# It's a Family Affair: Lower GI Functional Disorders

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Editor-in-Chief,Evidence-Based GI: An ACG Publication
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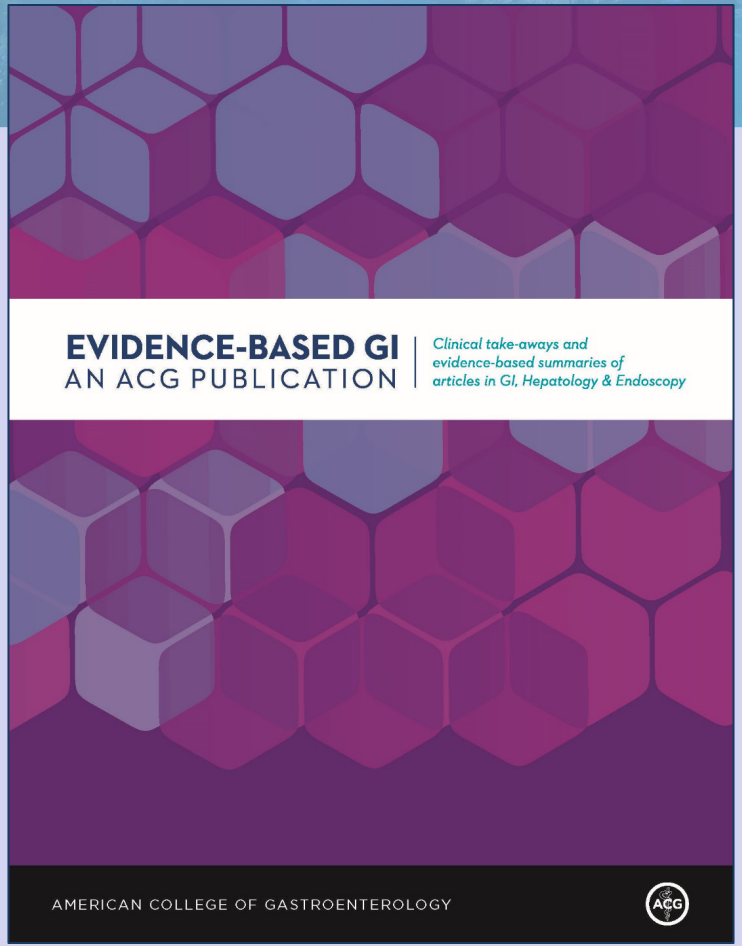
# Disclosures

