Workshop constipation

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Miss GL, 1988

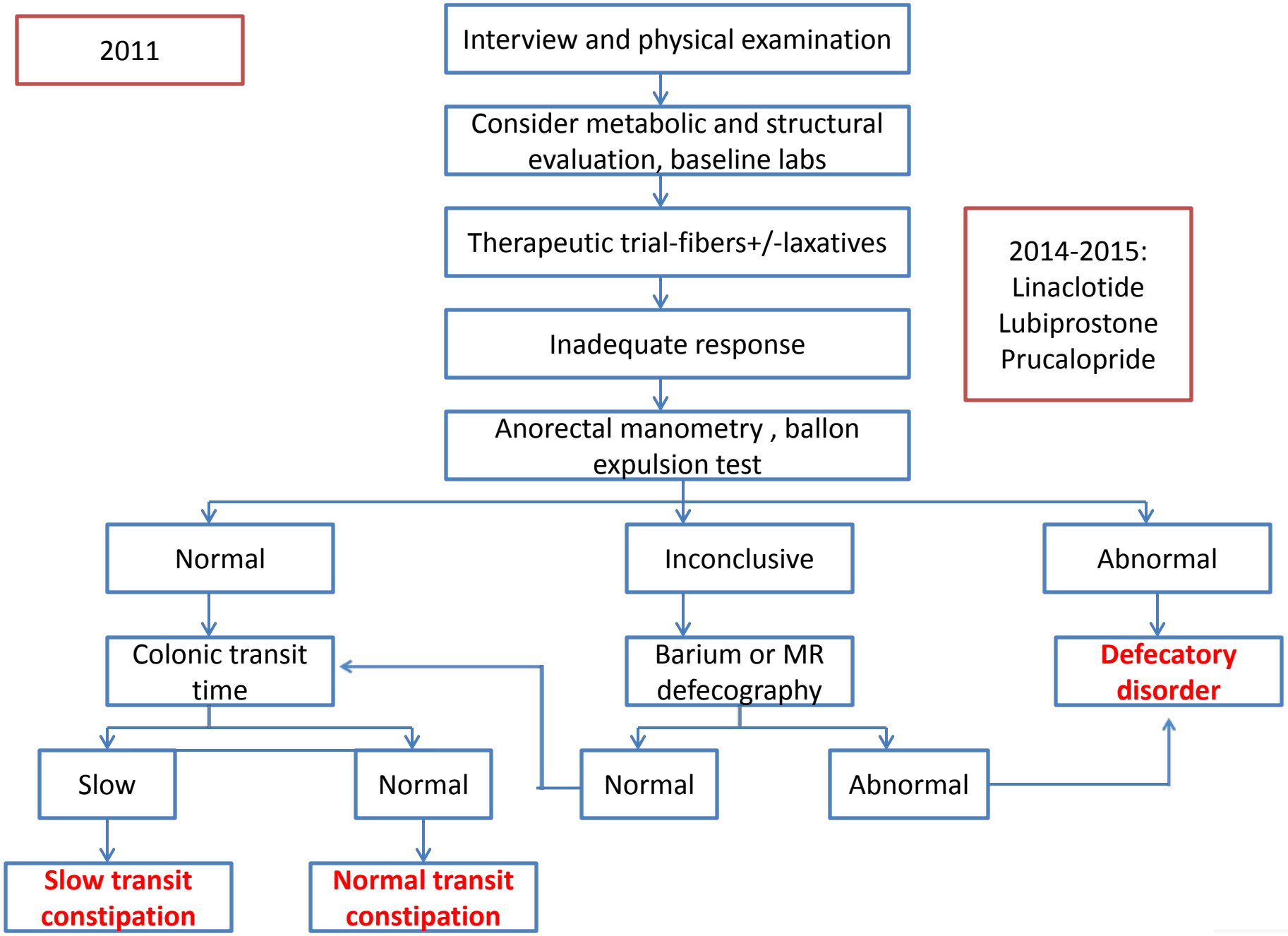
- Consulted in 2011 because of rectal bleeding
- Chronic constipation starting in adolescence, bowel movements every 2-4 weeks, excessive straining, incomplete rectal evacuation
- She takes Movicol 1-2bags/day
- No history of abus, no other medical problems and she is working in a nursery
- Colonoscopy: megadolicocolon with coprostasis in spite of double bowel preparation. Stage II hemorrhoids

Miss GL, 1988

- Biological tests: normal complete blood count, normal ESR, glycemia 4.3 mmol/l, creatinine 76 µmol/l, normal liver tests, normal thyroid function, normal electrolytes

- She is prescribed 3-4 Movicol bags/day with moderate improvement in constipation and persistence of abdominal bloating and discomfort

How do you proceed with this patient? (2011)



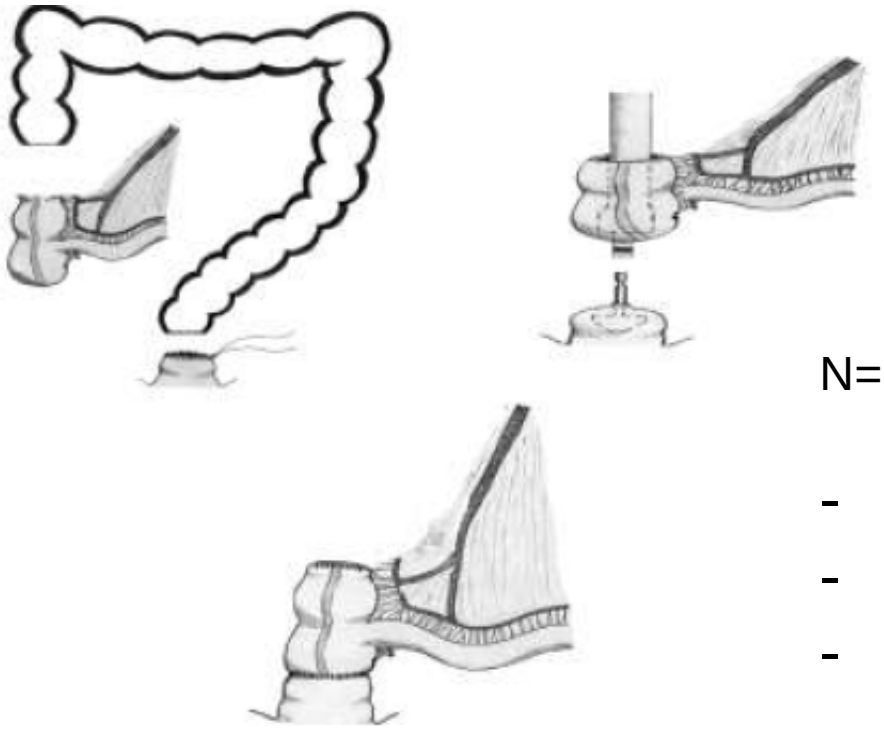
AGA Medical Position Statement on Constipation, Gastroenterology 2013;144:211-217

Miss GL, 1988

- Colonic transit time: 98.4 hours
- Several biofeedback seasons with little improvement of dyssynegia
- December 2013: subtotal colectomy (60 cm) with cecal-rectal anastomosis
- Histopathology: hypertrophy of the internal muscle layer, 4 polyp-like elevations containing a slight decrease of the neuronal cell numbers with focally hyperplasia and anarchic disposal of ganglia and nerves

«Sarli's procedure»

Subtotal colectomy with antiperistaltic caeco-rectostomy



Preservation terminal ileum
+ ileocaecal valve

N=10 women, FU 12m

- Bowel frequency: 1.3/day
- Normal continence
- No anti-diarrheal medication

Sarli *Dis Colon Rectum 2001*

«Sarli's procedure»

	studies	patients	
Bowel movements (4.5yrs FU)	3	43	**2.5/day**
Post-op complication	3	43	**9%**
- bowel bstruction			N=1
- diarrhoea			N=1
Success	3	43	**88%**

Bove A. World J Gastroenterol 2012

«Sarli's procedure»

N=43, 1991-2005, telephone questionnaire

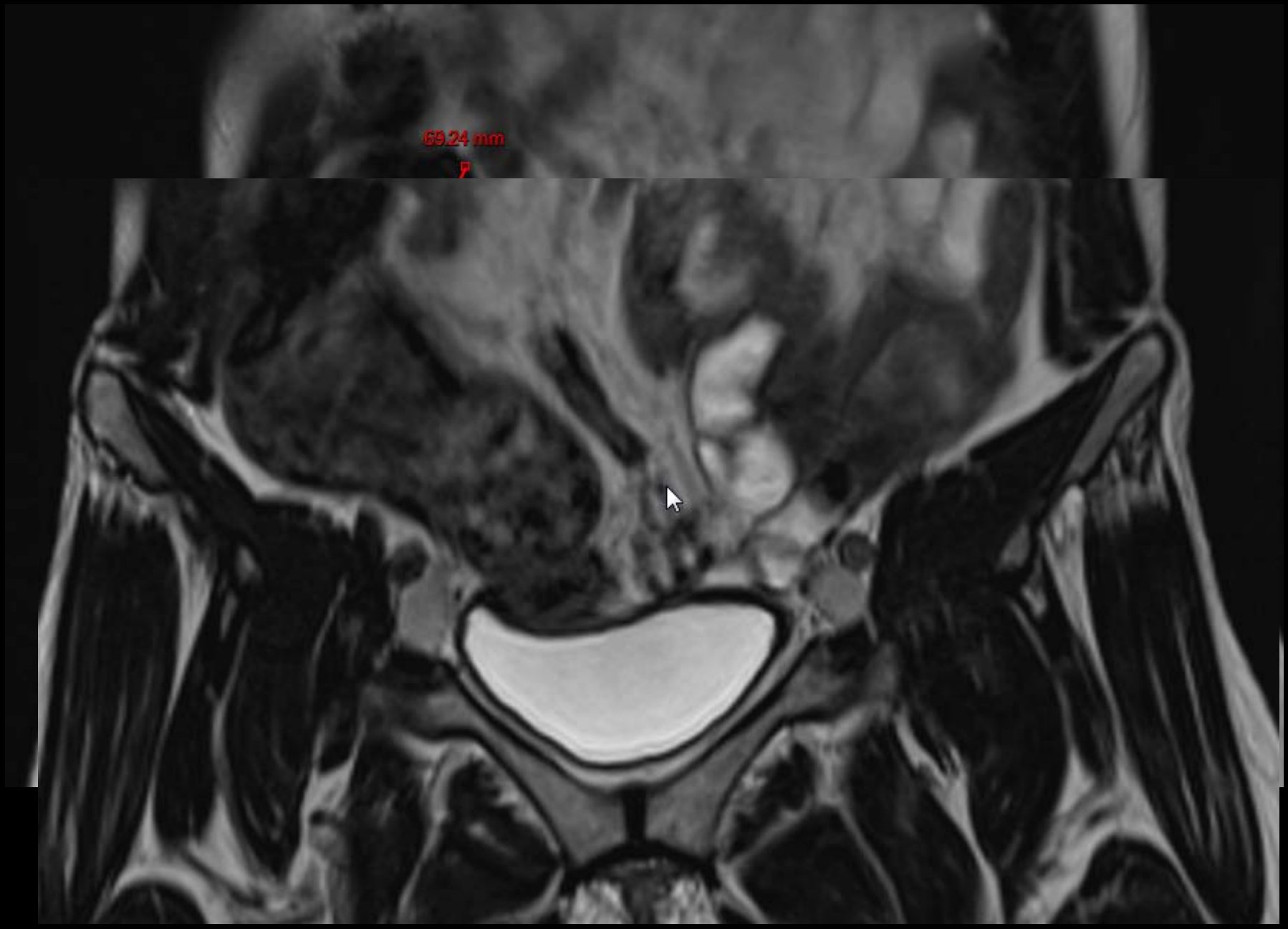
- 9.2% complications
- Mean GI-QLI 115.5 (±20.5) (healthy: 125)
- Mean Constipation score 20.3 → 2.6

