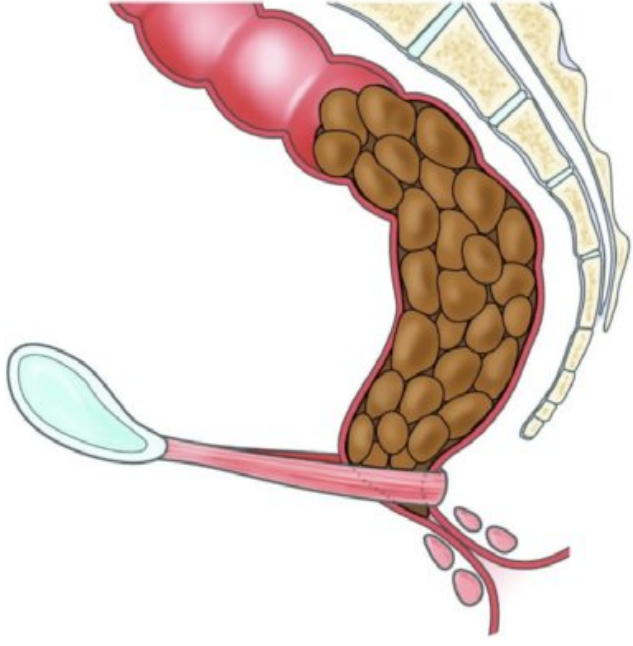
Constipation: slow transit versus outlet obstruction



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Constipation

Constipation (definition):
unsatisfactory defecation resulting from infrequent stools, difficult stool passage, or both.

Affects 8-15% of adult population

Chronic constipation: duration >4w

Normal transit

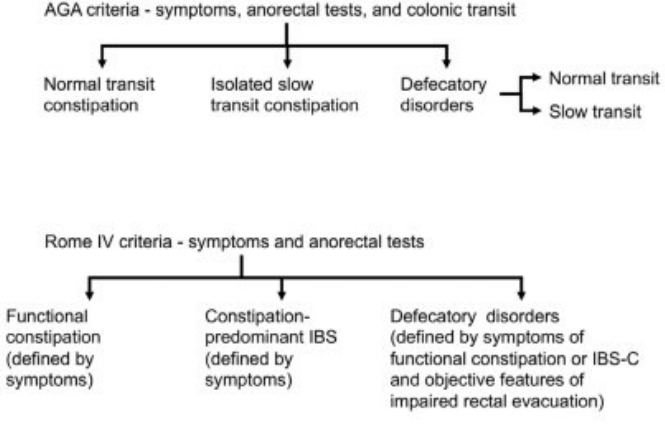
Slow transit

Defecatory disorders

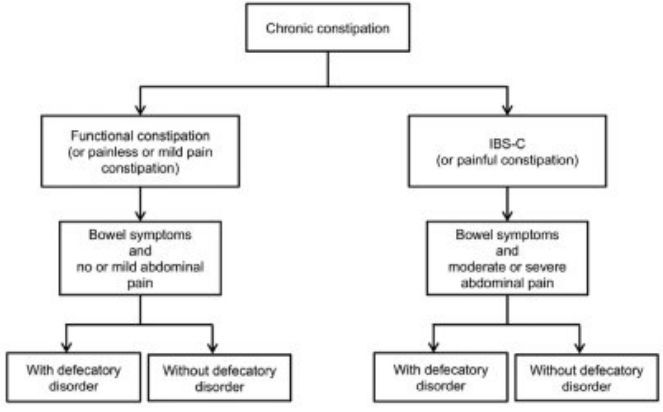
Scott SM et al. Neurogastroenterology & Motility. 2021;33:e14050

Constipation - classification

AGA vs. Rome IV criteria



Painless vs. painful constipation



Bharucha A et al. Gastroenterology 2020;158:1232–1249

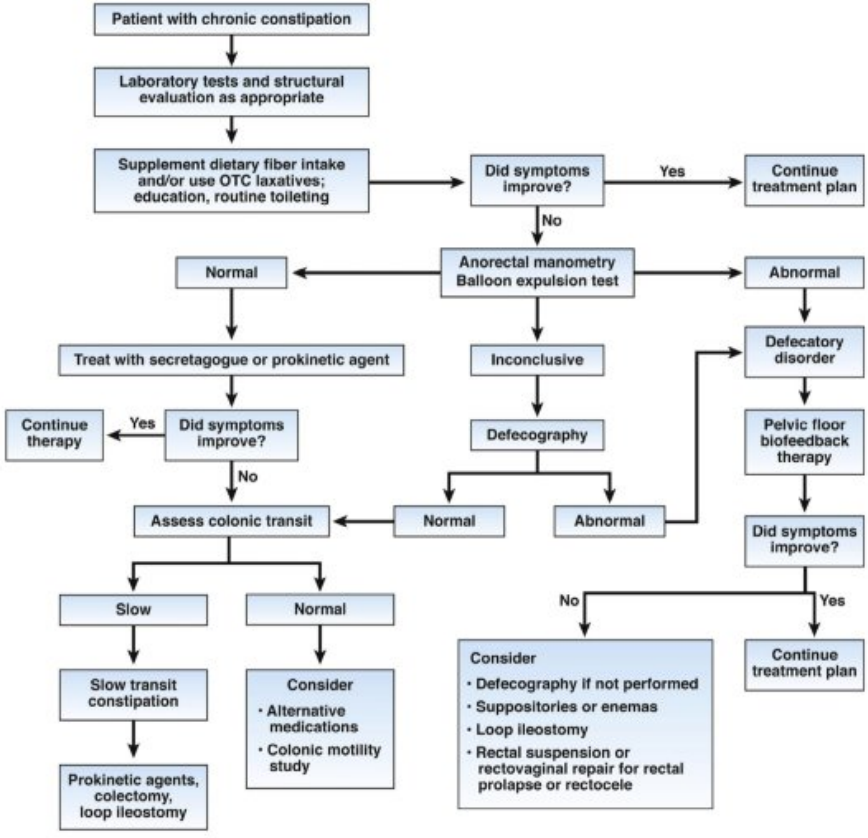
Constipation – common medical conditions