- Consultant:
  - AbbVie, Ardelyx, Exact, Ironwood, Salix, Sanofi, Phathom,
- Speaker:
  - AbbVie, Ardelyx, Ironwood, Phathom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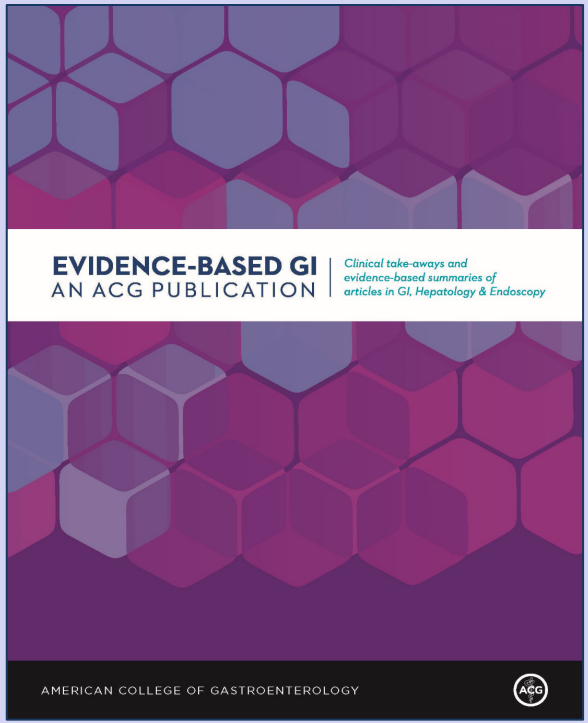
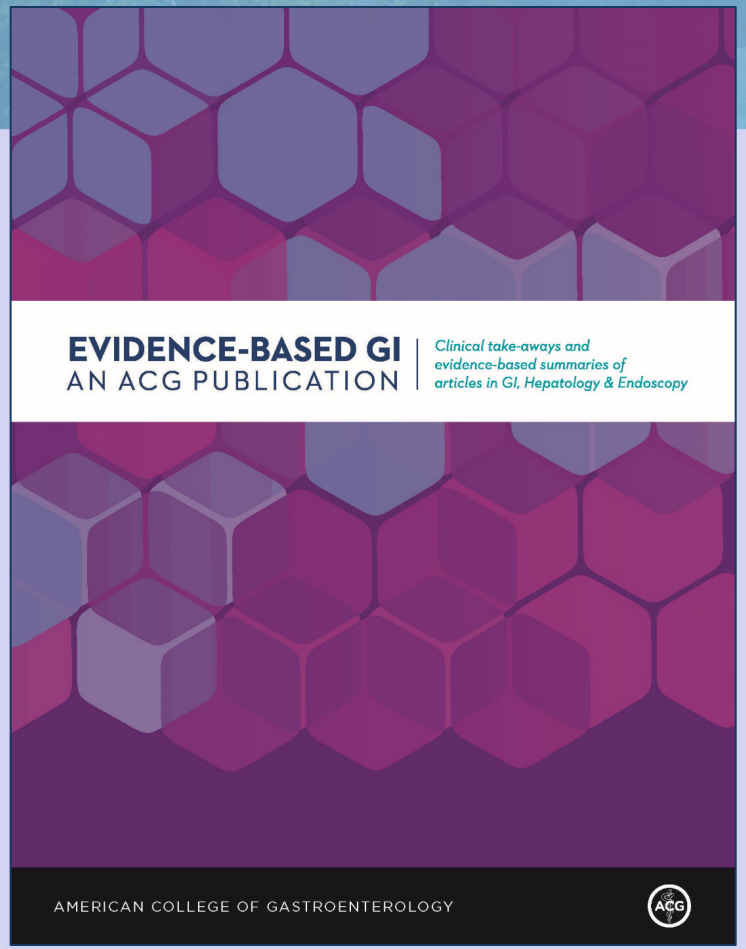
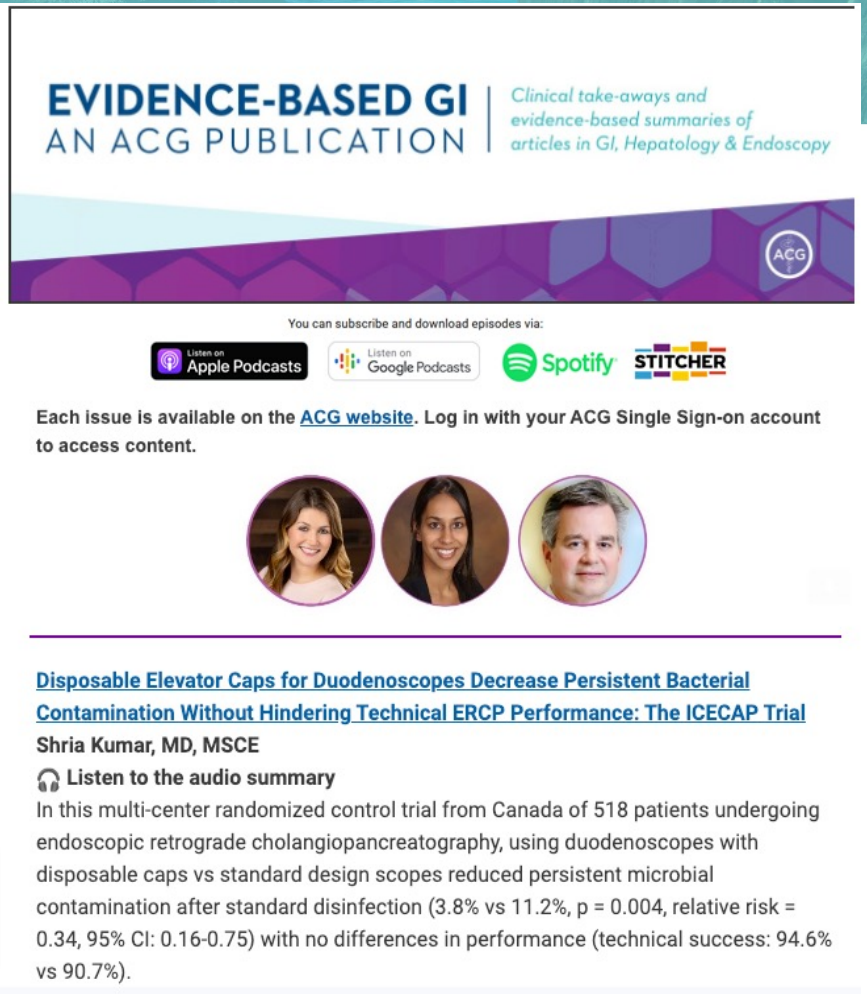



- **Monthly online ACG publication. Blast e-mail sent mid-month. Issues archived at ACG website.**
- **Summarizes important GI clinical research recently published in non-GI journals, including NEJM, JAMA, Lancet, etc.**
- **Each summary provides structured abstract and expert commentary**
- **Designed to be read on your phone**
- **Weekly podcasts and tweetorials**



