmaceuticals: Consultant, Grant/Research Support, organized educational symposium (latter is terminated); Mauna Kea Technologies: Advisory Committee/Board Member (Terminated); ModifyHealth: Stock Options; NeurAxis: Grant/Research Support; Trellus Health: Consultant, Stock Options; Atmo: Advisory committee; Food Marble: Consultant, Stock options, Vibrant: Advisory committee.

William D. Chey, MD, FACG:

AbbVie: Consultant; Allakos: Consultant; Alnylam: Consultant; American Medical Laboratories: Consultant; Ardelyx: Consultant; Arena: Consultant; Bayer: Consultant; Biomerica: Consultant, Grant/Research Support, Clinical Trial Participant; Commonwealth Diagnostics International: Grant/Research Support; Cosmo: Consultant; Digital Manometry: Intellectual Property/Patents, Patent Holder; Gastro Girl: Stock Options; Gemelli: Consultant; GI Health Foundation: Advisory Committee/Board Member; GI OnDEMAND: Advisory Committee/Board Member, Stock Options; IM Health: Consultant; International Foundation of GI Disorders: Advisory Committee/Board Member; Ironwood: Consultant; Isothrive: Consultant; Modify Health: Stock Options; My Nutrition Health: Intellectual Property/Patents, Patent Holder; Nestle: Consultant; Progenity: Consultant; QOL Medical: Consultant, Grant/Research Support, Clinical Trial Participant; Rectal Expulsion Device: Intellectual Property/Patents, Patent Holder; Redhill: Consultant; Ritter: Consultant; Rome Foundation: Advisory Committee/Board Member; Salix: Grant/Research Support; Salix/Valeant: Consultant; Takeda: Consultant; Urovant: Consultant; Vibrant: Consultant, Grant/Research Support

**All of the relevant financial relationships listed for these individuals have been mitigated*

8

Virtual Grand Rounds

universe.gi.org

American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation

Lin Chang, MD
G Oppenheimer Center for Neurobiology of Stress and Resilience
Goodman-Luskin Microbiome Center
Vatche and Tamar Manoukian Division of Digestive Diseases
David Geffen School of Medicine at UCLA

9

Virtual Grand Rounds

universe.gi.org

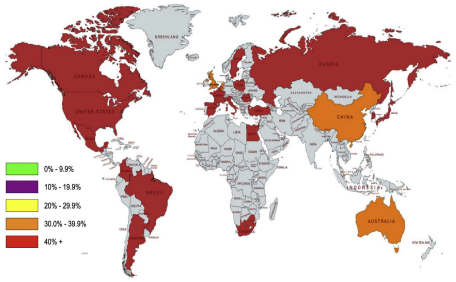
Objectives

- To review the AGA-ACG guidelines in the pharmacologic treatment of chronic idiopathic constipation (CIC)
- To use a case-based approach to describe how best to approach the treatment of patients with CIC

10

Virtual Grand Rounds

Impact of Chronic Constipation



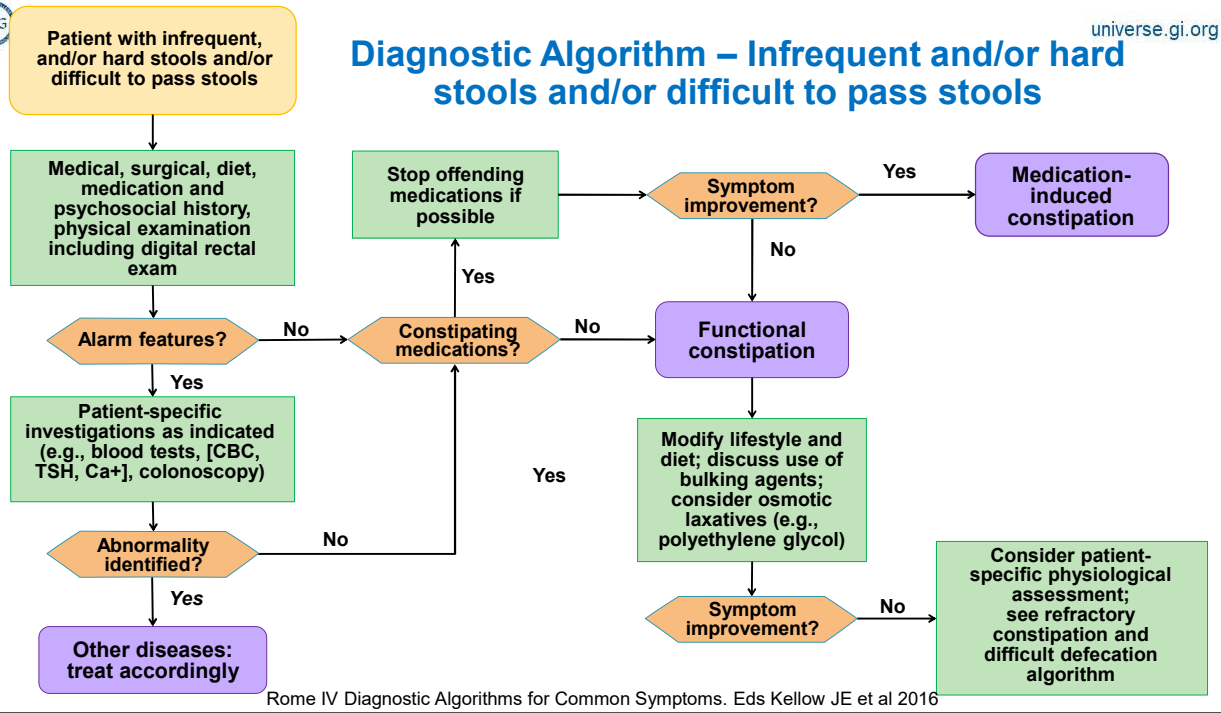
- **8-12% of US population affected**
  - Twice as many women as men
  - Most with years of symptoms before seeking help from a provider
- **60%** estimated it interfered with personal activities 4 days/month
- **4th most common GI symptom**, leading to > 3 million outpatient clinic visits/year in the US
- Patients' frustration and disability was greater than clinicians' perception
- **Billions of dollars** in health care expenditures

