Motility Disorder Extremes
Oropharyngeal, Colon and Anorectum

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Goal

Educate on clinically relevant oropharyngeal, colon and anorectal motility disorders encountered in practice

Why Are Motility Disorders Important?

- Motility disorders are common
  - You will see them!
  - Affects 15-20% of the adult population
- $$ There can be considerable expense in the work-up/management.
  - Cost effective evaluation is efficient
- Differential can be broad

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Oropharyngeal Dysphagia

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Define Dysphagia: sensation of difficulty or abnormality of swallowing

- Transfer dysphagia:
  - Difficulty *initiating* a swallow
    - Symptoms: Nasopharyngeal regurgitation, aspiration, retention

- Esophageal dysphagia:
  - Difficulty swallowing *seconds after initiation*
    - Sensation of food getting stuck

Lembo A. Up to Date 2017

NOT Oropharyngeal Dysphagia: **Globus**

Intermittent sensation of a lump in the throat

Occurs between meals, independent of swallowing

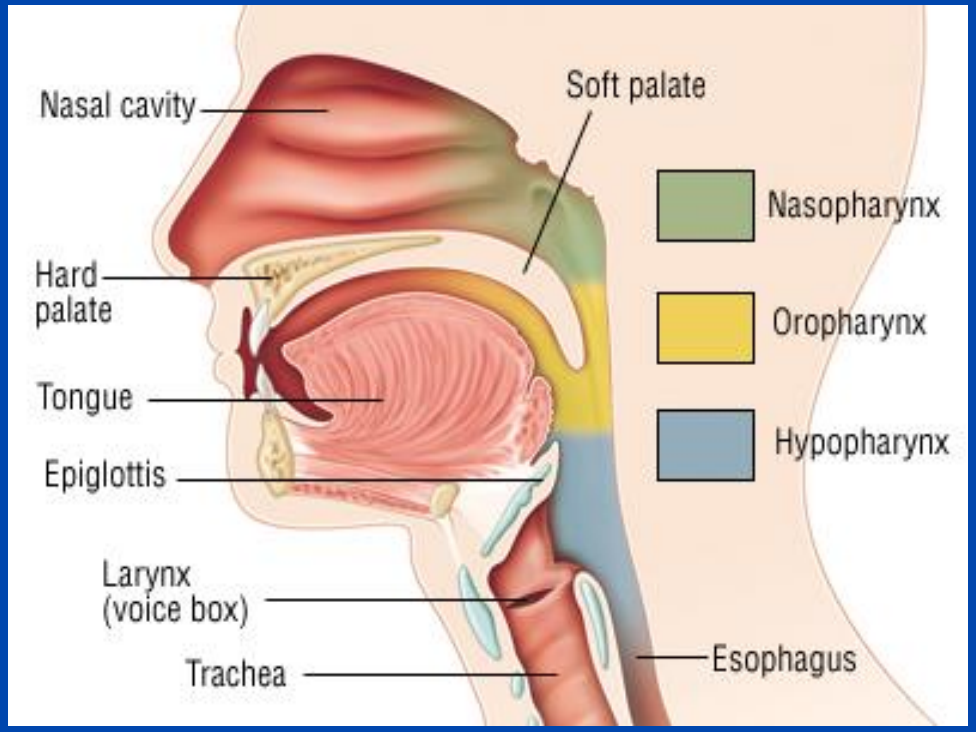
NO dysphagia, odynophagia, GERD, EoE or motility disorder causing symptoms

Aziz Q. et al. Gastroenterology 2016

Causes of Oropharyngeal Dysphagia

Structural	Iatrogenic	Infectious	Metabolic	Myopathic	Neurological
Cricopharyngeal bar	**Medications**	Mucositis	**Amyloidosis**	**Connective tissue disease**	**Brainstem tumors**
Zenker's	Postsurgical	Botulism	Cushing's	Dermatomyositis	Trauma
Cervical web	**Radiation**	Lyme disease	Thyrotoxicosis	Myasthenia gravis	**Stroke**
Oral tumors	Corrosive	Syphilis	Wilson disease	Sarcoidosis	Celebral palsy
Cleft palate				**Paraneoplastic syndromes**	Multiple Sclerosis
				Dystrophies	Post-polio
					Tardive dyskinesia
					Dementia
					Parkinson's