Marchesi F. W J Surg 2007

N=17 vs. N=20 IRA, mean FU 4yrs

• Bowel/day	2.4±0.9	vs.	3.4±0.8	p=0.001
• Wexner constipation	4.3±1.8	vs.	5.8±1.9	p=0.02
• GI-QLI	119±7	vs.	111±12	p=0.04

Jiang CQ. Int J Colorectal Dis 2008


69.24 mm

Miss GL, 1988

- February 2014: fecal impaction (rectal evacuation under GA) and laparoscopic adhesiolysis

- In March 2014: burning-like abdominal pain and diarrhea (5-6x/day and 1-2/night) and she lost 5 kilos (actual weight: 50.6 Kilos) without nausea, dysphagia or early satiety

→ **Second gastroenterological opinion. What would you do?**

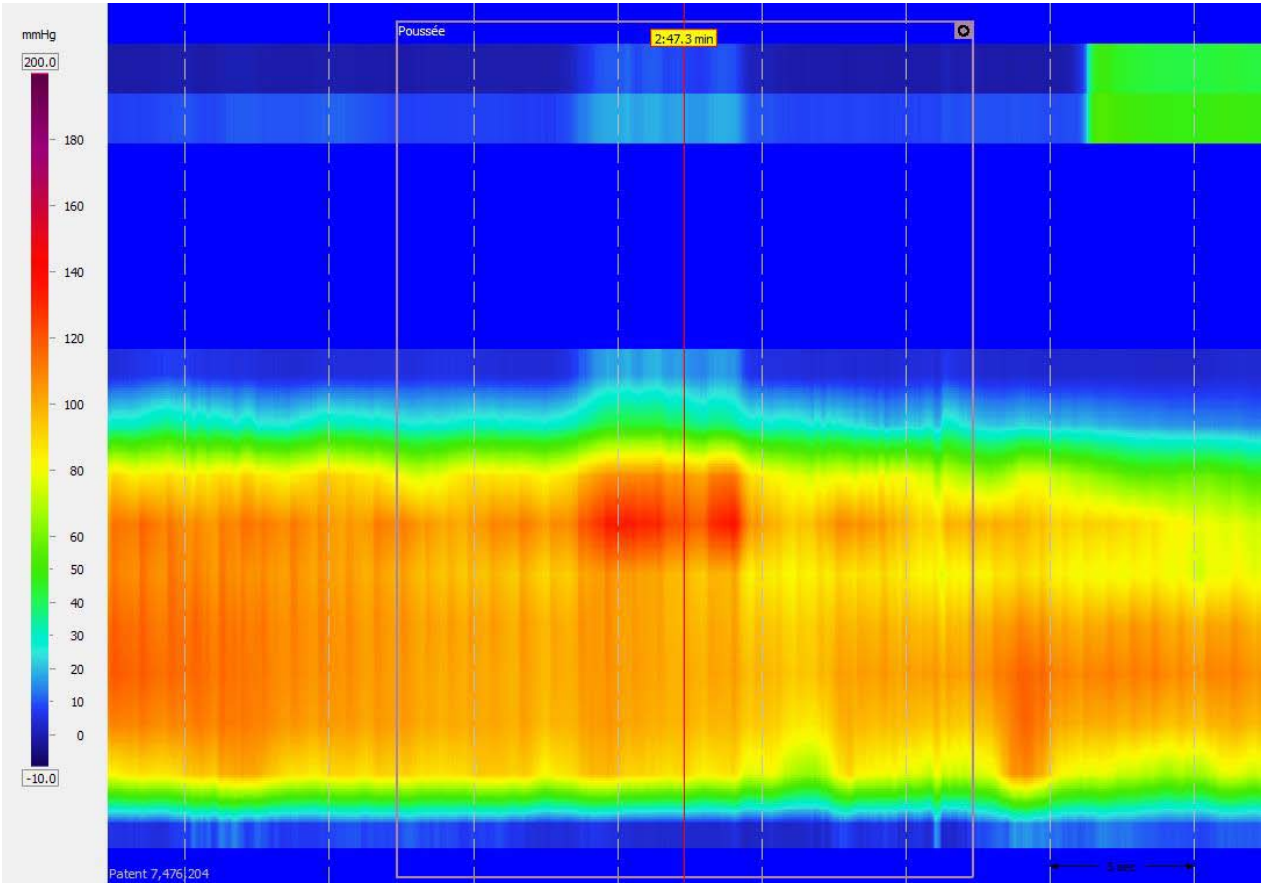
Second opinion

1. *Diagnostic field*

- Review of the colonic **histology** confirming the absence of visceral neuropathy or Hirschsprung disease. However an esophageal manometry and a gastric empting scintigraphy or small bowel manometry could be performed.

- **Colonic transit time**: should be offered after colonic preparation and the segmental repartition should be assed.

- Proposal to do **anorectal manometry** and **MR defecography**



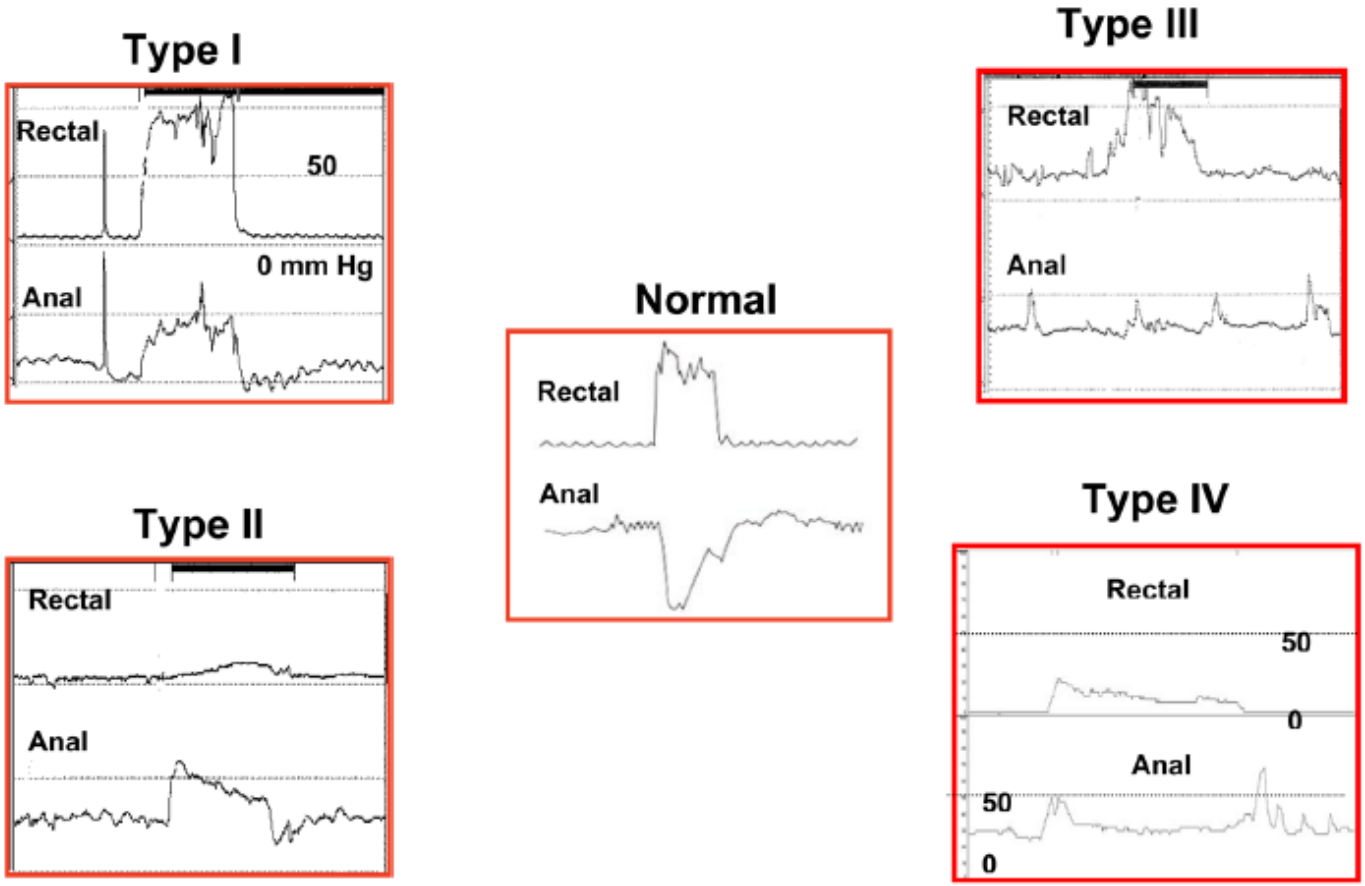
- Type 2 dyssynergia
- Disorders in rectal sensory function

Conclusions:

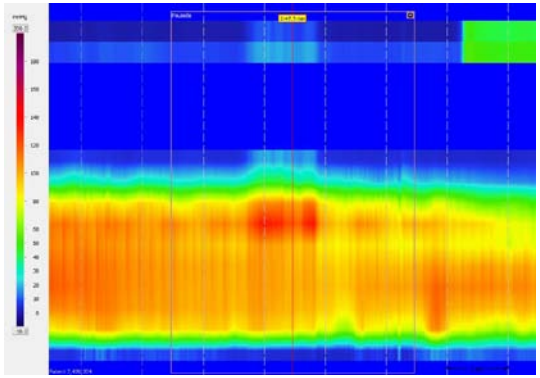
Colonic inertia secondary to obstructive defecation

Diarrhea secondary to partial colectomy or false diarrhea

Manometric patterns (Rao): attempted defecation



What would you do?