Harris LA, et al. *Adv Ther.* 2017;34(12):2661-2673
Sperber A et al. Gastroenterology. 2021 Jan;160(1):99-114.e3
Chang, Chey, Imdad, et al. *Gastroenterology* 2023;164(7):1086-1106 and *Am J Gastroenterology* 2023;118(6):936-954

11

universe.gi.org

Diagnostic Algorithm – Infrequent and/or hard stools and/or difficult to pass stools



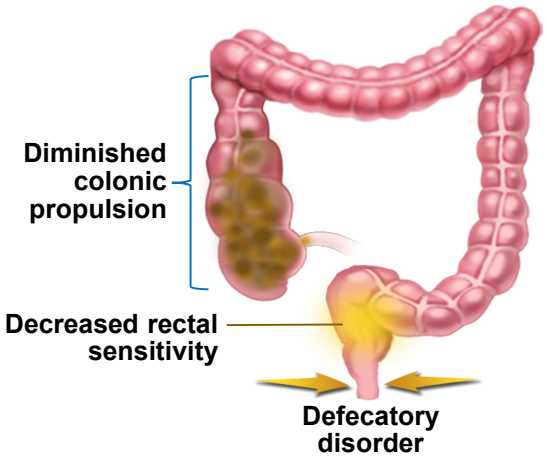
Rome IV Diagnostic Algorithms for Common Symptoms. Eds Kellow JE et al 2016

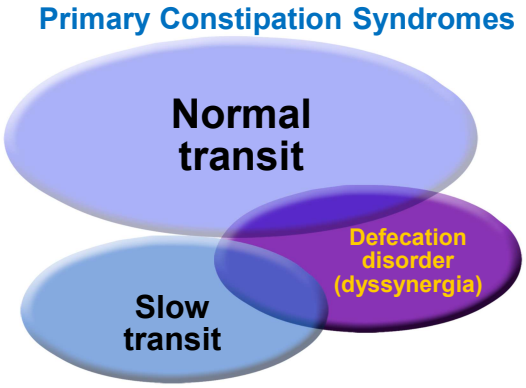
12

Virtual Grand Rounds

universe.gi.org

Functional Constipation Can Be Divided into Three Broad Categories: Normal-Transit Constipation, Slow-Transit Constipation and Defecatory Disorders





Schiller LR. Aliment Pharmacol Ther. 2001; 15:749
Mertz H et al. Am J Gastroenterol. 1999; 94:609

13

Virtual Grand Rounds

universe.gi.org

Rome IV Criteria: Functional Constipation

1. Diagnostic criteria* must include two or more of the following:* *

- Straining more than ¼ (25%) of defecations
- Lumpy or hard stools (Bristol Stool Form Scale 1-2) more than ¼ (25%) of defecations
- Sensation of incomplete evacuation more than ¼ (25%) of defecations
- Sensation of anorectal obstruction/blockage more than ¼ (25%) of defecations
- Manual maneuvers to facilitate more than ¼ (25%) of defecations (e.g., digital evacuation, support of the pelvic floor)
- Fewer than three SBM per week

2. Loose stools are rarely present without the use of laxatives

3. Insufficient criteria for irritable bowel syndrome

*Criteria fulfilled for the last 3 months with symptom onset more than 6 months prior to diagnosis

** For research studies, patients meeting criteria for opioid-induced constipation (OIC) should not be given a diagnosis of FC because it is difficult to distinguish between opioid side effects and other causes of constipation. However, clinicians recognize that these two conditions may overlap.

Adapted from Lacy BE et al. *Gastroenterology*. 2016;150:1393-1407.

14

Virtual Grand Rounds

universe.gi.org

Stool Form Depends on Water Content and Correlates With Transit Time

Bristol Stool Form Scale[1,2]

Type 1
Separate hard lumps, like nuts (hard to pass)

Type 2
Sausage-shaped but lumpy

Type 3
Like a sausage but with cracks on its surface

Type 4
Like a sausage or snake, smooth and soft

Type 5
Soft blobs with clear-cut edges (passed easily)

Type 6
Fluffy pieces with ragged edges; a mushy stool

Type 7
Watery, no solid pieces; entirely liquid

Slower → **Faster** (Transit)

Constipation

Less → **More** (Water content)

Lewis SJ, Heaton KW. Scand J Gastroenterol 1997; 32:920
Heaton KW, O'Donnell LJ. J Clin Gastroenterol 1994; 19:28

15

Virtual Grand Rounds

universe.gi.org

Chronic Idiopathic Constipation (CIC)

- Alternate term for Functional Constipation
- Diagnostic term adopted by regulatory agencies
- Use this term for the associated diagnosis for treatments approved for CIC
- Associate correct dose with CIC or IBS-C