Oropharynx anatomy

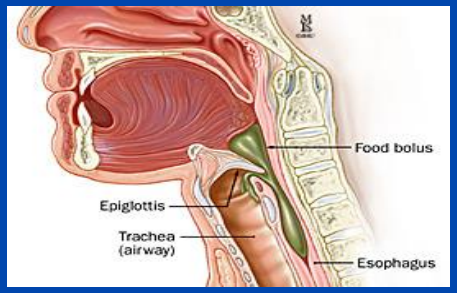


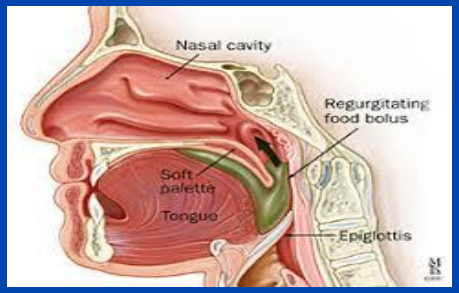
Diagnosing Oropharyngeal Dysphagia

Symptoms:

Difficulty initiating a swallow, associated with coughing, choking, or nasal regurgitation.

Aspiration





Nasal regurgitation

History – review symptoms and risk factors

- Higher risk with ETOH, Smoke, weight loss (cancer)
- Dry mouth or eyes (Sjogren's, radiation)
- Change in speech, hoarse, weak cough
- Food regurgitation
- Odynophagia
- Common after intubation

Stemple RN, et al. Ann Otol Rhinol Laryngol 2007;
Kawashima K, et al. Dysphagia 2004;
Kalf JG et al. Parkinsonism Relat Disord 2012.

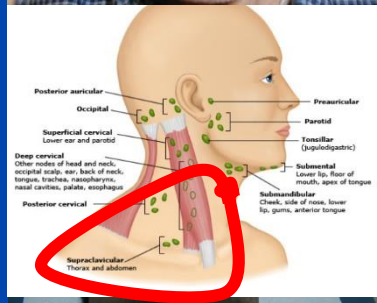
Physical Exam –

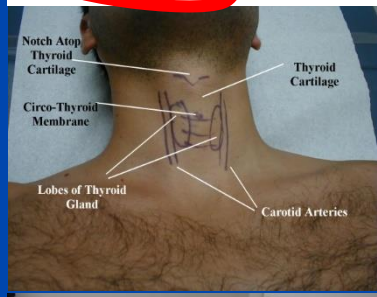
Examine the oral cavity, head and neck, and supraclavicular region.

Cranial Nerve Exam

Cranial Nerves

1. Olfaction (CN I)
2. Vision (CN II)
a. Visual fields
b. Visual acuity
c. Funduscopic examination
3. Pupillary light reflex (CNs II, III)
4. Eye movements (CNs III, IV, VI)
5. Facial sensation (CN V)
6. Facial strength
a. Muscles of mastication (CN V)
b. Muscles of facial expression (CN VII)
7. Hearing and vestibular function (CN VIII)
8. Palatal movement (CNs IX, X)
9. Dysarthria (CNs IX, X, XII)
10. Head rotation (CN XI)
11. Shoulder elevation (CN XI)
12. Tongue movements (CN XII)





Subsequent Evaluation

Patients with ***neuromuscular*** disease:

- videoflouroscopy with modified barium swallow
- esophageal manometry

Patients without systemic symptoms

- nasopharyngoscopy of swallowing
- videoflouroscopy with modified barium swallow
- esophageal manometry