- Failure to open appropriately the sphincter region
- Dyskinesia of the puborectalis muscle
- Inefficient rectal emptying

- Type 2 dyssynergia
- Disorders in rectal sensory function

Conclusions:

Colonic inertia secondary to obstructive defecation

Diarrhea secondary to partial colectomy or false diarrhea

Second opinion

2. *Therapeutic field*

- Biofeedback

- Botox injections in the puborectalis muscle

Miss GL, 1988

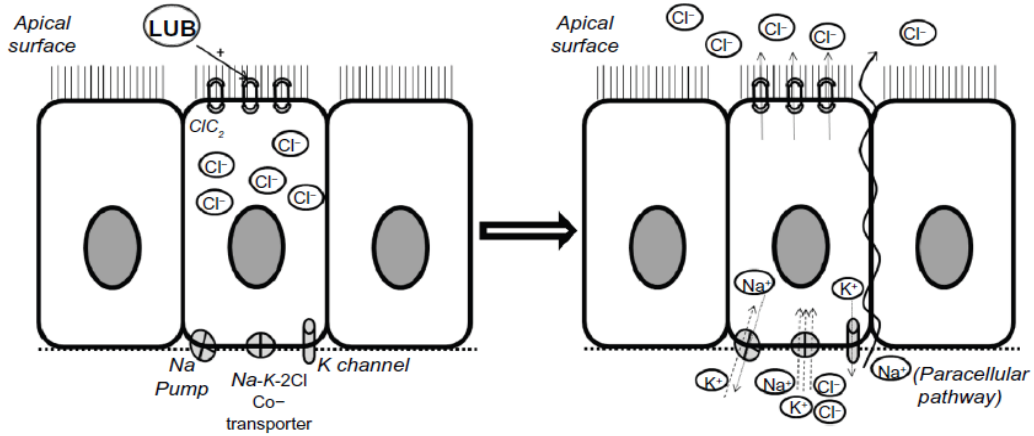
- Constipation starts again in June 2014 with 1 bowel movement/week, excessive straining and abdominal discomfort.

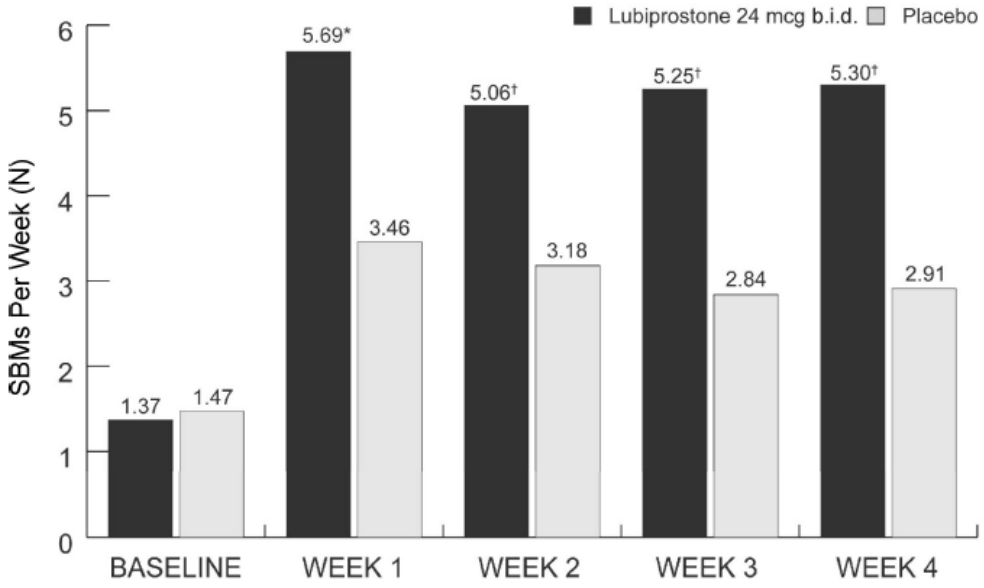
- She starts **Amitiza** 1x/day, than 2x/day and with occasionally Clyssie enema

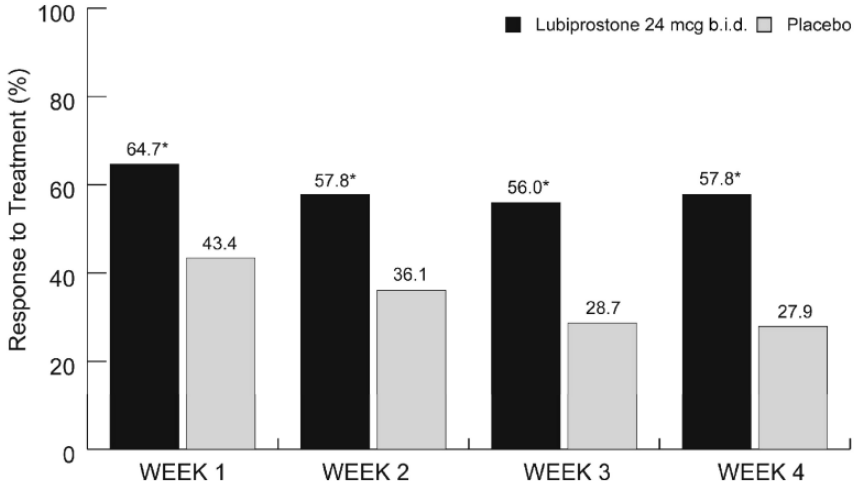
- She starts **biofeedbac**k in October 2014

- In December 2014: she is well taking Amitiza 3x/day (occasionally enema) and she is still doing physiotherapy

Amitiza =Lubiprostone







Johanson JF et al. Am J Gastroenterol 2008;103:170-177

Amitiza =Lubiprostone

- In rats and humans, lubiprostone contracts stomach longitudinal muscle and inhibits neuronally mediated contractions of colon circular muscle (Bassil AK et al. Br J Pharmacol 2008;154:126-135)

- Tested up to 52 weeks in IBS with constipation (8µgx2/day) showing significant improvement in abdominal pain and bloating

- Side effects: nausea (take it with meal) and diarrhea

- Also indicated for opioid-induced constipation

What should we do differently next time?

- Other laxative trials before considering surgery
- Complete constipation work-up before surgery (anorectal manometry, defecography, adequate colonic transit time, investigation of the upper gastrointestinal tract to consider)
- Complete treatment of obstructive defecation before surgery
- Treatment of choice in colonic inertia: total colectomy with ileo-rectal anastomosis.

Before surgery….

- **Repeat transit study**
  - mean interval of 14m between 2 studies
  - 3/12 patients excluded for surgery

N transit studies	success rate (2-96m FU)
≥ 2 studies	9/9 (100%)
1 study	13/21 (62%)

Nam YS. Dis Colon Rectum 2001

Author	No	Female (%)	Mean Age (yr)	FU (yr)	Success (%)
Beck et al, 1989[8]	14	100	41	1.2	100
Zenilman et al, 1989[9]	12	100	35	2	100
Pemberton et al, 1991[6]	38	84	40		100
Wexner et al, 1991[10]	16	92	45	1.2	94
Mahendrarajah et al, 1994[11]	9	100	38	1.3	88
Piccirillo et al, 1995[12]	54	78	49	2.2	94
Redmond et al, 1995[13]	34	92	43	7.5	90
Pikarsky et al, 2001[5]	30	70	60	8.9	100
FitzHarris et al, 2003[14]	75			3.9	95
Beck et al, 2005[15]	40			3	95
Glia et al, 2004[20]	17	94	46	5	71
Thaler et al, 2005[21]	17	100	47.8	4.9	100
Hassan et al, 2006[22]	59	97	41	6.1	100
Choe et al, 2006[23]	21			4.8	90
Zutshi et al, 2007[24]	35		38.6	10.8	77
Hsiao et al, 2008[25]	44	100	29		89
Jiang et al, 2008[26]	20	95	43	4	65
O'Brien et al, 2009[27]	13	100	39	8.1	100
Pinedo et al, 2009[28]	20	100	41.5	2.1	100
Riss et al, 2009[29]	12	100	46	7	50
di Fabio et al, 2010[30]	15	93	56	2.4	93
Sohn et al, 2011[31]	37	84	41	3.4	81.9

Success ~90%

McCoy JA. Clin Colon Rectal Surg 2012

Outcomes of IRA

	studies	patients		
Small bowel obstruction	26	913	**18%**	2-71%
Chronic diarrhea	19	843	**14%**	0-46%
Fecal incontinence	21	913	**15%**	0-52%
Abdominal pain	19	839	**35%**	0-90%
Re-operation	5	965	**14%**	0-50%
Permanent stoma	27	930	**9%**	0-28%
Mortality	26		**2.6%**	