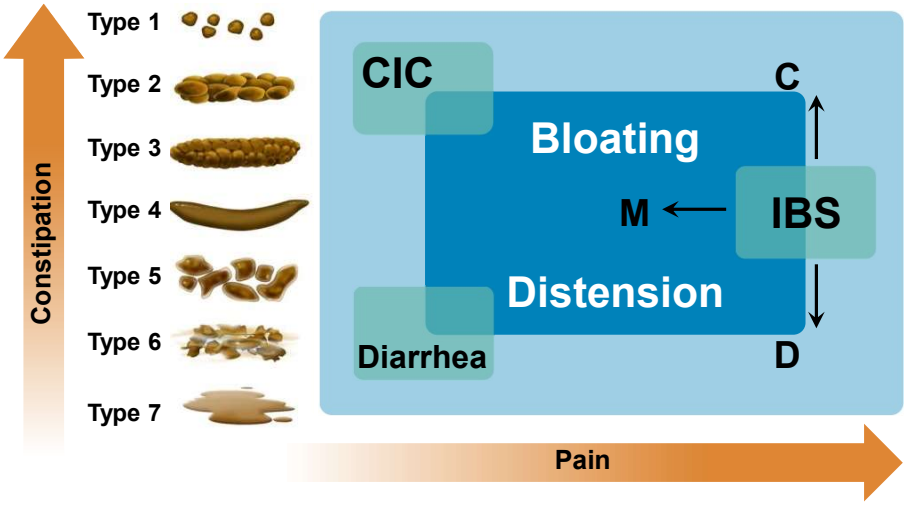
October 20-25, Vancouver, Canada

16

Virtual Grand Rounds

universe.gi.org

Rome IV Diagnostic Criteria Differentiate IBS-C From Chronic Idiopathic Constipation (CIC) by the Presence of Abdominal Pain



Adapted from Lacy BE et al. *Gastroenterology*. 2016;150:1393-1407.

17

Virtual Grand Rounds

universe.gi.org

Dietary & Lifestyle Approaches for CIC

- **Dietary modifications and supplementation**
  - **Increased fiber (25-30 g/day)**
    - Soluble preferred over insoluble
    - Increase dose gradually to minimize side effects
  - **Natural Laxatives**
    - Sorbitol: Prunes, Apples, Apricots, Cherries, Peaches, Pears
    - Stimulants: Aloe, Rhubarb
    - Other: Kiwi, Bananas, Mango, Papaya, Watermelon
- **Hydration***
- **Exercise***

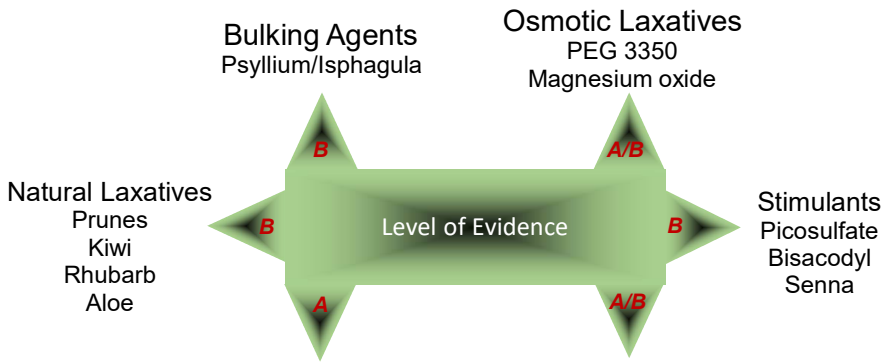
*Although increased fluid intake and exercise are generally recommended for constipation as a lifestyle measure, the incremental value of this in an individual who is already physically active, and consuming a good amount of fluids is questionable

CIC, chronic idiopathic constipation

Black CJ, Ford AC. *Med J Aust.* 2018;209:86-91. Ford AC, et al. *Am J Gastroenterol.* 2014;109:1547-1561. Chey WD, et al. *Gastroenterology.* 2021;160:47-62. Lacy BE, et al. *Gastroenterology*. 2016;150:1393-1407. Chey SW et al. Am J Gastroenterol 2021;116:1304-12; Rao SSC, Brenner DM. AJG. 2021;116(6):1156-1181

18

Pharmacological Treatments for Chronic Constipation:



Ford AC, et al. Am J Gastroenterol. 2014;109:S2-26
Rao, et al. Am J Gastroenterol 2021;116:1156

19

Virtual Grand Rounds

universe.gi.org

Joint ACG and AGA Guideline for CIC

- A joint society guideline on CIC with representatives from both AGA and ACG

  Evidence Review Committee (ERC): Conducted systematic reviews of each intervention and synthesized the data

  Practice Guideline Committee (PGC): Used information from the ERC to produce guideline recommendations

- Followed GRADE framework and methodology

Gastroenterology 2023;164:1086–1106

GUIDELINES

American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation

Lin Chang,[1,*] **William D. Chey,**[2,*] **Aamer Imdad,**[3,*] Christopher V. Almario,[4] Adil E. Bharucha,[5] Susan Diem,[6,7] Katarina B. Greer,[8,9] Brian Hanson,[6,10] Lucinda A. Harris,[11] Cynthia Ko,[12] M. Hassan Murad,[13] Amit Patel,[14] Eric D. Shah,[2,15] **Anthony J. Lembo,**[16,§] and **Shahnaz Sultan**[6,17,§]

CME

American Gastroenterological Association-American College of Gastroenterology Clinical Practice Guideline: Pharmacological Management of Chronic Idiopathic Constipation