- Drug effects
- Mechanical obstruction:
  - colon cancer, external compression from malignant lesion, strictures (diverticular or post ischemic), rectocele (if large), megacolon, anal fissure
- Metabolic conditions:
  - diabetes mellitus, hypothyroidism, hypercalcemia, hypokalemia, hypomagnesemia, uremia, heavy metal poisoning
- Myopathies:
  - amyloidosis, scleroderma
- Neuropathies:
  - Parkinson's disease, spinal cord injury or tumor, cerebrovascular disease, multiple sclerosis
- Other conditions:
  - depression, degenerative joint disease, autonomic, neuropathy, cognitive impairment, immobility, cardiac disease

Bharucha A et al. Gastroenterology 2020;158:1232–1249

Chronic constipation: algorithmic approach

1. Check for medical conditions
2. Treat with diet/fiber, OTC laxatives
3. Check for defecation disorders (anorectal manometry, defecography)
4. Treat with secretalogue / prokinetics
5. Assess colonic transit
6. Evaluate advanced therapies (prokinetics, colectomy, loop ileostomy, etc.)



Bharucha A et al. Gastroenterology 2020;158:1232–1249

Constipation: medical therapy overview

Treatment	Frequency	Dose		Number needed to treat		Cost per month	Comments
		CC	IBS-C	CC	IBS-C	(U$D in 2019)	
Bulking agents, psyllium	daily	var	var	2	10	< $10	start low dose
Macrogolum (PEG)	daily	17g	17g	3	n/a	$ 31	improve bowel symptoms but not pain
Lactulose	daily	20g	20g	n/a	n/a	$ 11	can produce bloating, only med approved during pregnancy
Bisacodil	daily	10mg	10mg	4	n/a	< $10	also supp. Can produce abd. Cramps
Senna	daily	17.2 - 34.4mg	17.2 - 34.4mg	n/a	n/a	< $10	widely used in US
Lubiprostone	twice daily	24 mcg	8 mcg	4	12	$ 350	indicated for opioid induced constipation
Linaclotide	daily	72 mcg	290 mcg	12	10	$ 400	reduces abdominal pain
Plecanatide	daily	3-6mg	6mg	11	9	$ 400	reduces abdominal pain
Prucalopride	daily	2mg	n/a	6	n/a	$ 400	prokinetic

Bharucha A et al. Gastroenterology 2020;158:1232–1249

Constipation: diagnostic investigations

Investigation	Screening, advanced, or experimental	Resources required [a]	Principal pathophysiological information provided	Other pathophysiological information provided
Tests of gut transit				
Radio-opaque markers	Screening	+	Delayed whole-gut transit	
Scintigraphy	Advanced	+++	Delayed colonic transit	Delayed regional GI and whole-gut transit (extension of technique)
Wireless motility capsule	Advanced	++	Delayed regional GI and whole-gut transit	Regional GI dysmotility; dysbiosis/ altered colonic fermentation?
3D-Transit capsule	Experimental	++	Delayed regional GI and whole-gut transit	Regional GI dysmotility
Tests of gut contractility				
Colonic manometry	Advanced	+++	Colonic dysmotility	
Colonic barostat	Advanced	++	Altered colonic tone	Colonic dysmotility
Real-time MRI	Experimental	+++	Colonic dysmotility (altered wall motion)	Alterations in colonic luminal volume

Abbreviation: MRI, magnetic resonance imaging.

[a]Relates to cost and availability (+ = cost-effective and/or widely available; +++ = expensive and/or of limited availability).

Scott SM et al. Neurogastroenterology & Motility. 2021;33:e14050

Constipation: diagnostic investigations

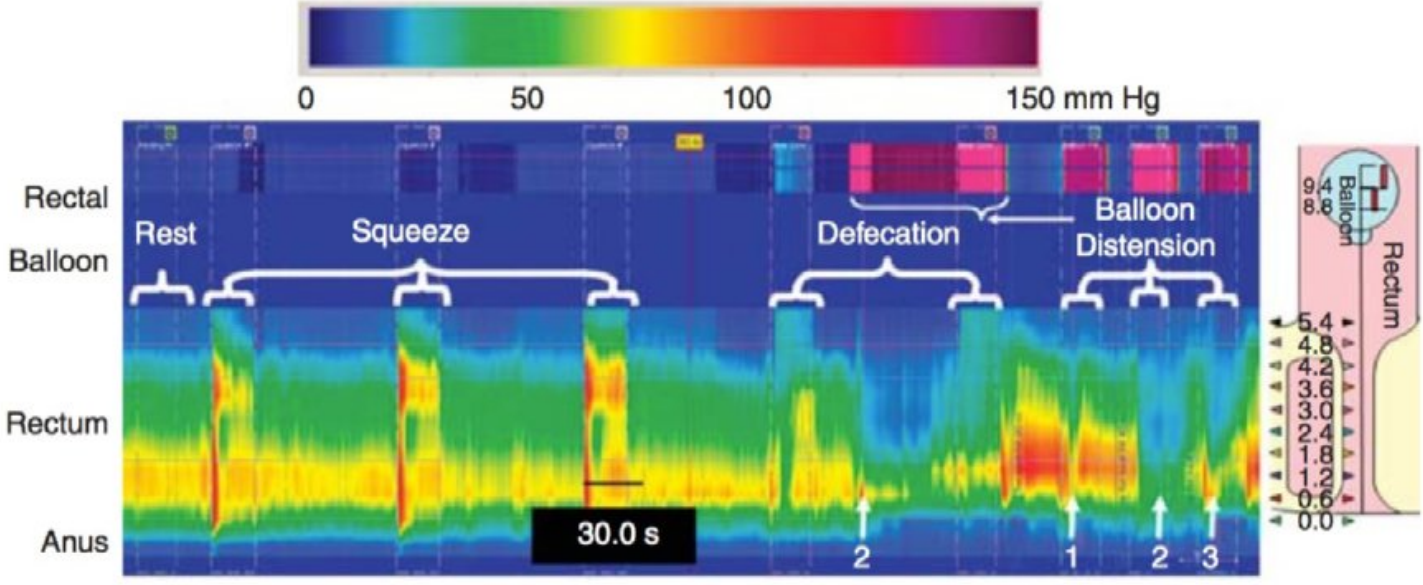
Investigation	Screening, advanced, or experimental	Resources required [a]	Principal pathophysiological information provided	Other pathophysiological information provided
Tests of evacuation				
Anorectal manometry	Screening	++	Abnormal recto-anal co-ordination; poor rectal propulsion; anal dyssynergia	Anal sphincter dysfunction
Balloon expulsion test	Screening	+	Impaired evacuation	
Transperineal ultrasound	Screening	++	Functional and/or structural obstructive features	
Barium defecography	Advanced	+++	Impaired evacuation; functional and/or structural obstructive features	Multi-compartmental abnormalities (when appropriately opacified)
MRI defecography	Advanced	+++	Impaired evacuation; functional and/or structural obstructive features	Multi-compartmental pelvic floor abnormalities
Fecobionics	Experimental	++	Impaired evacuation	Abnormal evacuation pressure patterns
Tests of sensation				
Balloon distension	Screening	+	Rectal hypo- and hypersensitivity	
Barostat	Advanced	++	Rectal hypo- and hypersensitivity	Abnormal rectal compliance and capacity