Bove A. Worls J Gastroenterol 2012

Knowles Ann Surg 1999

«Success» of IRA

39 studies

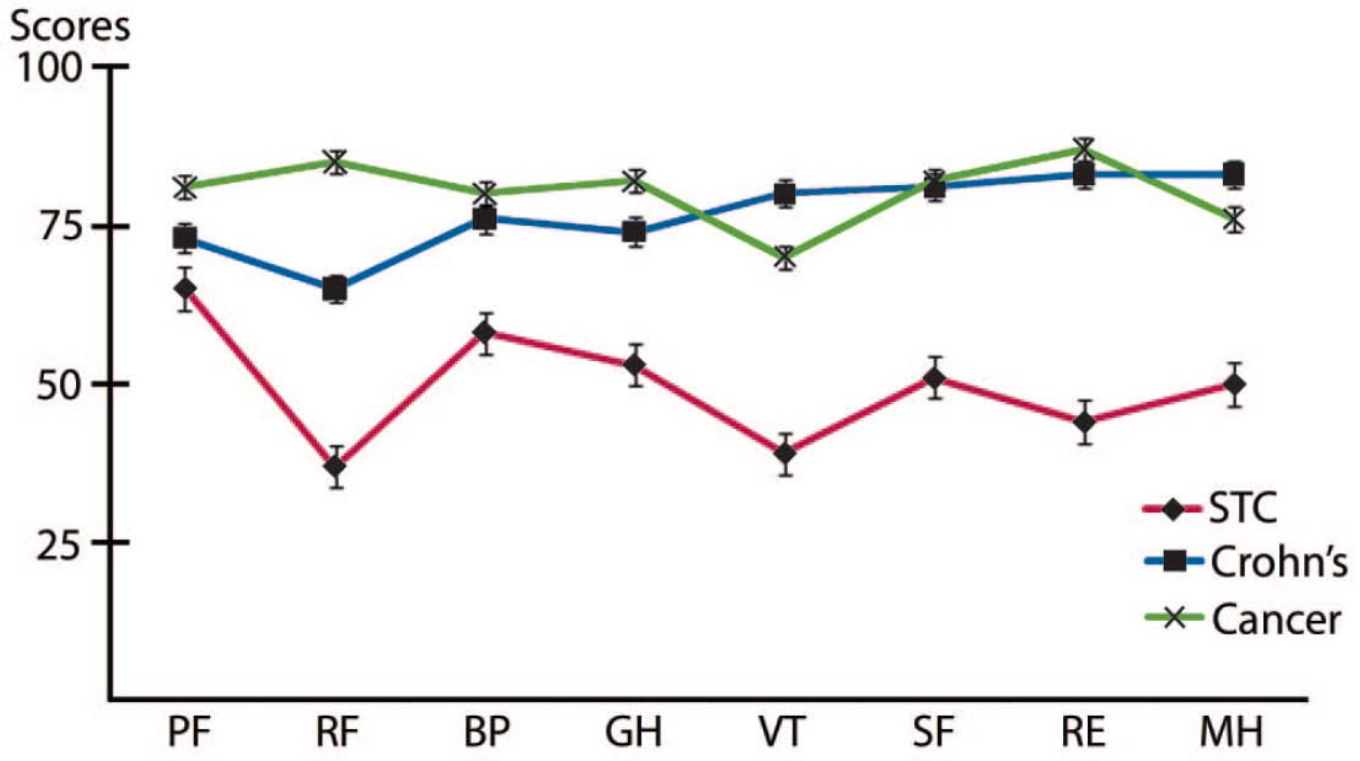
- → 6 no definition
- → 17 only patient feedback
- → 8 post-op functional tests
- → **8 post-op functional tests + patient feedback**

- → 15 «questionnaire»
- → 9 post-op interview done

Bove A. World J Gastroenterol 2012

QoL

SF-36



Di Fabio F. DCR 2010

Total colectomy + IRA

….when does it not work?

Total colectomy + IRA

….when does it not work?

- **Small bowel dysmotility (GID)**
  - Successful outcome 13% vs. 90% no GID
  - 80% recurrent constipation @5yrs

    Redmond JM. A J Gastroenterology 1995
  - 70% small bowel obstruction with GID

    Ghosh S. Scand J Gastroenterol 1996
  - Good outcome 5/9 patients vs. 7/7 no GID (p=0.09)

    Glia A . DCR 2004

Total colectomy + IRA

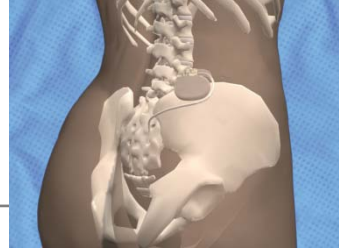
….when does it not work?

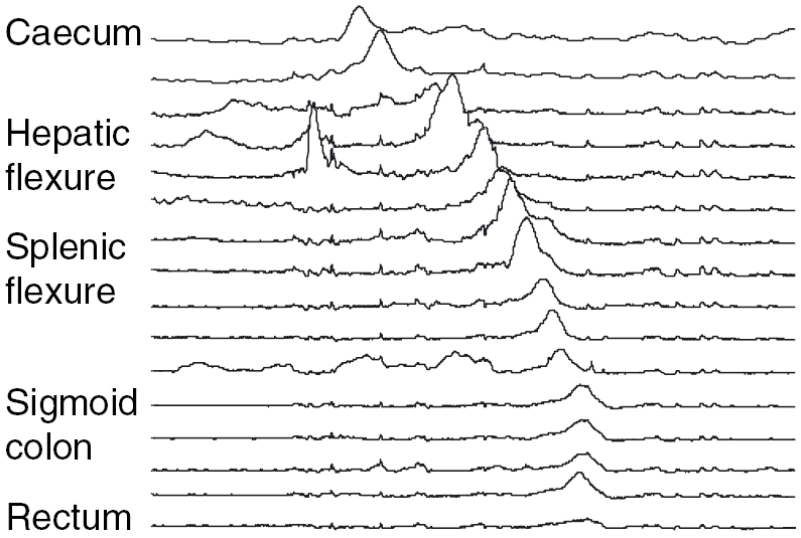
- **Small bowel dysmotility (GID)**

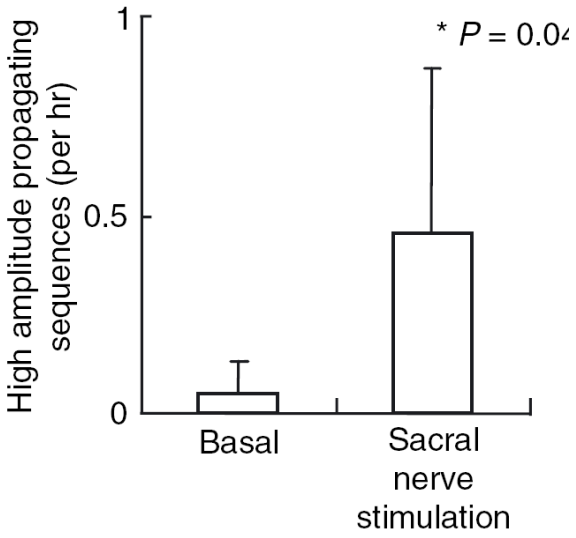
- **Psychological disturbances**
  - More stoma