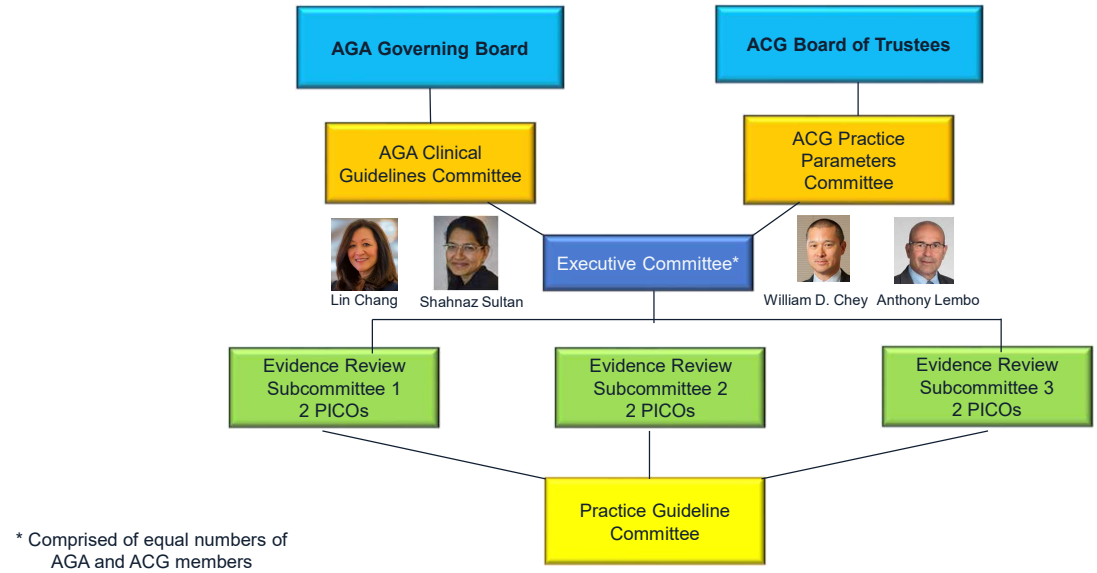
Lin Chang, MD, FACG[1,*], William D. Chey, MD, FACG[2,*], Aamer Imdad, MBBS, MPH[3,*], Christopher V. Almario, MD, MSHPM, FACG[4], Adil E. Bharucha, MD[5], Susan Diem, MD, MPH[6,7], Katarina B. Greer, MD, MS Epi[8,9], Brian Hanson, MD[6,10], Lucinda A. Harris, MD, FACG[11], Cynthia Ko, MD[12], M. Hassan Murad, MD[13], Amit Patel, MD, FACG[14], Eric D. Shah, MD, MBA, FACG[2,15], Anthony J. Lembo, MD, FACG[16,†] and Shahnaz Sultan, MD, MHSc, FACG[6,17,†]

20

Virtual Grand Rounds

A Collaborative Process for the First AGA-ACG Guideline on CIC

universe.gi.org



* Comprised of equal numbers of AGA and ACG members

21

Evidence Review Committee	GI Society	Expertise	Treatment
Subcommittee 1			
Lin Chang	AGA	Content expert	Fiber
Lucinda Harris	ACG	Content expert	Osmotic laxatives
Aamer Imdad	AGA	Methodologist	Lubiprostone
Subcommittee 2			
Bill Chey	ACG	Content expert	Stool softener
Tony Lembo	AGA	Content expert	Stimulant laxatives
Katarina Greer	ACG	Methodologist	Plecanatide
Subcommittee 3			
Adil Bharucha	AGA	Content expert	Linaclotide
Eric Shah	ACG	Content expert	Prucalopride
Brian Hanson	AGA	Methodologist	Colchicine
			Misoprostol
Methodology group			
M. Hassan Murad	AGA	Senior Methodologist	
Katarina Greer	ACG	Methodologist	
Brian Hanson	AGA	Methodologist	
Aamer Imdad	AGA	Methodologist	
Guideline committee			
Cynthia Ko	AGA	Chair	
Amit Patel	AGA	GI	
Christopher Almario	ACG	GI	
Susan Diem	AGA	Primary care	

22

Virtual Grand Rounds

universe.gi.org

Treatments

Fiber
- Psyllium/Isphagula
- Bran
- Inulin
- Methylcellulose

Osmotic Laxatives
- PEG 3350
- Magnesium oxide

Stimulant laxatives
- Picosulfate
- Bisacodyl
- Senna

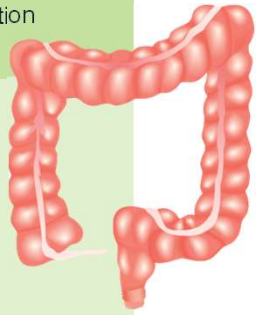
Prosecretory agents
- Lubiprostone
- Linaclotide
- Plecanatide

Prokinetic Agents
- Prucalopride

Patient Important Outcomes

Critical
- CSBMs per week
- SBMs per week
- AEs leading to treatment discontinuation

Other
- CSBM responder (≥3 + ↑ ≥1 from baseline)
- Diarrhea leading to treatment discontinuation
- Serious adverse events
- Global relief
- QOL improvement
- Stool form



CSBM, complete spontaneous bowel movements; SBM, spontaneous bowel movements; AE: adverse events; QOL, quality of life

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

23

Virtual Grand Rounds

universe.gi.org

Guideline Quality of Evidence

Quality Grade	Definition
High	We are very confident that the true effect lies close to the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.
Low	Our confidence in the estimate is limited. The true effect may be substantially different from the estimate of effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.
Knowledge gap	Available evidence is insufficient to determine true effect.

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

24

Virtual Grand Rounds

universe.gi.org

Guideline Strength of Recommendations

Implication	Strong recommendation	Conditional recommendation
For patients	**Most individuals in this situation would want the recommended course of action and only a small proportion would not.**	**The majority of individuals in this situation would want the suggested course of action, but many would not.**
For clinicians	**Most individuals should receive the intervention**. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	**Different choices will be appropriate for individual patients consistent with his or her values and preferences**. Use shared decision making. Decision aids may be useful in helping patients make decisions consistent with their individual risks, values and preferences.
For policy makers	The recommendation can be **adapted as policy or performance measure in most situations**	**Policy making will require substantial debate and involvement of various stakeholders**. Performance measures should assess whether decision-making is appropriate.