Abbreviation: MRI, magnetic resonance imaging.

[a]Relates to cost and availability (+ = cost-effective and/or widely available; +++ = expensive and/or of limited availability).

Scott SM et al. Neurogastroenterology & Motility. 2021;33:e14050

High resolution anorectal manometry (HRAM)



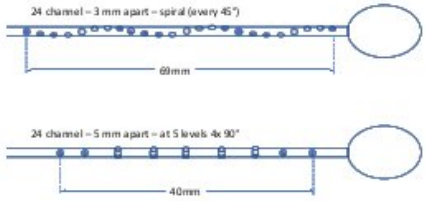
HRAM – London protocol

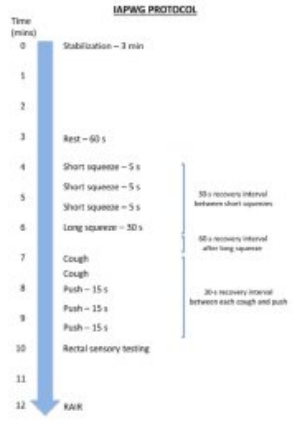
POSITION PAPER

Neurogastroenterology & Motility WILEY

The international anorectal physiology working group (IAPWG) recommendations: Standardized testing protocol and the London classification for disorders of anorectal function

Emma V. Carrington[1] | Henriette Heinrich[2] | Charles H. Knowles[1] | Mark Fox[2] | Satish Rao[3] | Donato F. Altomare[4] | Adil E. Bharucha[5] | Rebecca Burgell[6] | William D. Chey[7] | Guiseppe Chiarioni[8] | Philip Dinning[9] | Anton Emmanuel[10] | Ridzuan Farouk[11] | Richelle J. F. Felt-Bersma[12] | Kee Wook Jung[13] | Anthony Lembo[14] | Allison Malcolm[15] | Ravinder K. Mittal[16] | François Mion[17] | Seung-Jae Myung[13] | P. Ronan O'Connell[18] | Christian Pehl[19] | Jose María Remes-Troche[20] | R. Matthew Reveille[21] | Carolynne J. Vaizey[22] | Veronique Vitton[23] | William E. Whitehead[24] | Reuben K. Wong[11] | S. Mark Scott[1] | All members of the International Anorectal Physiology Working Group



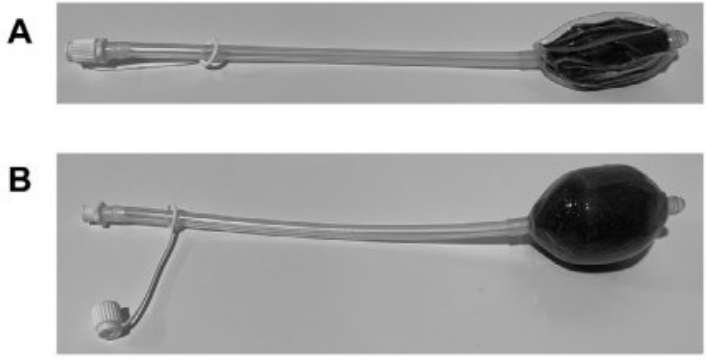


Carrington et al. Neurogastroenterology & Motility. 2020;32:e13679.

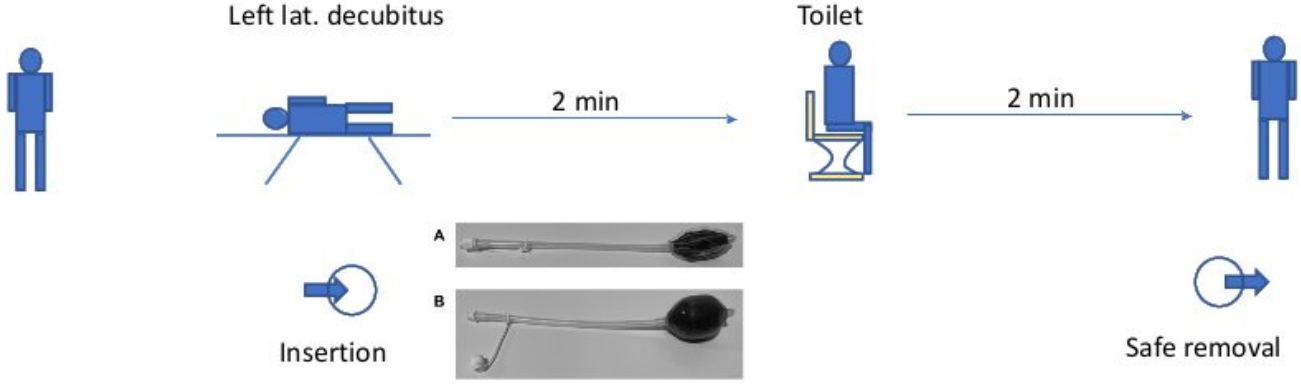
Clinical Gastroenterology and Hepatology 2023;21:1082–1090