Hasgawa H. Colorectal Dis 1999

SNM







- Increases frequency HAPS and propagating sequences >30cm

Dinning PG. Colorectal Dis 2006

- Benefit proven by cross-over study

Kenefick N. BJS 2002 and Ann R Coll Surg Engl 2006

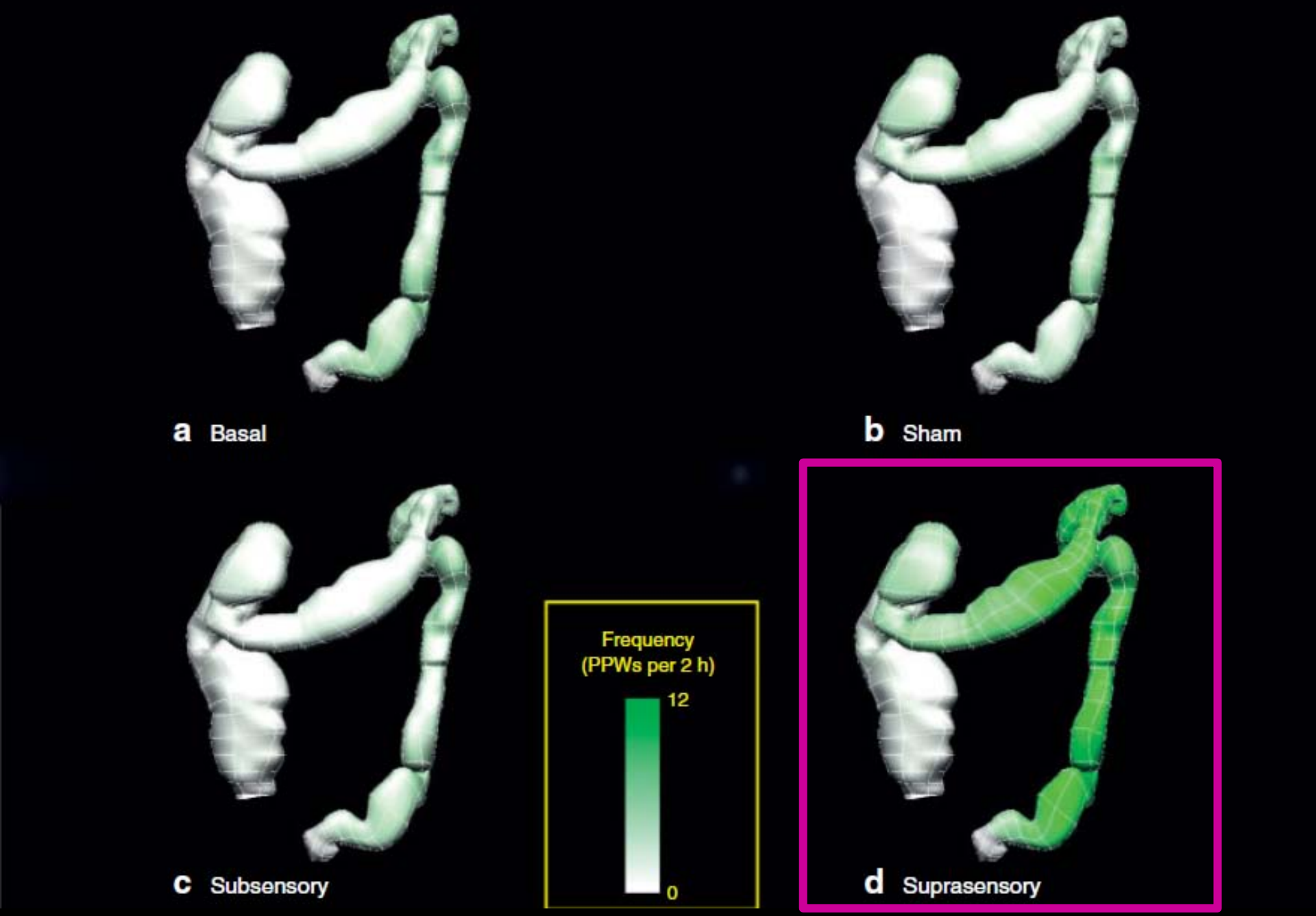
SNM

Reference	Year	Study type	Level of evidence*	Patient group	Type of constipation	No. who had PNE	No. with permanent SNS	PNE success rate (%)	Follow-up
Ganio *et al.*[18]	2001	Prospective uncontrolled	IV	Adults	Idiopathic	10	NA	NA	10 days
Malouf *et al.*[19]	2002	Prospective uncontrolled	IV	Adults	Slow colonic transit	8	NA	NA	3 weeks
Kenefick *et al.*[20]	2002	Prospective uncontrolled	IV	Adults	Slow colonic transit and evacuatory dysfunction	4	4	100	6 months (mean)
Kenefick *et al.*[21]*	2002	Double-blind crossover	IIb	Adults	Slow colonic transit and	NA	2	NA	4 weeks
Humphreys *et al.*[22]*	2006	Pro					15	NA	13 months (mean)
Holzer *et al.*[23]	2008	Prospective uncontrolled	IV	Adults	Slow colonic transit and evacuatory dysfunction	19	8	42	11 months (median)
Roth *et al.*[24]*	2008	Prospective uncontrolled	IV	Children	Idiopathic	NA	17	NA	27 months (median)
Naldini *et al.*[25]	2010	Retrospective	IV	Adults	Slow colonic transit	15	9	60	42 months (mean)
Kamm *et al.*[16]	2010	Prospective uncontrolled	IIb	Adults	Slow colonic transit and evacuatory dysfunction	62	45	73	28 months (median)
Sharma *et al.*[26]	2011							52	34 months (median)
Govaert *et al.*[27]	2012							58	37 months (median)
van Wunnik *et al.*[28]	2012				evacuatory dysfunction			92	6–12 months
Knowles *et al.*[11]	2012	Double-blind crossover	IIb	Adults	Evacuatory dysfunction	13	11	85	19 months (mean)

3 weeks PNE: 2/8 successfull

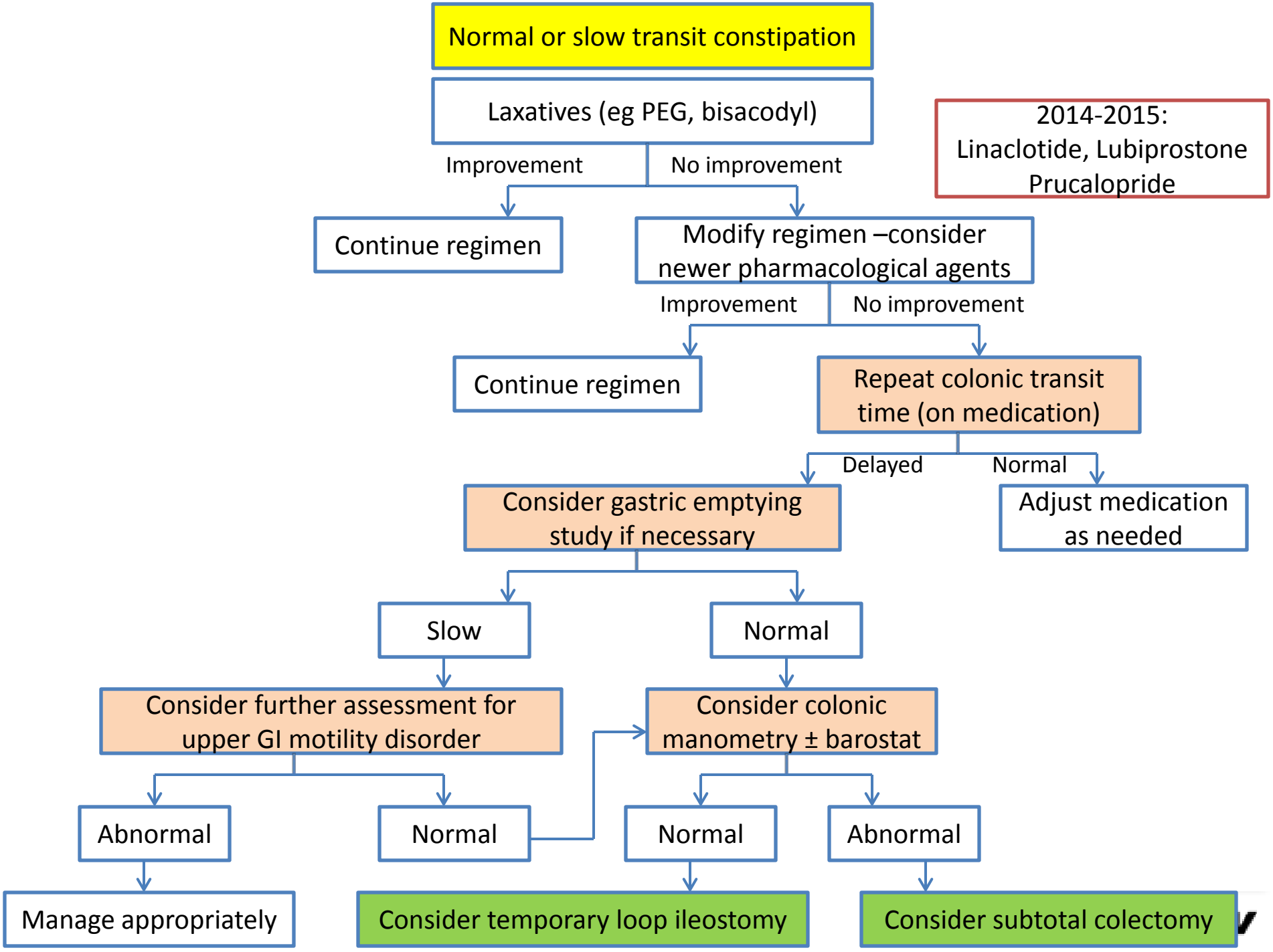
9/15 successfull
1.8 → 3.3 bowel/week (6 month)

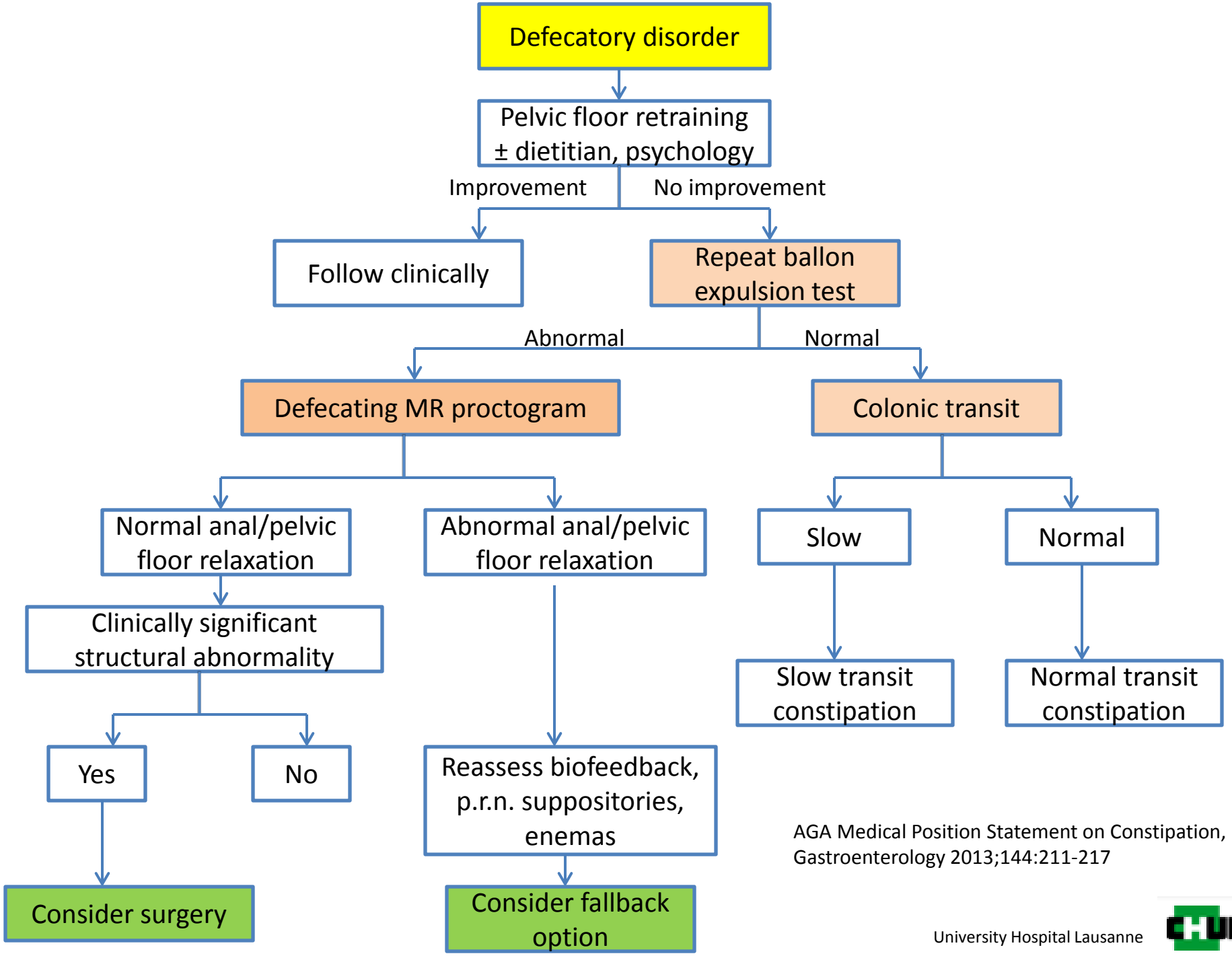
Thomas GP. BJS 2013



Dinning PG. BJS 2012

0.5-2V


Normal or slow transit constipation
Laxatives (eg PEG, bisacodyl)
2014-2015:
Linaclotide, Lubiprostone
Prucalopride
Improvement
No improvement
Continue regimen
Modify regimen –consider newer pharmacological agents
Improvement
No improvement
Continue regimen
Repeat colonic transit time (on medication)
Delayed
Normal
Consider gastric emptying study if necessary
Adjust medication as needed
Slow
Normal
Consider further assessment for upper GI motility disorder
Consider colonic manometry ± barostat
Abnormal
Normal
Normal
Abnormal
Manage appropriately
Consider temporary loop ileostomy
Consider subtotal colectomy