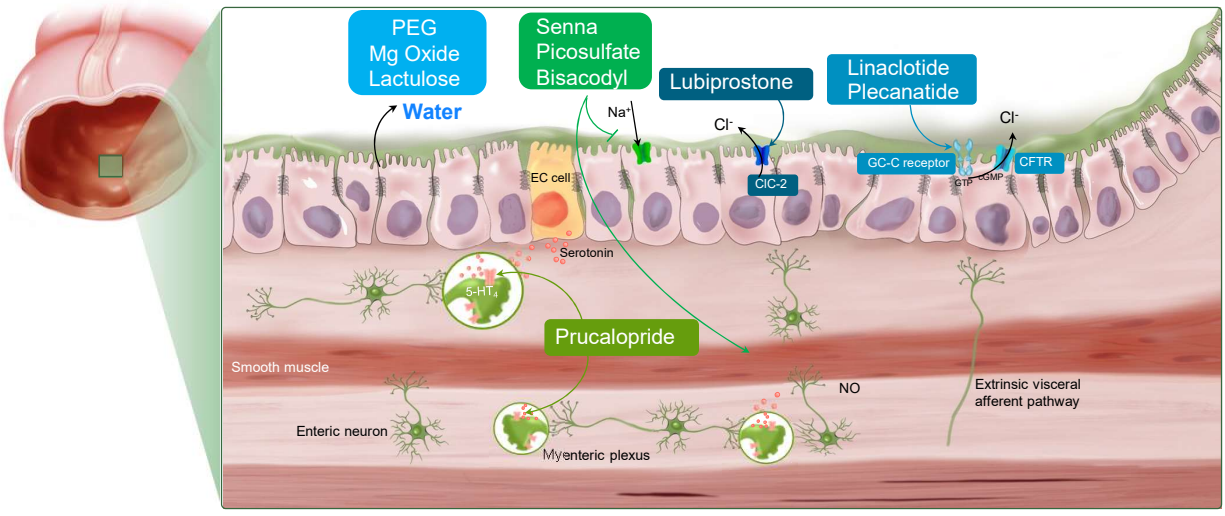
Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

25

Virtual Grand Rounds

universe.gi.org

Mechanism of Action of Pharmacologic Treatments for CIC



EC, enterochromaffin cells

Chang, Chey, Imdad, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

26

Virtual Grand Rounds universe.gi.org

Patient Case #1

27

Virtual Grand Rounds universe.gi.org

A 23-year-old woman presents with symptoms of constipation for the past year. She reports having a bowel movement every other day, hard stools and straining with about 30% of bowel movements. Although she has increased her daily dietary fiber and fluid intake, her symptoms have only partially improved and she asks about fiber supplementation to relieve symptoms of constipation. She denies bloody stools, history of anemia, unintentional weight loss, family history of colon cancer.

Which fiber supplement has been shown to significantly increase spontaneous bowel movements in randomized controlled trials?

a. Inulin

b. Bran

c. Psyllium

d. Methylcellulose

28

Virtual Grand Rounds

universe.gi.org

Fiber

TYPES OF FIBER

SOLUBLE FIBER
-traps water in intestine and softens stools
-may have prebiotic potential
Examples:
psyllium, inulin (fructan), methylcellulose, oats, barley, fruits, legumes

INSOLUBLE FIBER
-provides bulk to stools
Examples:
wheat bran, wheat rye other grains, skins of fruits

Four types of fiber reviewed in the guideline:
Bran, Inulin, Psyllium, Methylcellulose

- In 3 RCTs, patients with CIC who took psyllium had an increase in number of spontaneous bowel movements (SBMs) per week (no data on complete spontaneous bowel movements) AND improved global relief symptoms of chronic constipation. Psyllium did not significantly change stool consistency. No data on quality of life
- Bran (1 RCT) and inulin (2 RCTs) were not associated with a significant increase in the number of spontaneous bowel movements per week or improvement in global relief symptoms in RCTs of patients with CIC
- No RCTs for methylcellulose

RCTs: Randomized controlled trials
Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

29

Virtual Grand Rounds

universe.gi.org

Recommendation 1: In adults with CIC, the panel suggests the use of fiber supplementation over management without fiber supplements (Conditional recommendation, Low certainty of evidence)

Implementation considerations

- Dietary assessment is important to determine total fiber intake from diet and supplements
- Fiber supplements can be used as first-line therapy for CIC, particularly for individuals with low dietary fiber intake
- Among the evaluated fiber supplements, only psyllium appears to be effective (with very limited and uncertain data on bran and inulin)
- Adequate hydration should be encouraged with the use of fiber
- Flatulence is a commonly observed side effect with the use of fiber

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

30

Virtual Grand Rounds universe.gi.org

Patient Case #2

31

Virtual Grand Rounds universe.gi.org

During a routine checkup, a 35-year-old gentleman reports generally good health except for several years of mild constipation but recent worsening of constipation with less frequent bowel movements and more frequent hard stools, straining, bloating/gas. His family history is negative. Review of his medical records indicates a steady weight, an active lifestyle, good fluid intake, and a high fiber diet. His physical exam including vital signs and rectal exam is normal. Complete blood count (CBC), thyroid stimulating hormone (TSH), serum electrolytes, and glucose are normal.