An Office-Based, Point-of-Care Test Predicts Treatment Outcomes With Community-Based Pelvic Floor Physical Therapy in Patients With Chronic Constipation

Eric D. Shah,* Elizabeth A. Pelletier,* Carol Greeley,* Emily E. Sieglinger,* Jamie D. Sanchez,* Kayla A. Northam,* Jessica A. Perrone,* Michael A. Curley,* Christopher M. Navas,* Tracy L. Ostler,* Aimee R. Burnett Greeley,‡ Pablo Martinez-Camblor,§ Jason R. Baker,‖ Adrienne Harris,¶ Corey A. Siegel,* and William D. Chey#

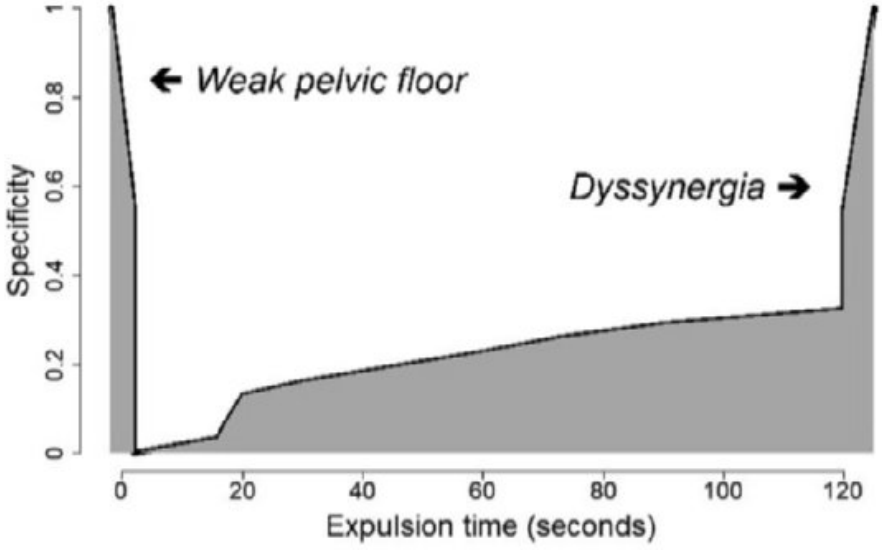


Rectal expulsion device (RED) - Protocol



Shah et al. Clin Gastroenterol Hepatol 2023;21:1082–1090

RED – Likelihood to respond to therapy



Expulsion time	Likelihood of response
<5 seconds or >120 seconds	48.9%
5-120 seconds	8.9%

Shah et al. Clin Gastroenterol Hepatol 2023;21:1082–1090

Pelvic floor training for dyssynergic defecation

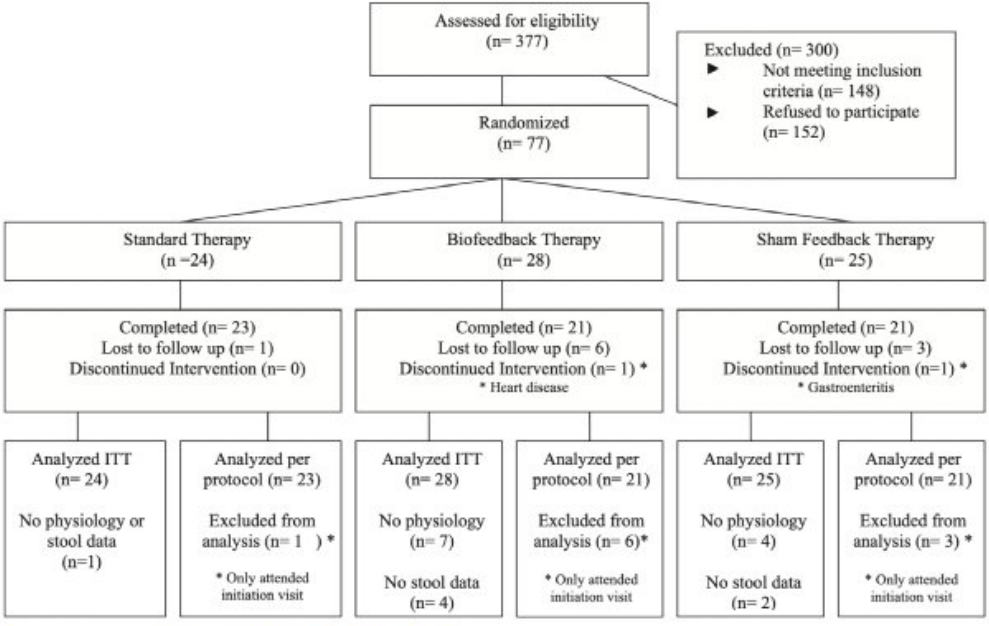
CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2007;5:331–338

Randomized Controlled Trial of Biofeedback, Sham Feedback, and Standard Therapy for Dyssynergic Defecation

SATISH S. C. RAO,* KARA SEATON,* MEGAN MILLER,* KICE BROWN,* INGRID NYGAARD,* PHYLLIS STUMBO,‡ BRIDGETTE ZIMMERMAN,‡ and KONRAD SCHULZE*

*University of Iowa Carver College of Medicine and ‡University of Iowa Clinical Research Center, Iowa City, Iowa