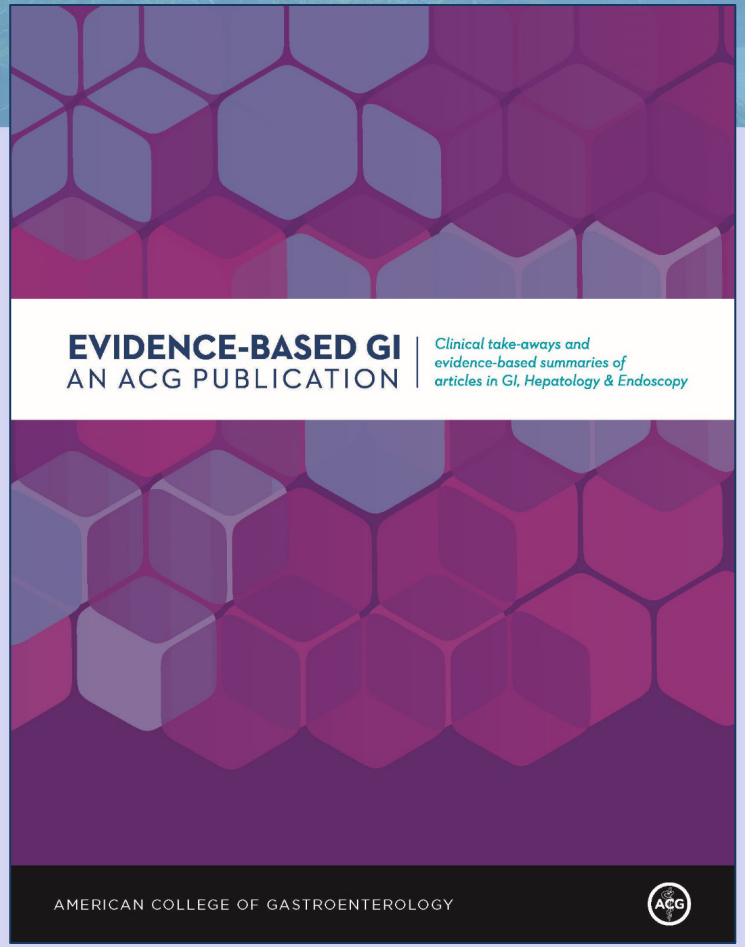




**Disposable Elevator Caps for Duodenoscopes Decrease Persistent Bacterial Contamination Without Hindering Technical ERCP Performance: The ICECAP Trial**

**Shria Kumar, MD, MSCE**

**Listen to the audio summary**

In this multi-center randomized control trial from Canada of 518 patients undergoing endoscopic retrograde cholangiopancreatography, using duodenoscopes with disposable caps vs standard design scopes reduced persistent microbial contamination after standard disinfection (3.8% vs 11.2%, p = 0.004, relative risk = 0.34, 95% CI: 0.16-0.75) with no differences in performance (technical success: 94.6% vs 90.7%).




*May 2023*

# TABLE OF CONTENTS

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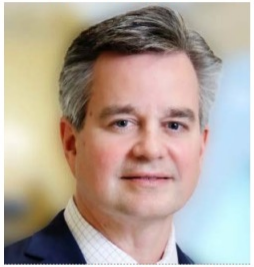
# Tenapanor (IBSRELA) for Treatment of IBS-C: Effective Over 26 Weeks



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*Philip Schoenfeld, MD, MSEd, MSc (Epi)*
*Editor-in-Chief*

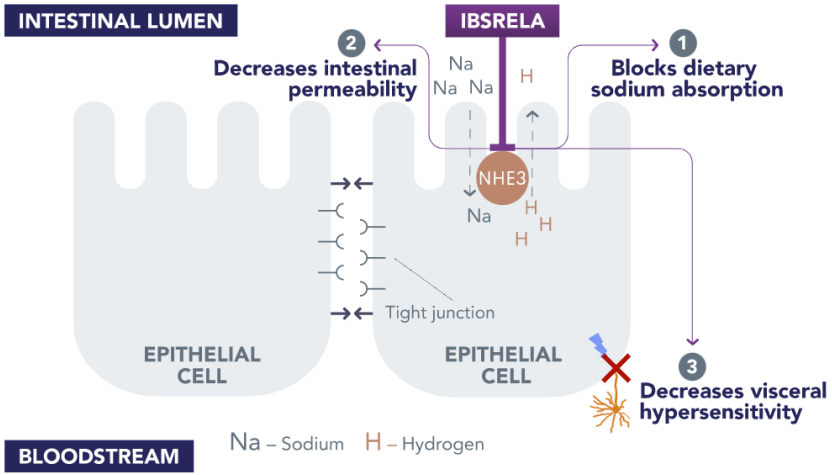
This article reviews Chey WD, Lembo A, Yang Y, Rosenbaum DP. Efficacy of Tenapanor in Treating Patients With Irritable Bowel Syndrome with Constipation: A 26-Week, Placebo-Controlled Phase 3 Trial (T3MPO-2). Am J Gastroenterol 2021; 116: 1294-1303. https://doi.org/10.14309/ajg.0000000000001056