Which of the following is the most appropriate treatment based on their certainty of evidence?

a. Lactulose
b. Magnesium oxide
c. Polyethylene glycol
d. Stimulant laxatives

32

Virtual Grand Rounds

universe.gi.org

Osmotic Laxatives

Three agents reviewed in the guideline:
PEG, Magnesium oxide, and Lactulose

- Across 3 RCTs, PEG was associated with greater efficacy in increasing the frequency of CSBMs and SBMs, improved stool form, decreased straining and increased global relief (compared with placebo)

Polyethylene Glycol (PEG)	
CSBM/week	2.9 CSBM/week higher (2.12 higher to 3.68 higher)
SBM/week	2.3 SBM/week higher (1.55 higher to 3.06 higher)
Responder rate	312 more per 1,000 (146 more to 569 more)
Global relief	454 more per 1,000 (159 more to 948 more)

CSBM, complete spontaneous bowel movements
SBM, spontaneous bowel movements

- Both magnesium oxide and lactulose demonstrate some beneficial effects on chronic constipation symptoms, however there were significant limitations in the evidence including few studies of short duration, small numbers of patients, different doses and formulations than those used clinically.

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

33

Virtual Grand Rounds

universe.gi.org

Recommendation 2: In adults with CIC, the panel recommends the use of PEG compared with management without PEG (Strong recommendation, Moderate certainty of evidence).

Implementation considerations

- A trial of fiber supplement can be considered for mild constipation before PEG use or in combination with PEG
- Response to PEG has been shown to be durable over 6 months
- Side effects include abdominal distension, loose stool, flatulence, and nausea

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

34

Virtual Grand Rounds universe.gi.org

Recommendation 3: In adults with CIC, the panel suggests the use of Magnesium Oxide (MgO) over management without MgO (Conditional recommendation, Very low certainty of evidence)

- 2 small RCTs
- MgO associated with increase in number of CSBM and SBM frequency, improved stool form and QOL, and higher treatment response vs placebo (RR 3.93, [CI 2.04-7.56])
- No differences in diarrhea leading to treatment withdrawal

Implementation considerations:

- The trials were conducted for 4 weeks, although longer term use is probably appropriate
- Trials used MgO, other Mg formulations have not been assessed in RCTs
- The panel suggests starting at a lower dose (500 mg), which may be increased if necessary
- Avoid use in patients with renal insufficiency due to risk of hypermagnesemia

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

35

Virtual Grand Rounds universe.gi.org

Recommendation 4: In adults with CIC who fail or are intolerant to OTC therapies, the panel suggests the use of lactulose over management without lactulose (Conditional recommendation, Very low certainty of evidence)

- Two RCTs studied the efficacy of lactulose syrup for the treatment of CIC in elderly participants
- Lactulose may have little to no effect on number of SBMs per week in one study and a large increase in global relief in the second study
- Studies did not report on number of CSBMs per week, diarrhea, serious adverse events, quality of life, or stool form.
- Approved by the FDA in the US for treatment of constipation at a dose of 10–20 g (15–30 mL or 1–2 packets) daily and is widely available in other countries

Implementation considerations:

- Bloating and flatulence are dose-dependent and common side effects, which may limit use in clinical practice

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

36

Virtual Grand Rounds universe.gi.org

What about stimulant laxatives?

37

Virtual Grand Rounds universe.gi.org

Recommendation 5: In adults with CIC, the panel recommends the use of bisacodyl or sodium picosulfate (SPS) short term or as rescue therapy over management without bisacodyl or SPS (Strong recommendation, Moderate certainty of evidence)

- Two RCTs showed SPS associated with increase in number of CSBMs and SBMs per week and improved stool form, responder rates, global relief and QOL vs placebo
- SPS associated with higher rate of diarrhea that led to treatment withdrawal

Implementation considerations:

- Short-term use is defined as daily use for 4 weeks or less
- While long-term use is probably appropriate, data are needed to better understand tolerance and side effects
- This is a good option for occasional use or rescue therapy in combination with other pharmacological agents for CIC
- The most common side effects are abdominal pain, cramping and diarrhea
- The panel suggests starting at a lower dose and increasing the dose as tolerated

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

38

Virtual Grand Rounds

universe.gi.org

Recommendation 6: In adults with CIC, the panel suggests the use of senna over management without senna (Conditional recommendation, Low certainty of evidence)

- One small RCT that showed that senna is associated with higher numbers of CSBMs and SBMs per week, responder rate and QOL vs placebo
- Increased diarrhea with senna vs placebo

Implementation considerations:

- While the trials were conducted for 4 weeks, longer term use is probably appropriate, but data are needed to better understand longer term tolerance and side effects
- The dose evaluated in trials is higher than commonly used doses in practice
- The panel suggests starting at a lower dose and increasing as tolerated if there is no response
- Abdominal pain and cramping may occur with a higher dose of senna

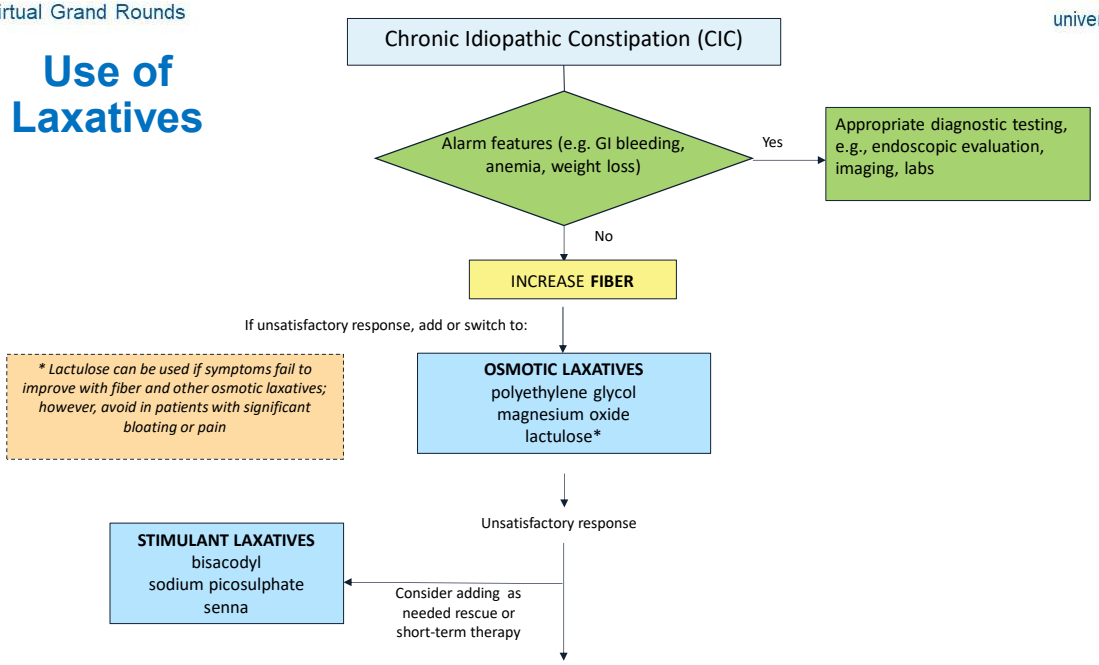
Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