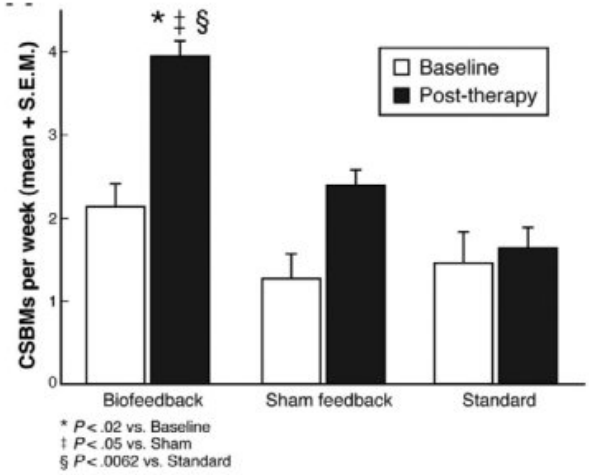
Pelvic floor training for dyssynergic defecation



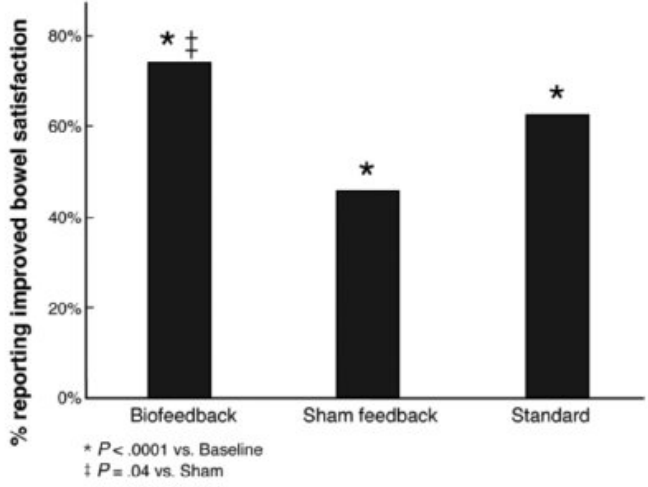
Rao et al. Clin Gastroenterol Hepatol 2007; 5:331–338

Pelvic floor training for dyssynergic defecation

Complete spontaneous bowel movements



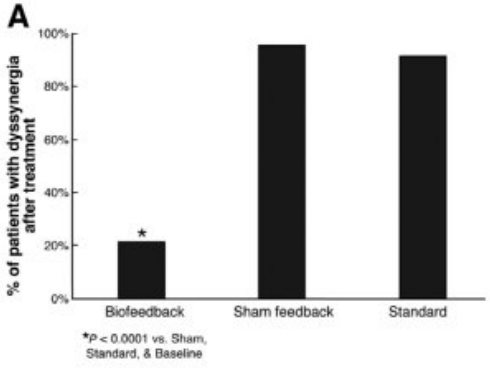
Improved bowel satisfaction



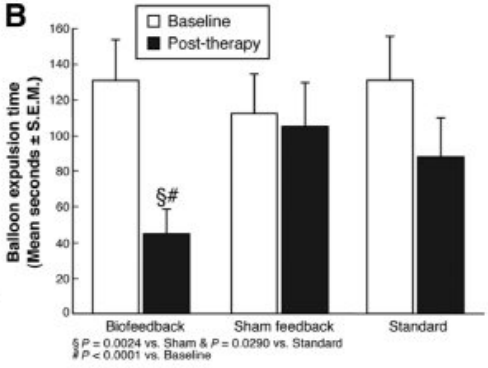
Rao et al. Clin Gastroenterol Hepatol 2007; 5:331–338

Pelvic floor training for dyssynergic defecation

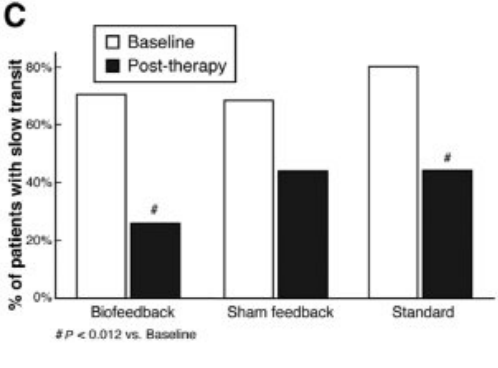
Dyssynergic defecation



Balloon expulsion time (sec)



Patients with slow transit



Rao et al. Clin Gastroenterol Hepatol 2007; 5:331–338

Pelvic floor training for dyssynergic defecation

Subjective and physiologic parameters

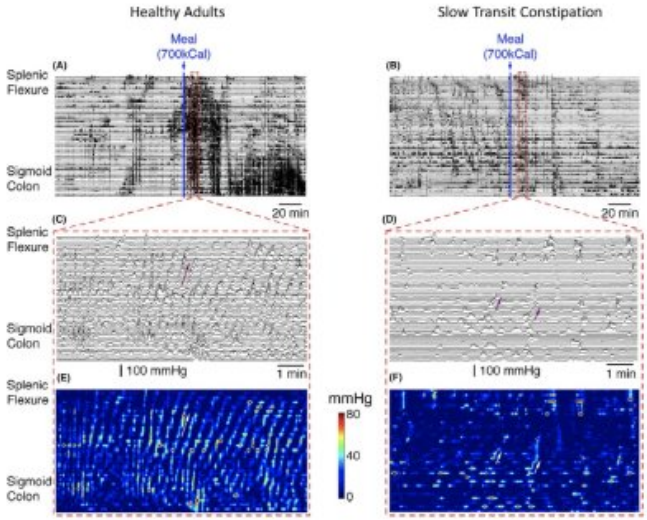
	Biofeedback		Sham feedback		Standard	
	Baseline	After	Baseline	After	Baseline	After
Subjective parameters						
No. of stools/wk	6.1 ± 0.1	7.1 ± 0.1[a]	6.2 ± 0.2	5.4 ± 0.1	5 ± 0.1	4.7 ± 0.1
Stool consistency (1–7)	3.5 ± 0.2	3.9 ± 0.2	3.5 ± 0.2	3.4 ± 0.2	3.4 ± 0.2	3.5 ± 0.2
Stool strain score (1–3)	1.99 ± 0.1	1.85 ± 0.1	2.0 ± 0.1	1.8 ± 0.1	1.9 ± 0.1	1.9 ± 0.1
Laxative consumption (%)						
Types I–II	70%	85%	64%	76%	67%	75%
Types III–IV	30%	11%	32%	16%	33%	21%
Digital assistance (%)	36%	14%[b,c]	32%	32%	33%	24%
Physiologic parameters						
Anal resting pressure	67 ± 3[d]	60 ± 4	60 ± 5	54 ± 4	56 ± 4	55 ± 4
Anal residual pressure (*mm Hg*)	81 ± 6[d]	39 ± 5[e]	67 ± 6	68 ± 6	60 ± 5	61 ± 5
Intrarectal pressure (*mm Hg*)	32 ± 5	49 ± 4[e]	39 ± 4	38 ± 4	34 ± 4	34 ± 3
Defecation index	0.4 ± 0.1[d]	1.7 ± 0.2[e]	0.7 ± 0.1	0.7 ± 0.2	0.6 ± 0.1	0.6 ± 0.1
First sensation threshold (*mL*)	43 ± 9[a]	29 ± 7[b]	39 ± 8	33 ± 11	27 ± 9	20 ± 2
Urge to defecate threshold (*mL*)	185 ± 17	171 ± 15	200 ± 15	191 ± 13	186 ± 14	184 ± 22