*Correspondence to Philip Schoenfeld, MD, MSEd, MSc (Epi), Editor-in-Chief. Email: EBGI@gi.org*

## Tweetorial provided by:

**Romy Chamoun, MD**
@RomyChamoun
EBGI Ambassador
PGY-3, Lankenau Medical Center

- Blocks NHE3
- FDA-approved for IBS-C
- Minimally absorbed
- Blocks dietary sodium absorption, decreases intestinal permeability and visceral hypersensitivity (animal studies)
- 50mg po bid before breakfast and dinner



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Adapted from:
Chey, W; Lembo, A. J.; Yang, Y; Rosenbaum, D.P. Efficacy of Tenapanor in Treating Patients With Irritable Bowel Syndrome With Constipation: A 26-Week, Placebo-Controlled Phase 3 Trial (T3MPO-2), The American Journal of Gastroenterology: June 2021 - Volume 116 - Issue 6 - p 1294-1303
doi:10.14309/ajg.0000000000001056

## Key Study Definitions

👉Weekly combined response :

⬇️ in average weekly worst abdominal pain of ≥30.0% from baseline

**+**

⬆️ of ≥1 weekly complete spontaneous bowel movements (CSBM) from baseline

👉6/12-week combined responder rate:

**%** of pts who had a weekly combined response for at least 6/12 weeks.

## Key Study Endpoints

🥇 **Primary Endpoint:**

- The 6/12-week combined rate.

🥈 **Key Secondary Endpoint:**

- 6/12-week CSBM and abdominal pain responder

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Adapted from:

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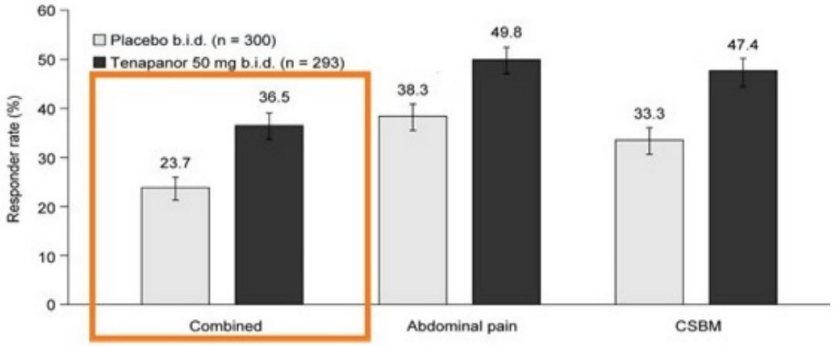


| | | | |
|---|---|---|---|
| Risk difference versus placebo, % (95% CI) | 12.9 (5.5, 20.2) | 11.5 (3.6, 19.4) | 14.1 (6.3, 21.9) |
| *P* value | <0.001 | 0.004 | <0.001 |

**Figure 1.** ≥ 6/12 week responders for FDA-combined endpoint, abdominal pain endpoint, and CSBM endpoint.

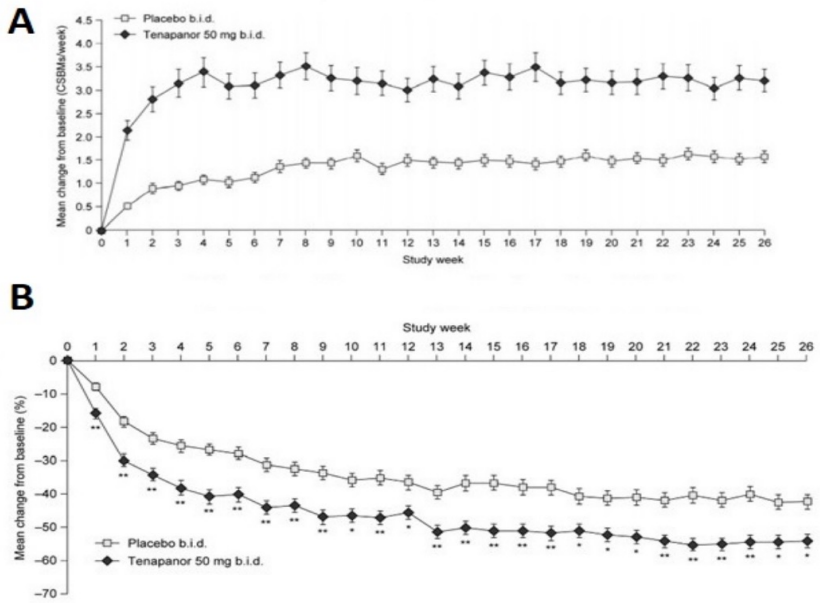


**Figure 2.** Weekly change in CSBMs (A) and abdominal pain (B).

## My Practice

Inadequate relief w/ **initial** course of a guanylate cyclase-C agonist (linaclotide or plecanatide)

Tenapanor 50 mg po bid (with breakfast and dinner)

**Tips:**

- Combine Tenapanor + peppermint oil capsules PRN for cramping
- Combine with neuromodulator: prefer duloxetine 30-60mg daily in IBS-C
- Refer to dietician for instruction in low-FODMAP diets

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# It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy

Philip Schoenfeld, MD, MSEd, MSc (Epi)

*Chief (Emeritus)-Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI*

This article reviews Sey MSL, Von Renteln D, Sultanian R, et al. A Multicenter Randomized Controlled Trial Comparing Bowel Cleansing Regimens for Colonoscopy After Failed Bowel Preparation. Clin Gastroenterol Hepatol 2022; In Press.