39

Virtual Grand Rounds

universe.gi.org

Use of Laxatives



Gastroenterology. 2023;164:1107

40

Virtual Grand Rounds universe.gi.org

Patient Case #3

41

Virtual Grand Rounds universe.gi.org

40-year-old woman is referred for chronic constipation. She has severe bloating, decreased stool frequency (< 2/week), and a sense of incomplete evacuation for at least 5 years. Abdominal pain occurs when she has not had a BM for at least 5 days. She has tried fiber supplements, and multiple over-the-counter laxatives (polyethylene glycol, magnesium citrate, bisacodyl) with suboptimal results. She also endorses intermittent nausea and headaches which limits her quality of life but denies weight loss, bloody stools, FH of colon cancer. Recent evaluations have included a normal CBC, TSH, serum electrolytes, glucose, and head CT. Physical exam demonstrates mild LLQ abdominal tenderness and a normal digital rectal exam.

What treatment would you recommend next?

a. Lubiprostone
b. Linaclotide
c. Prucalopride
d. Tenapanor

42

Virtual Grand Rounds universe.gi.org

Recommendation 7: In adults with CIC who do not respond to OTC agents, the panel suggests the use of lubiprostone over management without lubiprostone (Conditional recommendation, Low certainty of evidence).

- Three 4-week RCTs with 24 mcg bid dose of lubiprostone showed that it was associated with increased number of SBMs per week, responder rate, global relief, and stool form vs placebo
- No data on CSBMs per week, QOL
- Lubiprostone associated with higher rate of diarrhea that led to treatment withdrawal

Implementation considerations:

- Can be used as a replacement or as an adjunct to OTC agents
- Duration of treatment in trials was 4 weeks, but the drug label does not provide a limit
- Nausea may occur; however, the risk of nausea is dose-dependent and seems to be lower when taken with food and water
- Lubiprostone is now generic

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

43

Virtual Grand Rounds universe.gi.org

Recommendation 8-9: In adults with CIC who do not respond to OTC agents, the panel recommends the use of linaclotide or plecanatide, over management without these medications (Strong recommendation, Moderate certainty of evidence)

- Linaclotide and plecanatide each studied in three 12-week RCTs
- Both were associated with increased numbers of CSBMs and SBMs per week, responder rate, global relief, and stool form vs placebo
- Both associated with higher rate of diarrhea that led to treatment withdrawal than placebo

Implementation considerations:

- Can be used as a replacement or as an adjunct to OTC agents
- May be associated with side effects of diarrhea leading to discontinuation of treatment
- Duration of treatment in trials was 12 weeks, but the drug label does not provide a limit. Studies in IBS-C up to 6 months (linaclotide)
- Dose at least 30 minutes before first meal of the day (linaclotide); Can be dosed with or without food (plecanatide)

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

44

Virtual Grand Rounds

universe.gi.org

Recommendation 10: In adults with CIC who do not respond to OTC agents, the panel recommends the use of prucalopride over management without prucalopride (Strong recommendation, Moderate certainty of evidence)

- Five 12-week RCTs with 2 mg daily dose of prucalopride showed that it was associated with increased in number of CSBMs per week, responder rate, and global relief vs placebo
- No data on number of SBMs per week and could not pool variable scales of stool form
- Prucalopride was associated with higher rate of diarrhea that led to treatment withdrawal

Implementation considerations:

- Duration of treatment in trials was 4–24 weeks , but the drug label does not provide a limit
- Can be used as a replacement or as an adjunct to OTC agents
- General prokinetic effects may be useful in patients with upper GI symptoms/gastroparesis
- May be associated with side effects of headache, abdominal pain, nausea, and diarrhea
- Can be taken with or without food

Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

45

Virtual Grand Rounds

universe.gi.org

Summary

46

Virtual Grand Rounds

universe.gi.org

Summary of Recommendations for CIC

In patients with CIC, the AGA and ACG	Treatment	Strength of Recommendation	Certainty of Evidence
Recommends using	**Polyethylene glycol**	Strong	Moderate
	Bisacodyl & Sodium picosulfate	Strong	Moderate
	Linaclotide	Strong	Moderate
	Plecanatide	Strong	Moderate
	Prucalopride	Strong	Moderate
Suggests using	**Fiber**	Conditional	Low
	Magnesium oxide	Conditional	Very low
	Lactulose	Conditional	Very low
	Senna	Conditional	Low
	Lubiprostone	Conditional	Low