[a] $P = .019$, biofeedback vs standard for number of stools.
[b] $P = .03$ vs baseline.
[c] $P = .02$ vs sham feedback.
[d] $P < .002$ vs sham and standard.
[e] $P < .003$ vs baseline, sham, and standard.

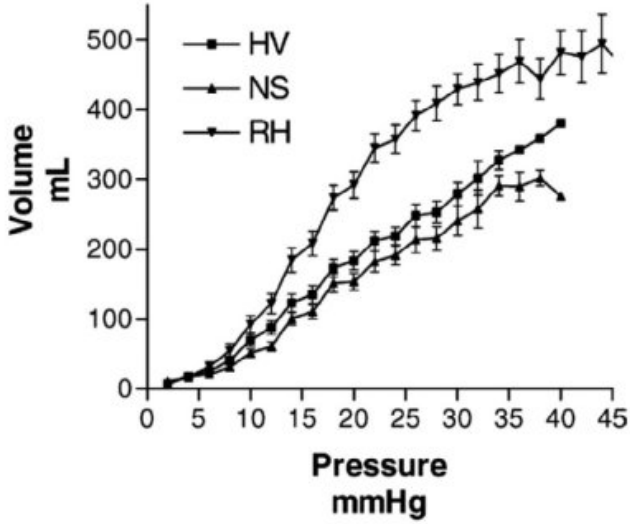
Rao et al. Clin Gastroenterol Hepatol 2007; 5:331–338