Philip Schoenfeld, MD, MSEd, MSc (Epi)
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**Tweetorial provided by:**

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- **Risk Factors for colonic dysmotility and inadequate bowel preparation despite compliance**
  - Obesity
  - Current opioid use
  - Diabetes mellitus
  - History of using constipation treatments
  - Current use of anticholinergics (including TCA)

- **In non-compliant patient**
  - Additional patient education is more helpful than prescribing supratherapeutic regimen.

❖ **Risk Factors for colonic dysmotility and inadequate bowel preparation despite compliance**

- Obesity
- Current opioid use
- Diabetes mellitus
- History of using constipation treatments
- Current use of anticholinergics (including TCA)

❖ **In non-compliant patient**

- Additional patient education is more helpful than prescribing supratherapeutic regimen.

## Prior Trials with Bowel Preparations

**Gimeno-Garcia et al.** *Am J Gastroenterol 2017; 112: 951-58.*

- 10 mg bisacodyl on the day before the procedure + a low-residue diet for 3 days pre-procedure.
- 4L PEG-3350 as split-prep vs 2L PEG + ascorbic acid as split-prep
- 4L PEG-3350-superior for adequate bowel cleansing (81.1% vs 67.4%, P< 0.01, ITT analysis)

→ Does not answer if supratherapeutic purgative regimens are more effective!

- No prior RCT assessing patients who successfully completed 4L PEG split-prep but still had inadequate cleansing.
- Multi-center, single-blind RCT
- Intervention: 4L PEG split prep + 15mg bisacodyl (taken at 2pm on day before scope) vs 6L PEG split prep + 15mg bisacodyl
- Outcome: Adequate bowel prep based on BBPS $\geq$6 with $\geq$2 in each segment
- Patient Demographics: 37% obese, 41% with IBS-C or CIC, 10% on opioids. Prior bowel prep: 35% used 4L PEG; 38% used 2L PEG; 12% used sodium picosulfate

# It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy



| Outcome | | Split-dose 4L + bisacodyl (n = 97) | Split-dose 6L + bisacodyl (n = 99) | *P*-value |
|---|---|---|---|---|
| **Adequate cleansing** | Defined as BBPS ≥ 6 | 83 (91.2%) | 78 (87.6%) | 0.44 |
| | Defined as adequate to identify polyps > 5mm | 82 (91.1%) | 76 (85.4%) | 0.24 |
| **Secondary endpoints** | Cecal intubation rate, n (%) | 87 (96.7%) | 82 (92.1%) | 0.19 |
| | Adenoma detection rate, n (%) | 34 (37.4%) | 28 (31.5%) | 0.41 |
| **Adherence** | Diet + consumed 100% of prep | 67 (81.7%) | 53 (68.0%) | 0.05 |
| | Diet + consumed 80% of prep | 71 (86.6%) | 57 (73.1%) | 0.03 |

Adapted from Sey MSL et al. Clin Gastroenterol Hepatol 2022.

# It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy

| My Practice-Before This Trial | |
|---|---|
| **Reactive prescription:** prior inadequate bowel cleansing | **Proactive Prescription:** any patient with 2 or more risk factors for inadequate cleansing |
| 6L PEG-3350 split-prep with 4L PEG consumed between 6 and 10 PM on the night before the procedure and 2L taken 4-6 hours before colonoscopy. | |
| Adequate cleansing Successes per BBPS | |
| 87.7% | 91.5% |
| **Remember,** patient education is the preferred intervention in non-compliant patients. | |

# It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy

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| 87.7% | 91.5% |
| **Remember,** patient education is the preferred intervention in non-compliant patients. | |

***Switched to 4L PEG split-prep + 15 mg bisacodyl at 2pm on day before scope***

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# Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach

**Philip Schoenfeld, MD, MSEd, MSc (Epi)**

*Chief (Emeritus), Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI.*

*Editor-in-Chief*

This summary reviews Rao S, Quigley EMM, Chey WD, et al. Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation. Gastroenterology 2023; In Press. doi.org/10/1053/j.gastro.2023.02.013

**Tweetorial Provided by:**

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**PGY-3, UCLA**

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# "Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach"