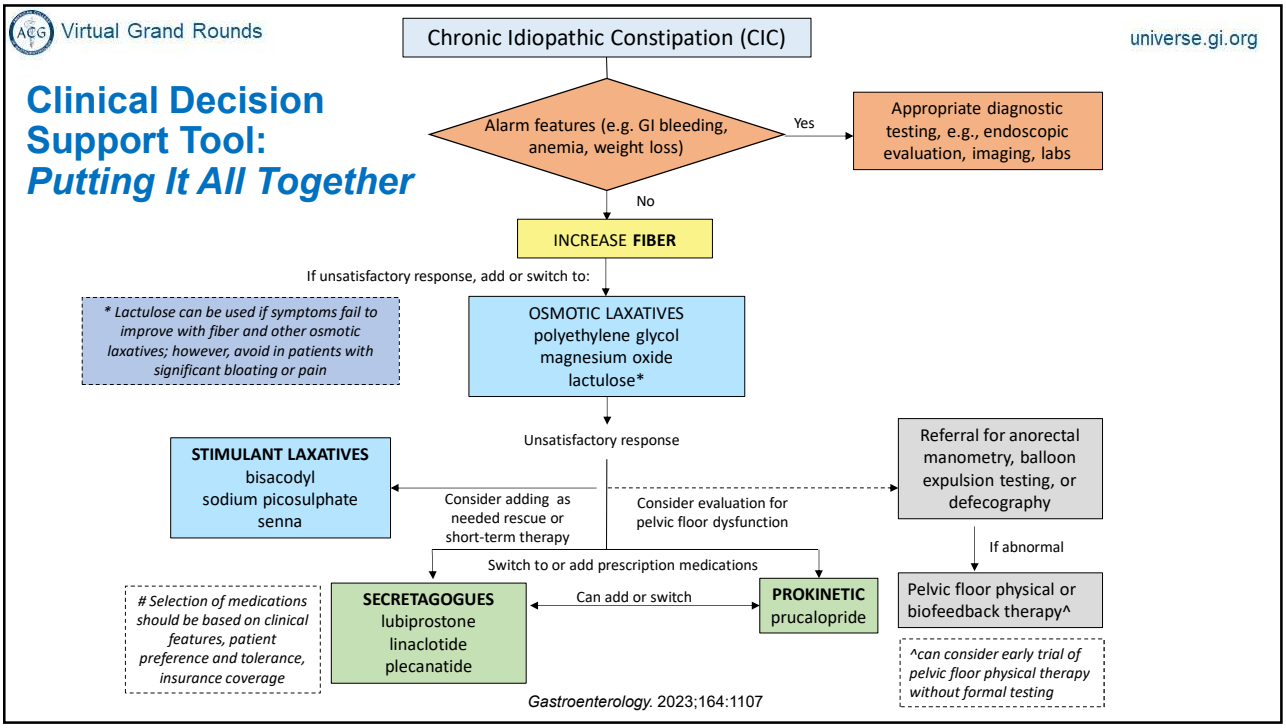
Chang L, Chey WD, Imdad A, et al. *Gastroenterology.* 2023;164(7):1086-1106 and *Am J Gastroenterology 2023;*118(6):936-954

47

Virtual Grand Rounds

universe.gi.org

Clinical Decision Support Tool: *Putting It All Together*



Gastroenterology. 2023;164:1107

48

Virtual Grand Rounds universe.gi.org

FDA Approved Prescription Options

Drug	Description/Mechanism	Dosing and Administration
Chloride channel activator		
Lubiprostone	Prostaglandin E1 analogue; activates chloride channel type 2 (CIC-2) on apical surface of intestinal epithelium	24 mcg orally twice daily with food and water
Guanylate cyclase-C (GC-C) agonists		
Linaclotide	14-amino acid peptide; binds to membrane-bound GC-C receptor on luminal epithelial cells in a pH-independent manner; may be active throughout the small intestine and colon	72 mcg or 145 mcg orally once daily, depending on individual presentation or tolerability
Plecanatide	16-amino acid peptide; binds to GC-C receptor in a pH-dependent manner with increased activity in the acidic portion of the proximal small intestine	3 mg orally once daily with or without food
Selective serotonin-4 (5-HT_4) receptor agonist		
Prucalopride	Dihydrobenzofurancarboxamide compound with high affinity for 5-HT_4 receptors; stimulates GI motility, especially colonic	2 mg orally once daily, with or without food (1 mg daily in patients with severe renal impairment)

Ford AC et al. *Am J Gastroenterol.* 2014;109(Suppl 1):S2-26; . Camilleri M et al. *Nat Rev Dis Primers 2017;3:* 10.1038/nrdp.2017.95; Shah ED et al. *Am J Gastroenterol.* 2018;113:329-338.

49

Virtual Grand Rounds universe.gi.org

Concluding Remarks

- Constipation is a multi symptom condition
- The main causes of functional constipation are slow colon transit, normal colon transit and disordered defecation
- Diet, lifestyle modification and OTC laxatives are primary therapies for patients with CIC
- When patients fail to respond to laxatives, diagnostic testing should be considered
- Prosecretory and prokinetic prescription options are effective for CIC patients
- A collaborative, integrated approach is best for severely affected patients

50

Virtual Grand Rounds universe.gi.org

Q&A

51

Virtual Grand Rounds universe.gi.org

Questions?

Lin Chang, MD, FACG

William D. Chey, MD, FACG

52


CONNECT AND COLLABORATE IN GI
ACG & CCF IBD Circle
ACG Hepatology Circle
ACG Functional GI Health and Nutrition Circle
ACG GI Circle
Connect and collaborate within GI
ACG Women in GI Circle
ACG's Online Professional Networking Communities
LOGIN OR SIGN-UP NOW AT: acg-gi-circle.within3.com

53