Constipation: advanced investigations

Colonic HRM – healthy vs. slow-transit

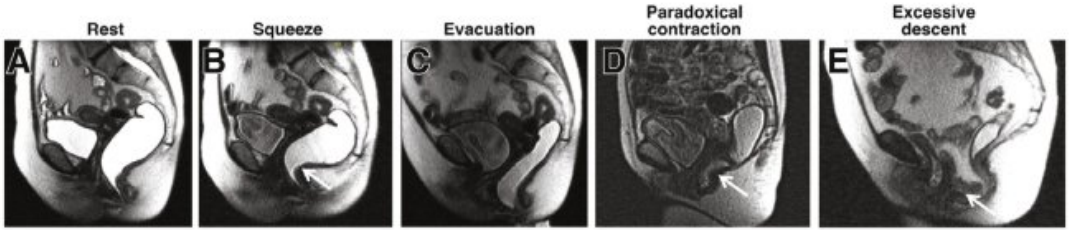


Rectal barostat – healthy vs. hyposensitivity

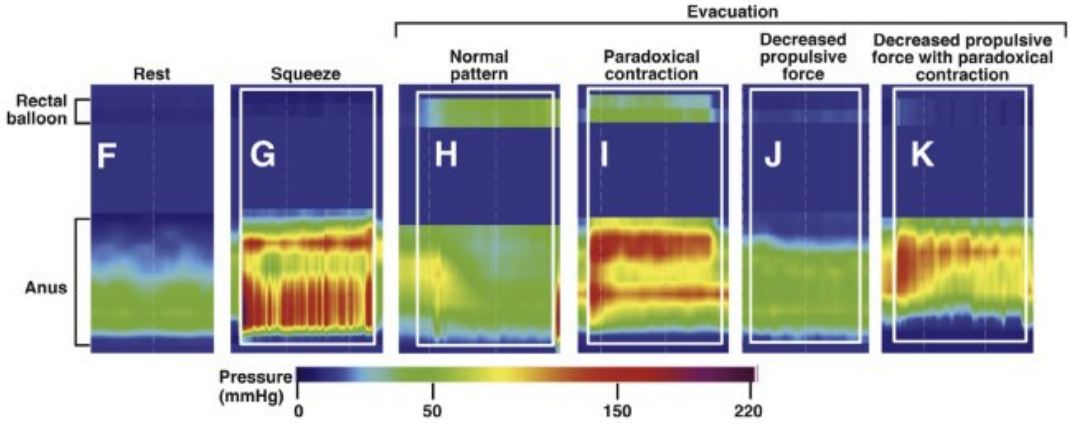


Scott SM et al. Neurogastroenterology & Motility. 2021;33:e14050

Combining data from diagnostic investigations



MR-defecography



HRAM

Bharucha A et al. Gastroenterology 2020;158:1232–1249

Gastroenterology 2023;164:1202–1210

FUNCTIONAL GI DISEASE

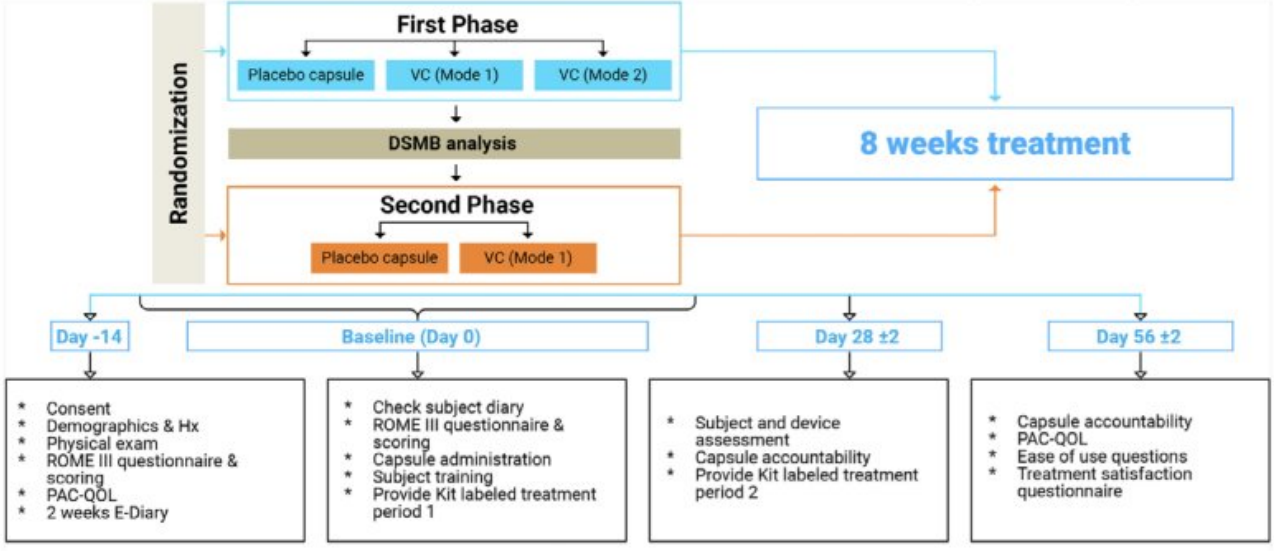
Randomized Placebo-Controlled Phase 3 Trial of Vibrating Capsule for Chronic Constipation

Satish S. C. Rao,[1] Eamonn M. M. Quigley,[2] William D. Chey,[3] Amol Sharma,[1] and Anthony J. Lembo[4]

[1]Division of Gastroenterology/Hepatology, Augusta University, Augusta, Georgia; [2]Lynda K. and David M. Underwood Center for Digestive Disorders, Houston Methodist Hospital and Weill Cornell Medical College, Houston, Texas; [3]University of Michigan, Ann Arbor, Michigan; and [4]Beth Israel Hospital, Boston, Massachusetts

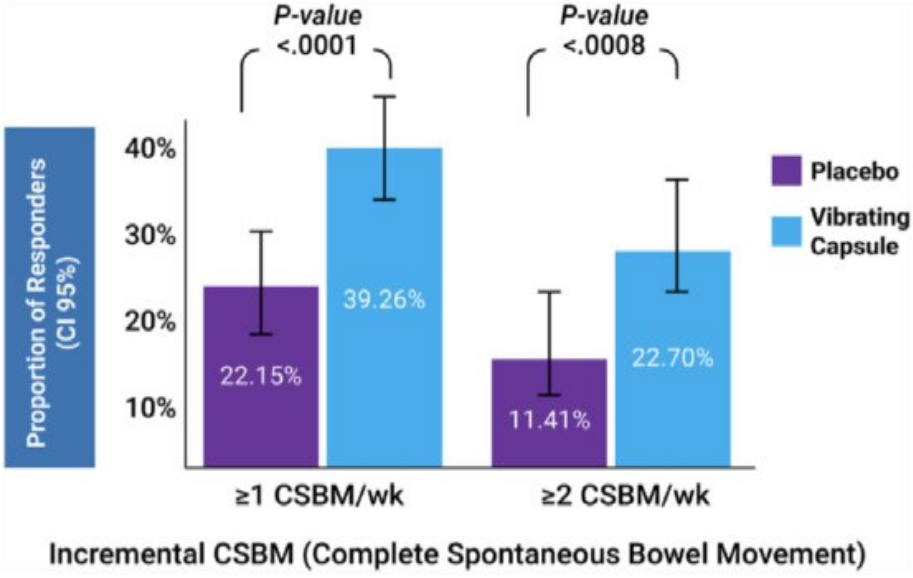
Study protocol

1 capsule orally between 9-10 PM each night, 5 times a week (excluding Wednesdays and Sundays).



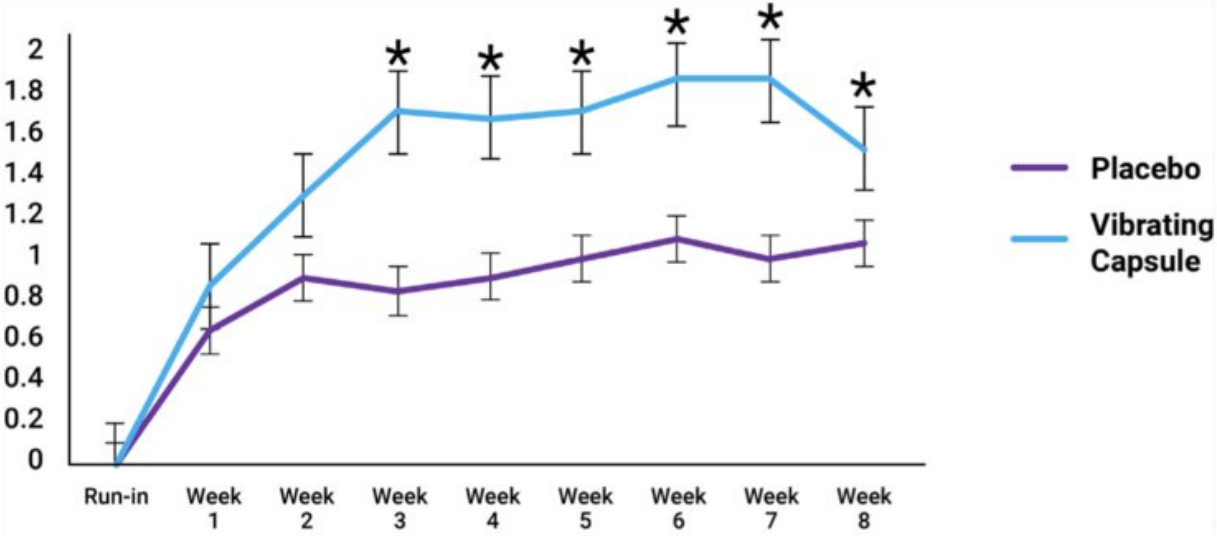
Rao et al Gastroenterology 2023;164:1202–1210