Summary of Rao et al. *Gastroenterology* 2023

## Pharmacologic

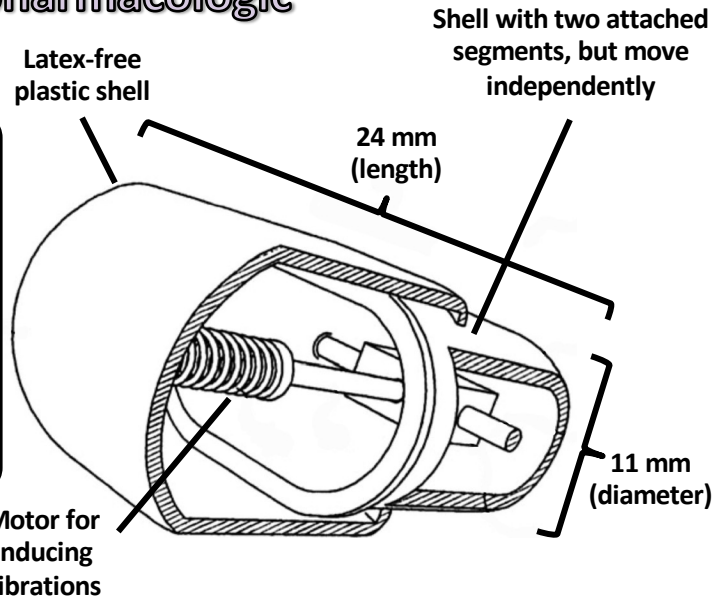
NEW

## Non-pharmacologic

Treatments for chronic idiopathic constipation

- Secretagogues
- Enemas
- Suppositories
- Osmotic laxatives
- Stimulant laxatives
- Fiber

- 2 vibration cycles/2 d period
- Each cycle lasts 2 hr
- Cycle: 3 sec stim + 16 sec rest
- ie, approx. 3 cycles/min




## Importance

"Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach"
Summary of Rao et al. *Gastroenterology* 2023

## Chronic Idiopathic Constipation (CIC)

2️ of the following:
- <3 💩 per wk
- Straining >25%
- Hard 💩 >25%
- 👉 maneuver >25%
- Blockage sensation >25%
- Incomplete sensation >25%

- 🚫 IBS
- Rare loose 💩 without laxatives

## Spontaneous BM (SBM)

- BM w/o use of rescue medicine in preceding 48 hrs & w/o use of digital maneuvers

## Complete Spontaneous BM (CSBM)

- SBM *plus* subject report of feeling complete evacuation

## Primary Endpoints

- 📈 1+ CSBM ($CSBM_1$) per week

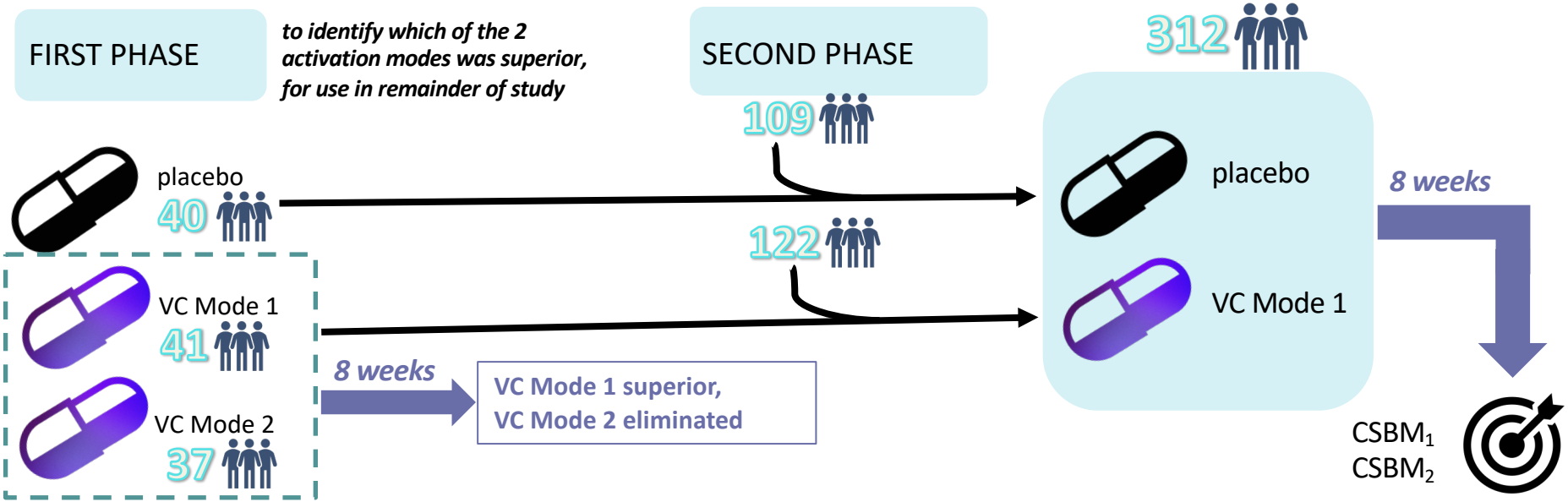
*or*

- 📈 2+ CSBM ($CSBM_2$) per week

during ≥6 of 8 wks of treatment (compared with baseline)