AGA Medical Position Statement on Constipation, Gastroenterology 2013;144:211-217

Constipation 2nd case

MN, 1981

- Constipation since her infancy with 2 bowel movements/week, getting worst when she has stressful periods (Fructine and Metamucil)
- No sign of obstructive defecation
- Normal colonoscopy in 2002 (21 years old)
- In **2004** she lose weight (35.5 kilos, 1.53 cm, BMI 15 kg/m^2)
- She consults in **2005** for constipation (bowel movement every 4 days), abdominal bloating and discomfort while taking Fructine 2x/day

MN, 1981

- Laboratory normal, except for a moderate higher morning blood cortisol and a lower IgF1, consistent with a previous eating disorder
- She works as a nurse and she takes no constipating drug
- Transit time of 110 hours (uniform distribution within the colon)
- Normal digital rectal examination
- Proposed treatment: Zelmac (no effect), then Transipeg + Padma Lax + acupuncture with a moderate improvement

MN, 1981

- **2006**: fluctuant symptoms with some constipation periods of 3-4 days, intermittent abdominal bloating (no effect of Flatulex, Infloran)

- **2007**: worsening of abdominal bloating and pain with aggravation in stand up position, abdominal CT showing a dilated right colon and coprostasis

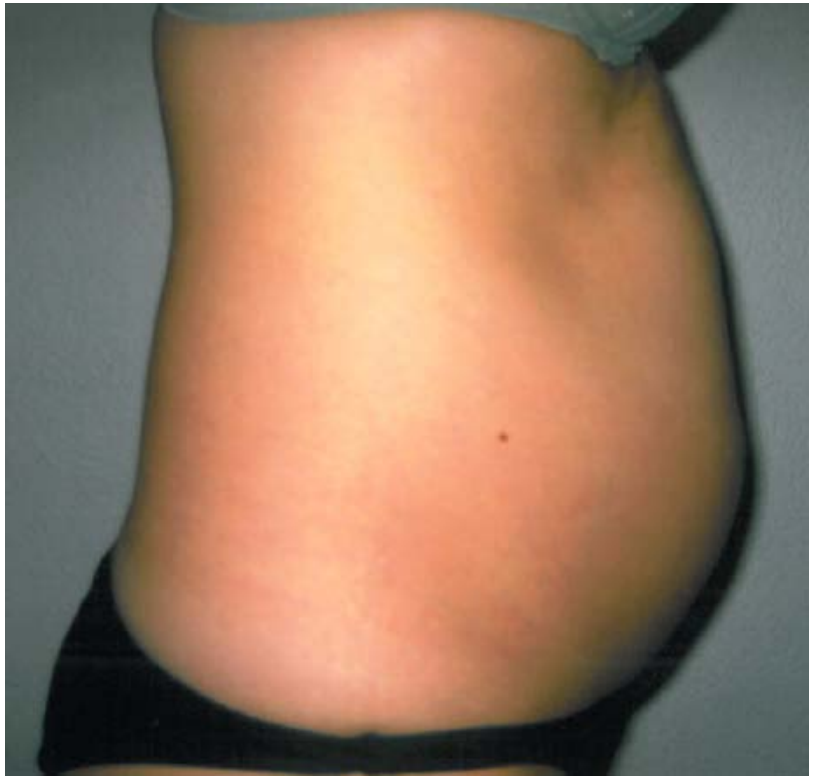
- **2007**: hospitalized at CHUV (main symptoms: bloating and abdominal pain): enteroclyss CT normal, colonoscopy and gastroscopy normal, normal biological tests, breath test suggesting lactose intolerance and psychological examination suggesting a depressive reaction secondary to worsening somatic pain → Diagnose: **Irritable bowel syndrome and lactose intolerance.**

MN, 1981

- Therapeutic suggestions CHUV: abdominal massage, abdominal TENS, Citalopram, avoid diary products, Transipeg et Padma Lax (bowel movements every 2 days)

- **2008**: persistence of abdominal bloating and pain, she stops working, persistence of the depression reaction (Fluoxetine)

- Progressive severe symptoms with no response to various medications (Debridate, Duspatalin, Neostigmine, hydro-colonotherapy, Somatostatin, Dulcolax)



What would you do?

MN,1981

- **July 2008**: left colectomy (resection of 70 cm dilated sigmoid and descending colon, hystopathologically normal)

- **November 2008**: abdominal bloating +++, bowel movement every day with Laxoberon 5-10 drops/day

- **2008**: normal anorectal manometry

- **January 2009:** normal small bowel manometry:
  - Probably "*functional gastrointestinal condition*" (no histological lesion, worsening with stress) secondary to long standing abuse of medication and/or behavioral disturbance
  - No enteric pathology

- **April 2009**: right colectomy and adhesiolysis

Segmental colectomy

- 100% failure rates *Pretson DM. BJS 1984, Gray EJ. Ann Surg 1971*
- Segmental colonic transit studies
  - n=18 63% satisfaction *de Graaf EJ. BJS 1996*
  - n=40 n=3 IRA after 1 year *You YT. Ann Surg 1998*
  - n=28 median FU 50 month
    n=5 failure (18%) *Lundin E. BJS 2002*
- Deteriorate with time *Kamm MA. Int J Colorectal Dis 1991*
  Knowles CH Ann Surg 1999

Trial ileostomy ?

MN, 1981

- **June 2009**: 3 mm ileo-rectal stenosis, endoscopically dilated to 15 mm in one season → perforation, temporary ileostomy
- She still complains of abdominal bloating during the ileostomy period even if normal ileostomy transit
- Restoration of continuity in **Sept 2009**
- **2010**: her 5th surgery: adhesiolysis because of abdominal pain and bloating
- 2010: several analgesics: Lyrica, Tramal, Oxycontin

MN, 1981

- **Good improvement since 2011** when she starts wearing an abdominal support belt and she starts dating her future husband.
- She gives birth to a healthy boy in **Oct 2013**
- **2014**: she has no complains (still wearing a support belt) and she works at partial time

What can we learn from this case?

- Is it constipation or IBS with constipation?
- “Functional gastrointestinal disorder” secondary to long standing laxative abuse ?
- Abdominal bloating becomes a leading symptom
- Again: left colectomy as initial treatment
- Again: complete constipation work-up after the first surgery
- Place of the newer constipation medicine (Constella, Amitiza)?
- Large caliber anastomotic dilation during one endoscopic season (3mm → 15 mm)

Constipation vs IBS with constipation

Rome III criteria for constipation

Symptoms for ≥6 months and ≥2 of the following for more than ¼ of defecations during the past 3 months:

- Straining
- Lumpy or hard stools
- Sensation of incomplete evacuation
- Sensation of anorectal obstruction/blockade
- Manual maneuvers to facilitate defecations; <3 defecations/week
- Loose stools are not present and there are insufficient criteria for IBS

Rome III criteria for IBS with constipation

Recurrent abdominal pain or discomfort at least 3 days per month in the past 3 months associated with two or more of the following:

- Improvement with defecation
- Onset associated with change in frequency of stool
- Onset associated with change in form (appearance) of stool
- < 25% of bowel movements were loose stools

Constipation vs IBS with constipation

Rome III criteria for constipation

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- Straining
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- Manual maneuver defecations; <3 de
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with change in

with change in
) of stool

ovements were

loose stools

1. Probably "functional abdominal disorder" secondary to long standing laxative abuse
2. Bloating in a patient with possibly weak abdominal wall

Chronic stimulant laxative use

	Group 1 (n = 29) (%)	Group 2 (n = 26) (%)
Loss of haustral marking	8 (27.6)	0*
Colonic dilatation	13 (44.8)	6 (23.1)
Redundancy of colon	10 (34.5)	5 (19.2)

*$p < 0.005$.

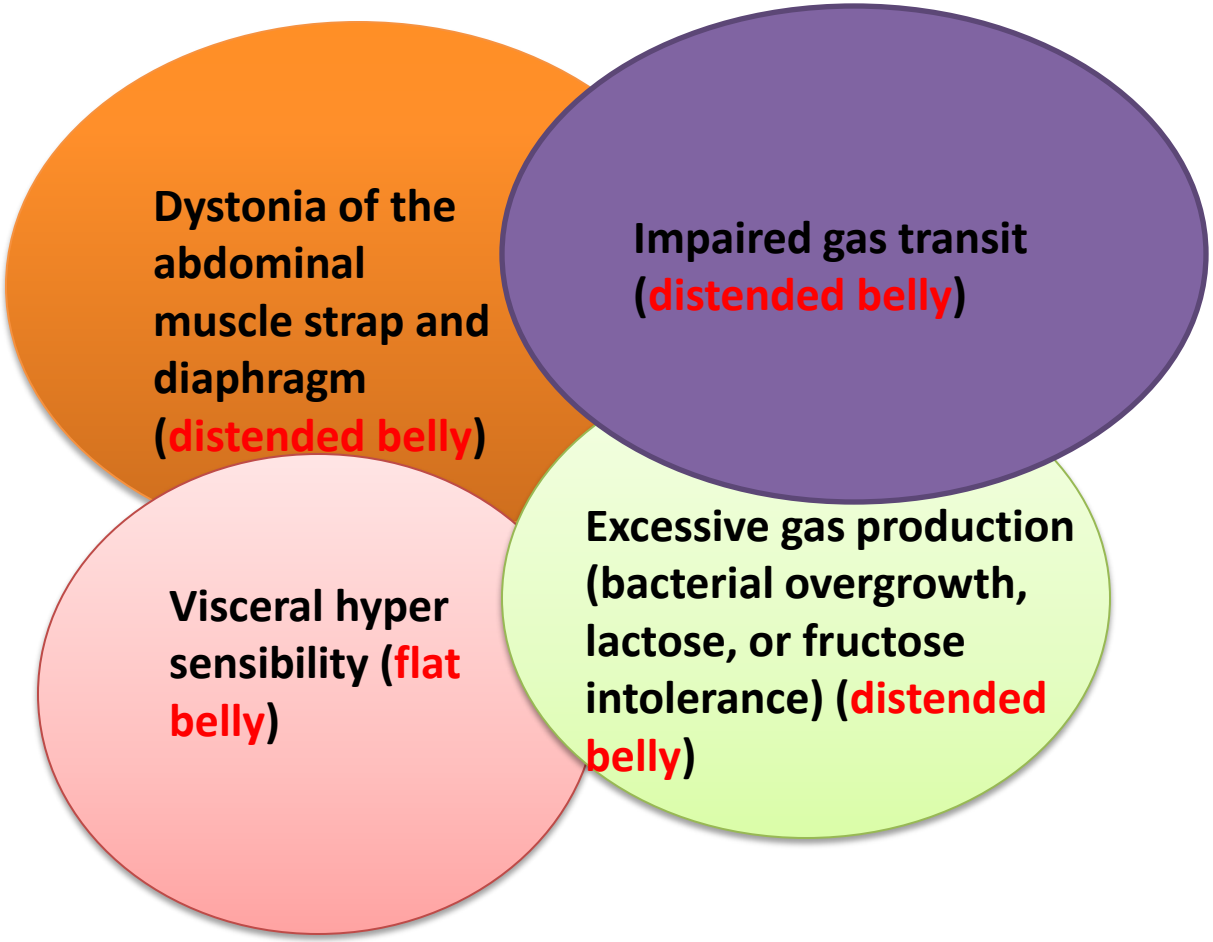
Effects of long standing laxative use:

- Stimulant laxatives cause increased activity of the intrinsic neuronal pathways of the colon. Later, neuronal damage and death occurs, resulting in denervation injury and atrophy of the colonic smooth muscle

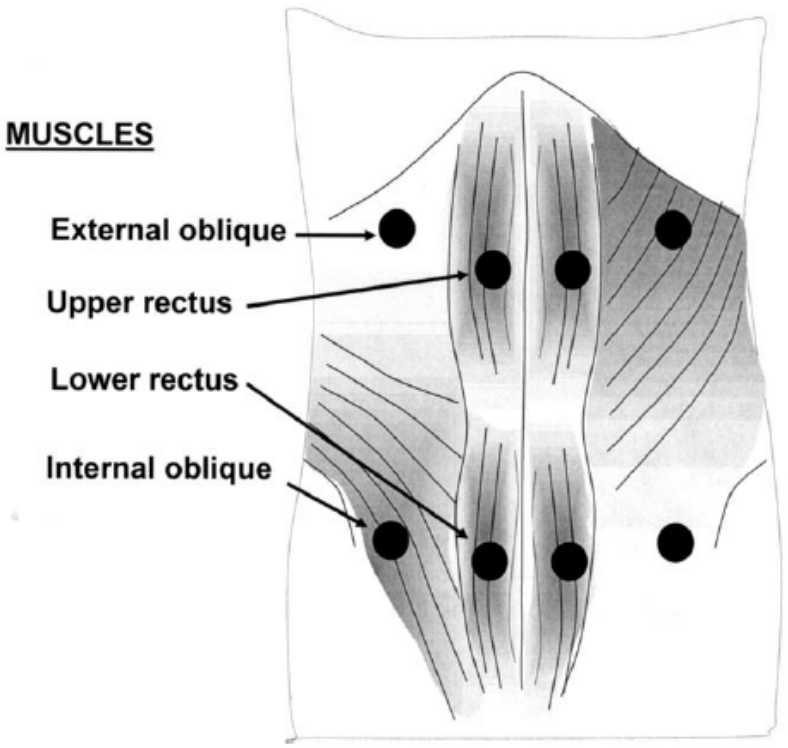
- Animal studies suggest that chronic stimulant laxative intake results in degeneration of colonic myenteric plexus

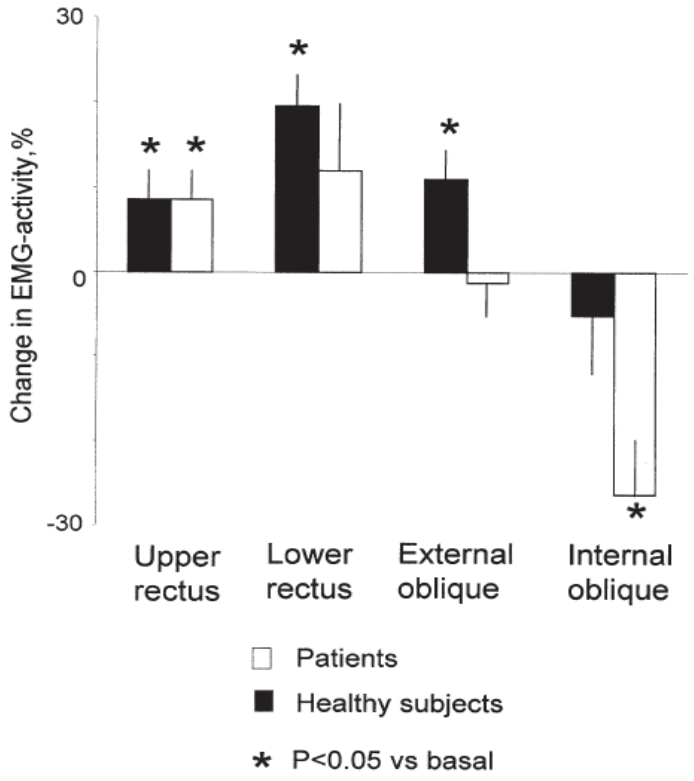
Joo Jae et al. J of Clinical gastroenterology 1998, Volume 6:283-286

Abdominal bloating



Dysfunction of the abdominal muscle strap

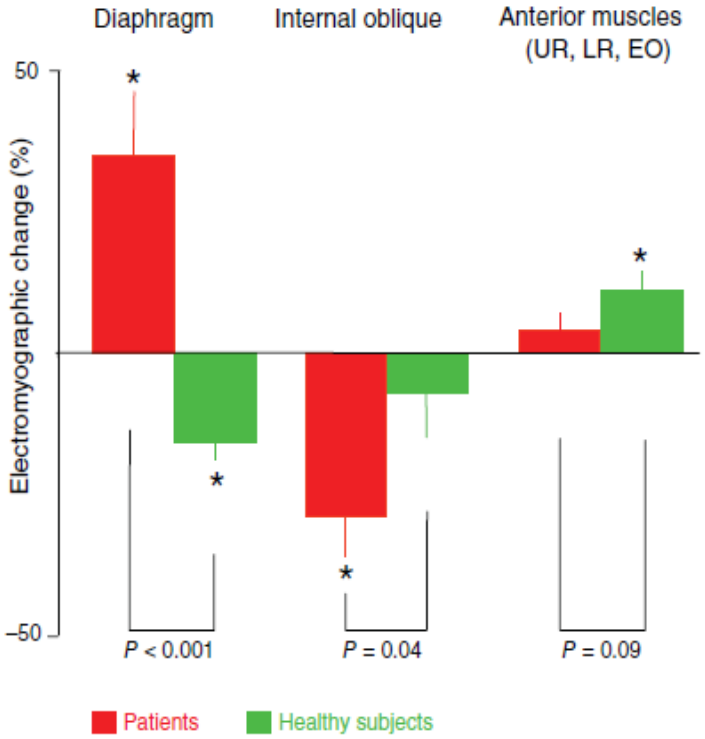


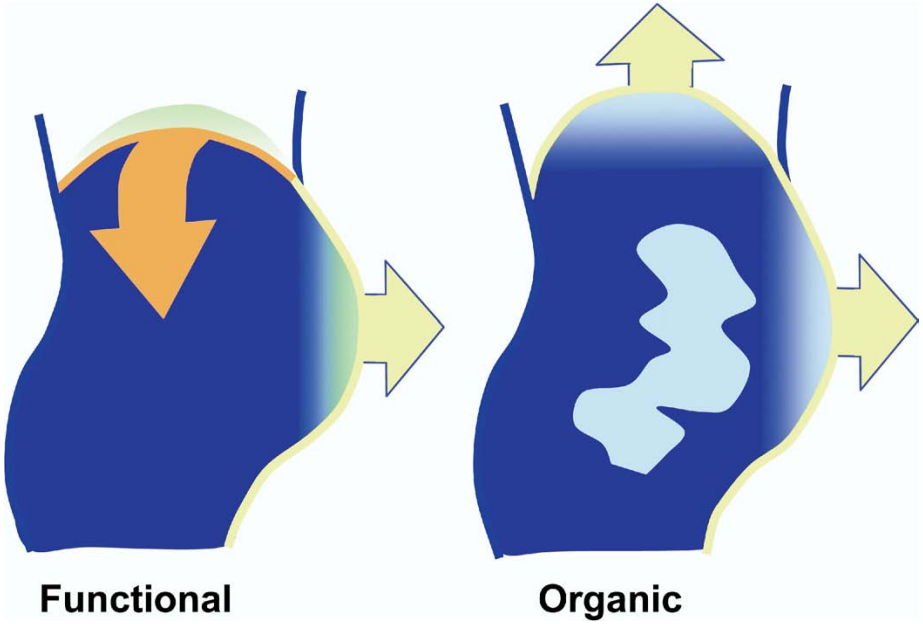


- The same volume load produced significantly more abdominal distention in patients with bloating.
- The decrease in activity of the internal oblique correlated with increments in girth
- The colonic gas distribution was similar in patients and healthy subjects