Results: Incremental CSBM



Rao et al Gastroenterology 2023;164:1202–1210

Results: change from baseline in mean weekly CSBM rate



Rao et al Gastroenterology 2023;164:1202–1210

Sacral nerve stimulator for slow-transit constipation

ANNALS OF SURGERY

RANDOMIZED CONTROLLED TRIAL

Sacral Neuromodulation Versus Conservative Treatment for Refractory Idiopathic Slow-transit Constipation

The Randomized Clinical No.2-Trial

Heemskerk, Stella C.M. MSc[*,†,‡]; Dirksen, Carmen D. PhD[*,†]; van Kuijk, Sander M.J. PhD[*,†]; Benninga, Marc A. MD, PhD[§]; Baeten, Coen I.M. MD, PhD[‖]; Masclee, Ad A.M. MD, PhD[¶,#]; Melenhorst, Jarno MD, PhD[¶,#,**]; Breukink, Stéphanie O. MD, PhD[¶,#,**]

Heemskerk et al Ann Surg 2023; e-pub ahead of print Nov 23, 2023

Sacral nerve stimulator for slow-transit constipation

- **Study design**: multicenter, open-label, pragmatic, randomized trial performed in two Dutch hospitals
- **Inclusion criteria**: age 14-80y, idiopathic slow-transit constipation STC (transit time >67h), a defecation frequency <3 per week and refractory (i.e. unresponsive) to maximal conservative (non-operative) treatment
- **Exclusion criteria:** outlet obstruction, rectal prolapse, and previous colon surgery
- **Randomization** (3:2):
  - sacral neuromodulation (SNM)
  - personalized conservative treatment (PCT)
- **Primary end-point**: average defecation frequency ≥3 per week after six months

Heemskerk et al Ann Surg 2023; e-pub ahead of print Nov 23, 2023

SNM vs. PCT for slow-transit constipation (STC)

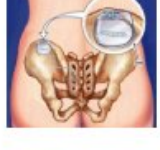
110
Enrollment
(Inclusion/exclusion)

67
Randomization

26
PCT
ITT 4%
6-mo f/u
ITT 4%
12-mo f/u

41
SNM (test)

31
SNM (implant)

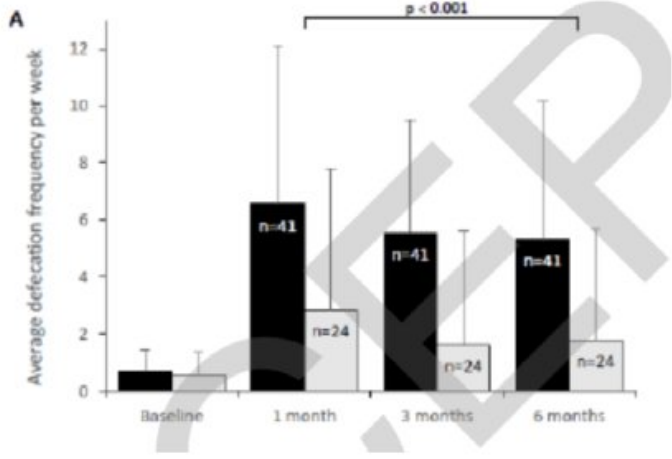


ITT 54%
6-mo f/u
ITT 47%
12-mo f/u

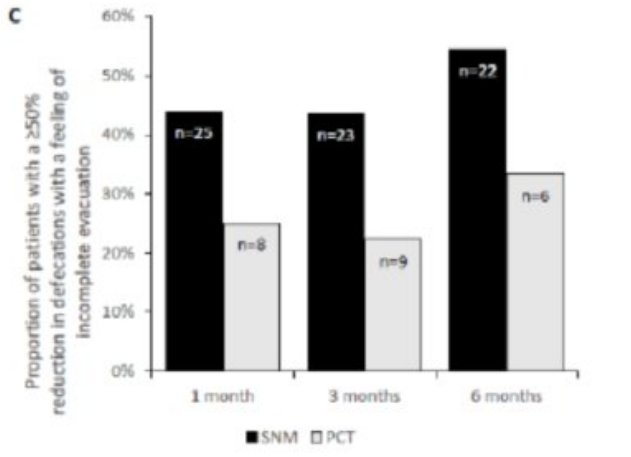
Heemskerk et al Ann Surg 2023; e-pub ahead of print Nov 23, 2023

SNM vs. PCT for slow-transit constipation (STC)

Average defecation frequency/week



Reduction of feeling of incomplete evacuation



Heemskerk et al Ann Surg 2023; e-pub ahead of print Nov 23, 2023

Take home messages

- Constipation is a common medical condition (8-15% of population)

- Approach to patient with chronic constipation
  1. Trial of diet/fiber supplements/OTC laxatives
  2. Test for defecatory disorders (HRAM/BET, defecography)
  3. Trial of secretalogues/prokinetics
  4. Test for slow-transit constipation (radiomarker, scintigraphy)
  5. Advanced testing and (non-medical) therapies

- Ongoing research in device-assisted treatment