# Definitions & Endpoints

"Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach"
Summary of Rao et al. *Gastroenterology* 2023

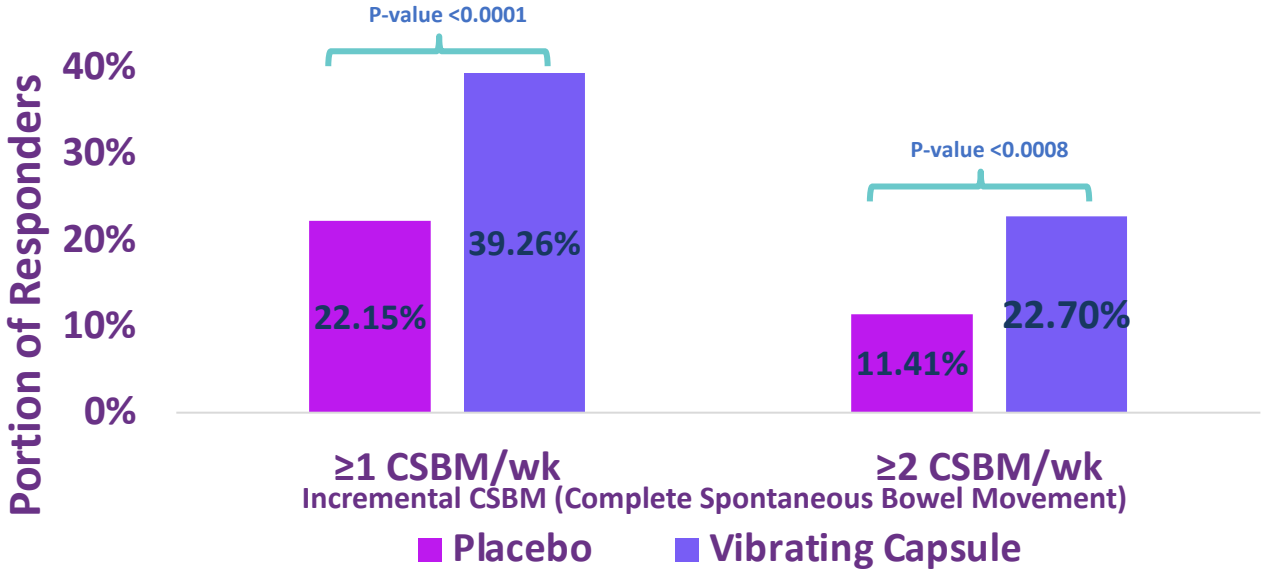



**Mode 1: starts vibrating from 12PM next day**
**Mode 2: starts vibrating from 6AM next day**

## Study Design

"Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach"
Summary of Rao et al. *Gastroenterology* 2023

## Effect of Vibrating Capsule on CSBM, Primary Outcomes




## Results

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# "Vibrating Capsules for Chronic Constipation: The New Non-Pharmacologic Approach"

Summary of Rao et al. *Gastroenterology* 2023

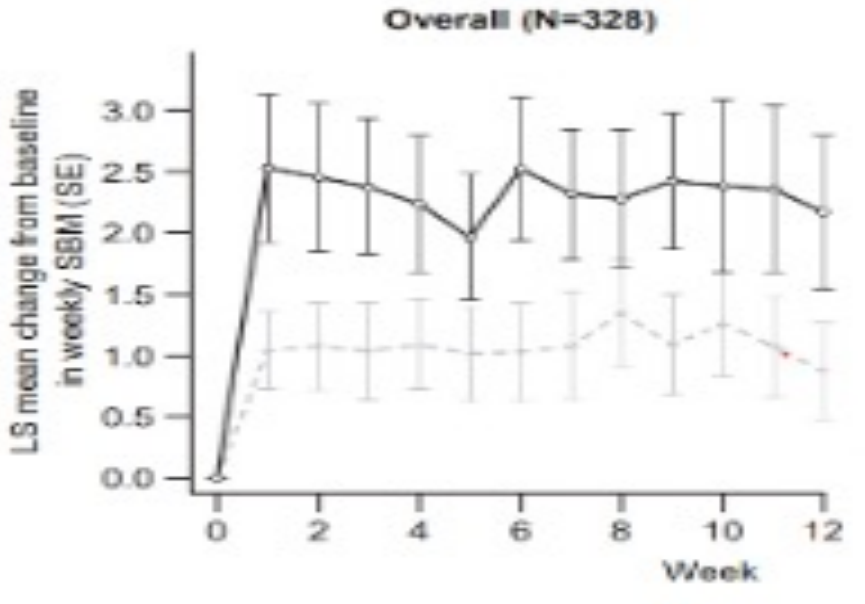
- Limited capsule supply in 2023
- Available at motility centers of excellence
- Only one vibration cycle was evaluated
- Need longer trials (i.e., >8 weeks)
- Need to find CIC subgroups that respond
- Not evaluated in IBS-C
- Unclear insurance reimbursement
- $89 per month (out-of-pocket)