Tremolaterra F et al, Gastroenterology 2006;130:1062-1068

Abdomino-phrenic dyssynergia



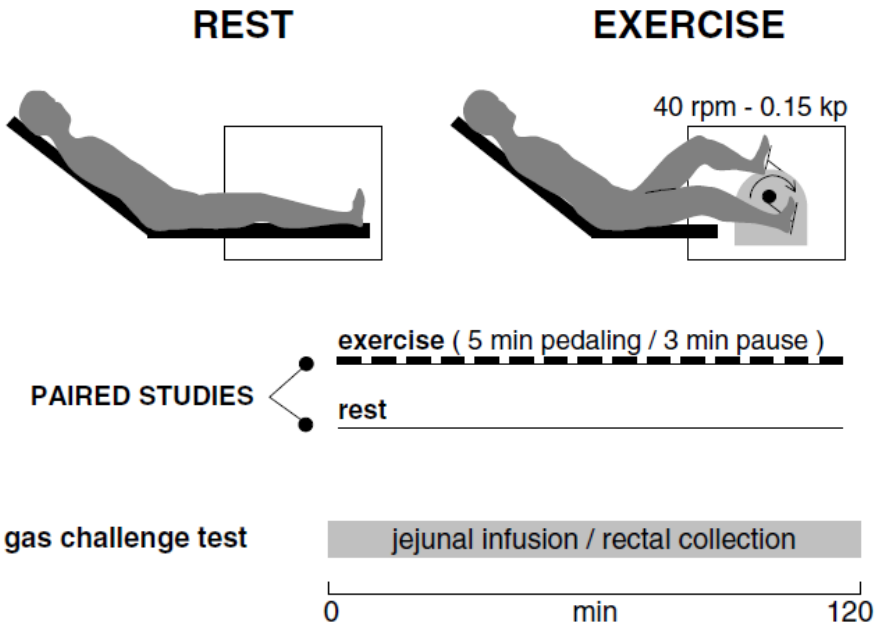


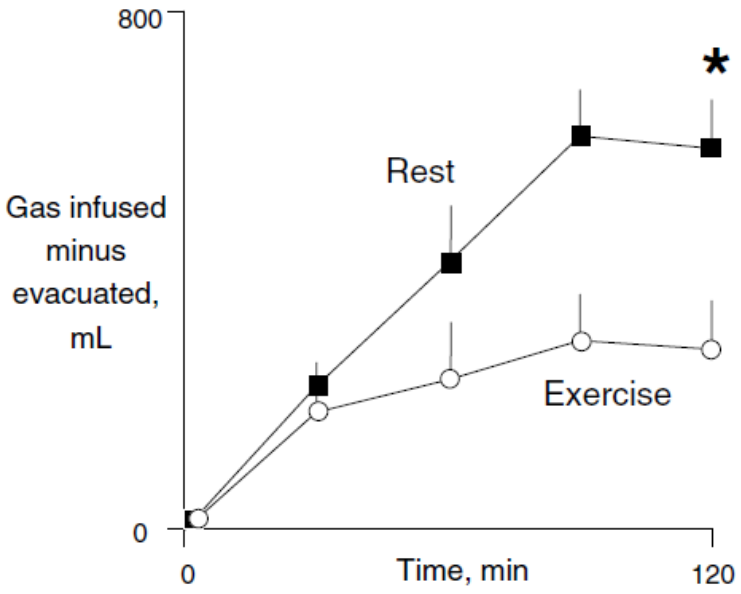
47 patients with IBS without diarrhea
12 normal subjects
9 patients with intestinal dysmotility

Villoria A et al, Am J Gastroenterol 2011;106:815-819

Accarino A et al, Gastroenterology 2009;136:1544-1561

Abdominal wall and exercises

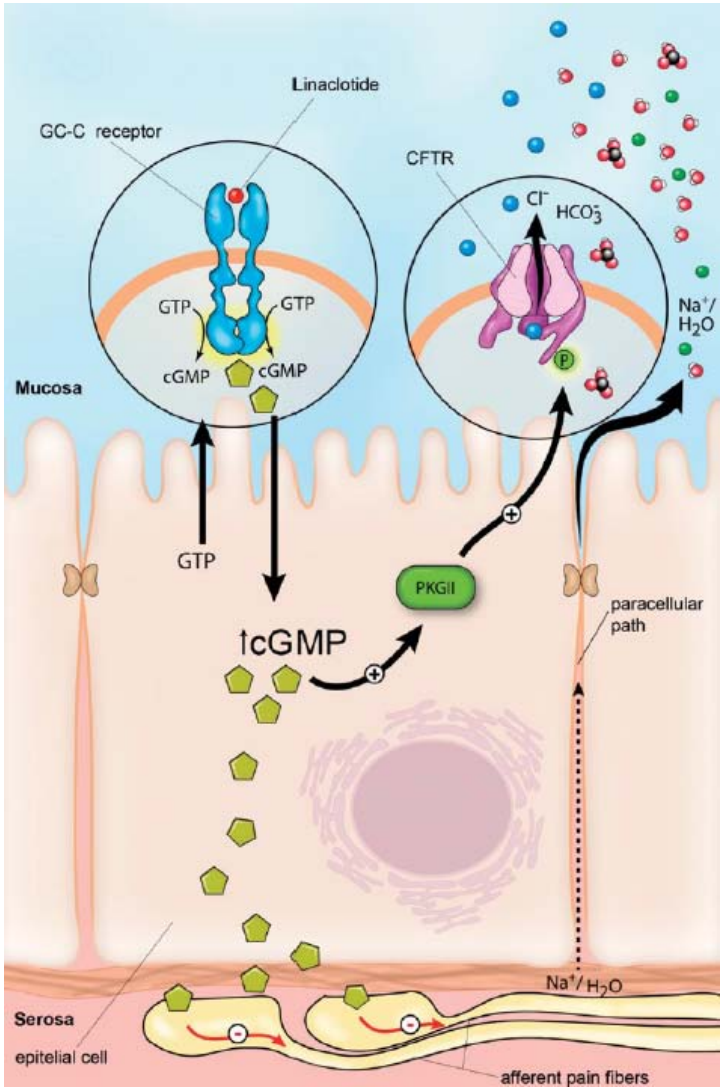


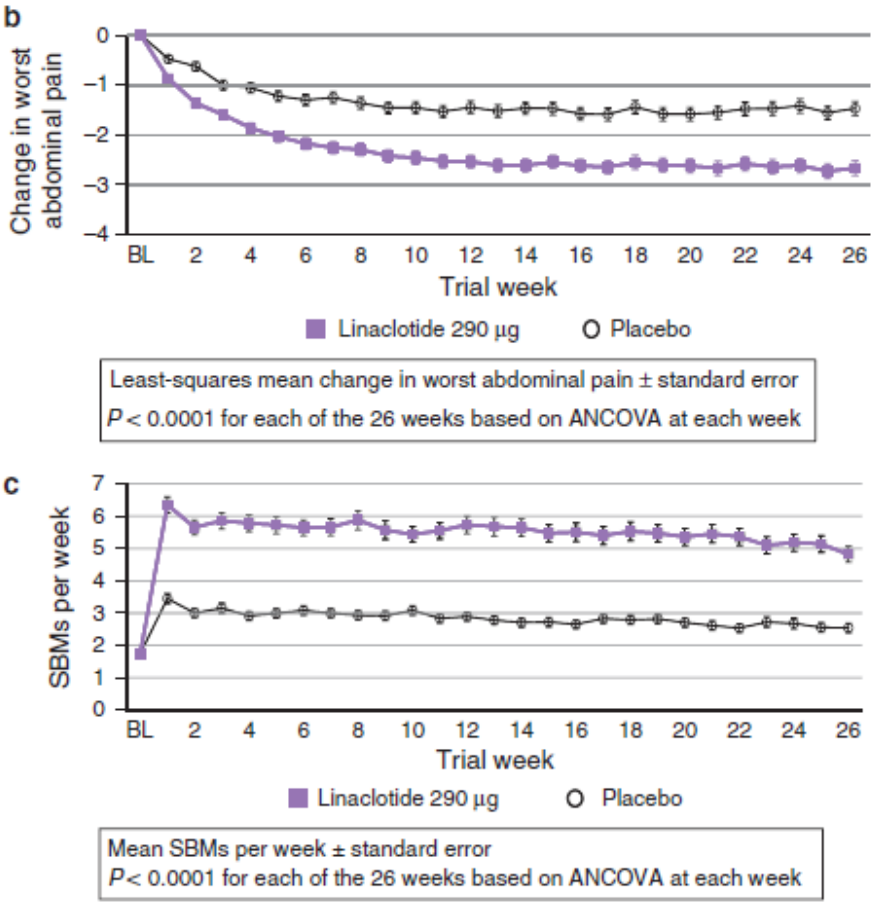


8 patients

Villoria A et al, Am J Gastroenterol 2006;101:2552-2557

New constipation medication: Constella





804 patients, NNT=5

Chey WD et al. Am J Gastroenterol 2012;107:1702-1712

Endoscopic balloon anastomotic dilation

Study (first author)	Patients n	Type of dilatation	Success (%)	Average number of dilatations
Araujo, 2008 [5]	24	endoscopic	22 (92)	2.3
Di Giorgio, 2004 [6]	30	endoscopic	30 (100)	2.6
Venkatesh, 1992 [12]	17	endoscopic	16 (96)	–
Johansson, 1996 [9]	14	endoscopic	12 (86)	3.7
Skreden, 1987 [10]	12	endoscopic	10 (83.3)	2
Ambrosetti, 2008 [4]	12	endoscopic	12 (100)	1.4
Placer, 2010 [16]	26	endoscopic	23 (88.5)	2.0
Delaunay-Tardy, 2003 [13]	27	endoscopic	21 (77.1)	2.0
Pietropaolo, 1990 [12]	42	endoscopic vs. bougienage	41 (97.6)	–
Suchan, 2003 [15]	94	endoscopic & fluoroscopic	67% (63/94)	2.5
Di, 2005 [8]	17	fluoroscopic	71% complete 29% partial	1.0

805 procedures, 1.4% complications: 1.1% perforations, abscesses 0.2% and pyrexia 0.1%
Recurrence: 4-20%

Ragg J et al. Dig Surg 2012;29:287-291

Endoscopic balloon anastomotic dilation

ASGE: "The rule of 3 has been used when deciding how much to dilate a stricture with a bougie dilator in 1 session. This rule states that after moderate resistance is encountered, no more than 3 dilators of progressively increasing diameter should be passed in that season."

ASGE Tools for endoscopic stricture dilation; Gastrointestinal Endoscopy 2013;Vol78,No3

Prospective trial randomized patients with symptomatic benign postoperative anastomotic colorectal strictures :
- dilation with either 18 mm TTS balloon vs dilation with an over-the-wire 35 mm pneumatic balloon

Results:
- success in all patients without complications
- 1.6 sessions vs 2.6 session (p=0.009)
- longer response duration : 560 days vs 245 days, p=0.016

Di Giorgio et. Gastroeintest Endosc 2004;60:347-359