# Linaclotide for Pediatric Functional Constipation- First prescription treatment for pediatic FC!

- Double-blind, placebo-controlled, Phase 3 RCT
- 328 pediatric patients (6-17 years old) with modified ROME III criteria for functional constipation (mean SBM/week: 1.2)
- Intervention: 72 ucg linaclotide vs placebo X 12 weeks
- Primary Outcome: Increase in SBMs/week

**Di Lorenzo C, Nurko S, et al. Gastro 2023; P145**

# Linaclotide for Pediatric Functional Constipation



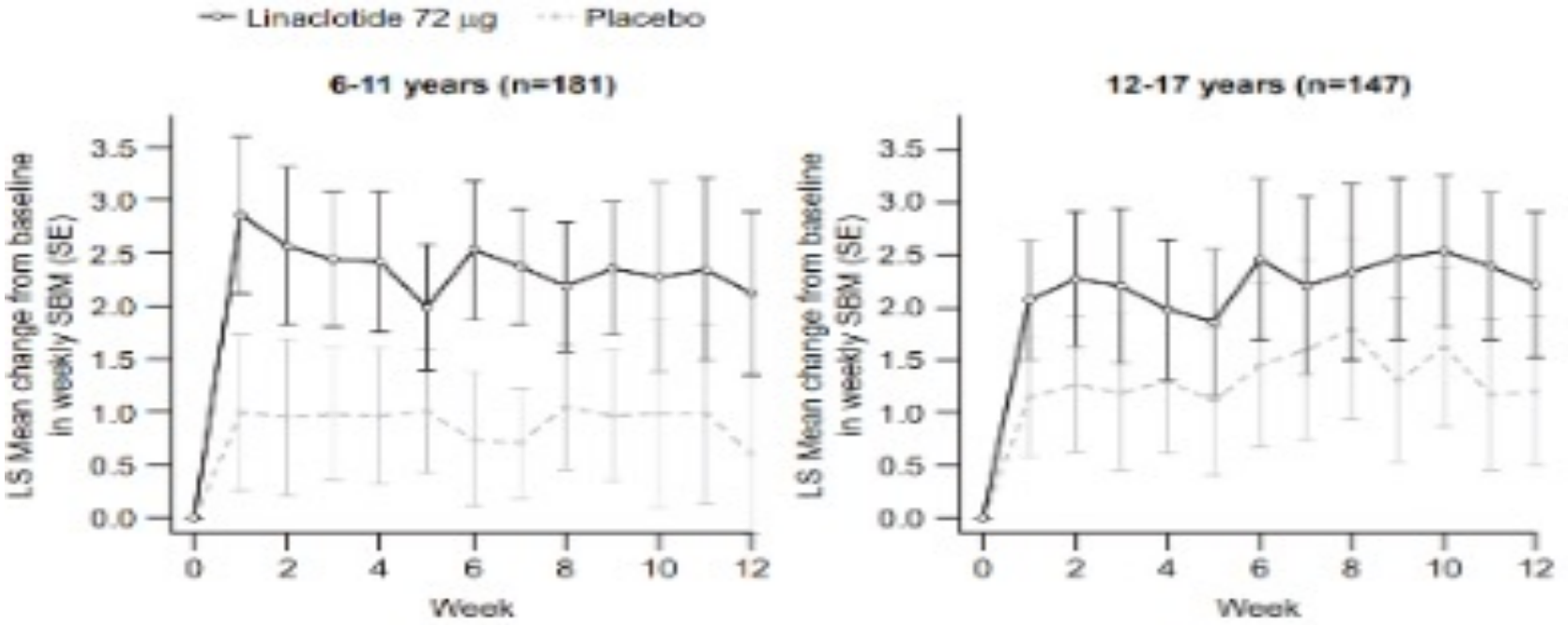

-Increase in 12-week SBM frequency significantly greater with linaclotide: 2.22 vs 1.05, p = 0.0001

-Significant improvement in stool consistency, based on Bristol stool scale, with linaclotide vs placebo

Adverse events: diarrhea < 5% and < 2% discontinued drug due to diarrhea

**Di Lorenzo C, Nurko S, et al. Gastro 2023; P145**

# Trend for Larger Increase in SBM/week in linaclotide-treated 6-11 year olds vs linaclotide-treated 12-17 year olds




**My Practice: Use 145 ucg dose for selected 12-17 year olds with functional constipation. Most likely approved for use in summer 2023. Probably will be approved for long-term use.**