Nasopharyngoscopy to evaluate swallowing

Why: allows assessment of symmetry, sensation, pooling, and aspiration

Disadvantages: cannot evaluate

cricopharyngeus or esophagus

Fiberoptic endoscope




Videoflouroscopy modified barium swallow

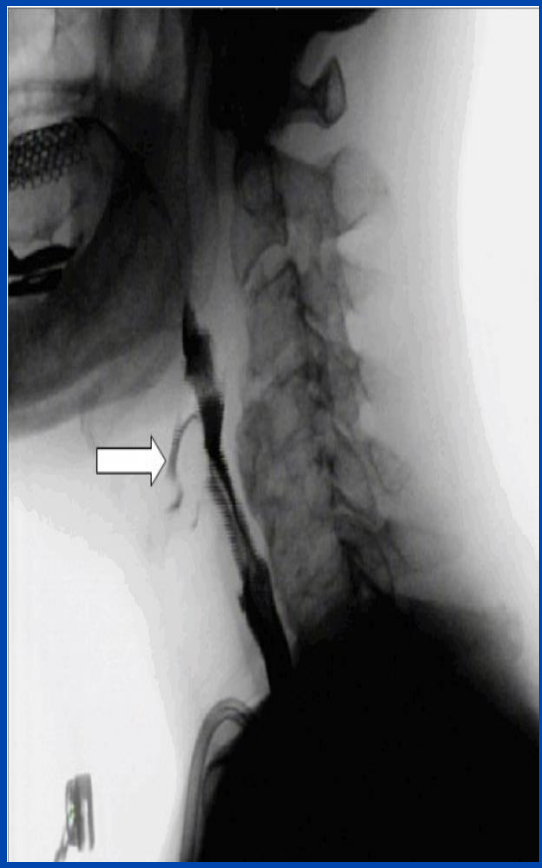
Who: suspect neuromuscular process and structural

Why: detects severity of dysfunction and aspiration

Drawbacks: interobserver reliability is high

only for aspiration

Stoeckli SJ et al. Dysphagia 2003

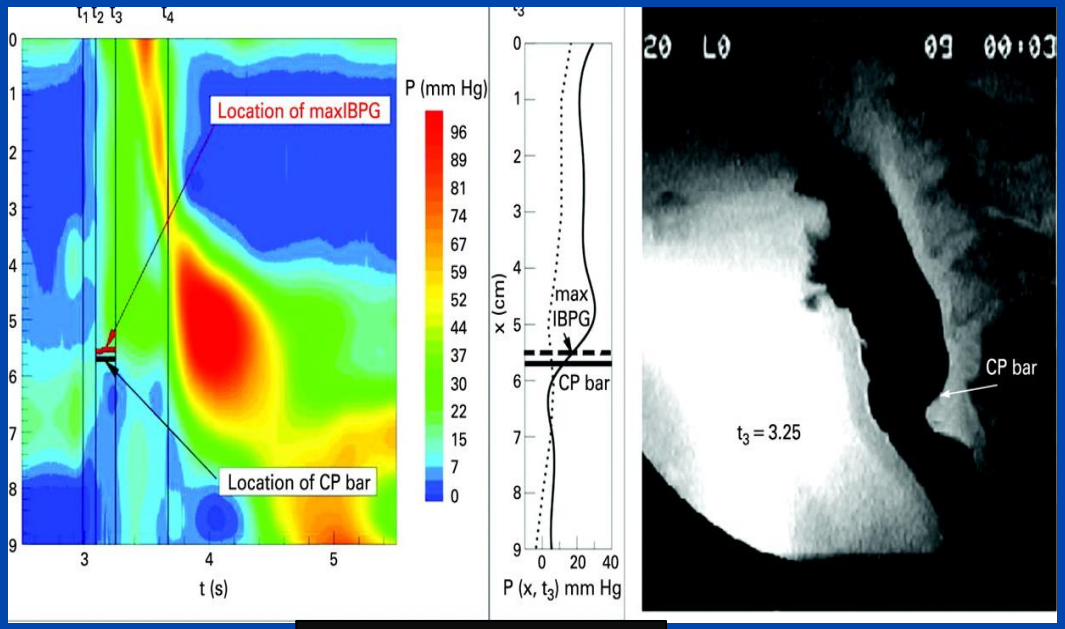


Manometry

Evaluate *pressures* and *timing* in pharyngeal contraction and deglutitive UES relaxation

Identify underlying etiology.

Patients who may benefit from surgical myotomy.



Cricopharyngeal Bar

Management oropharyngeal dysphagia

Goals: improve food transfer and prevent aspiration

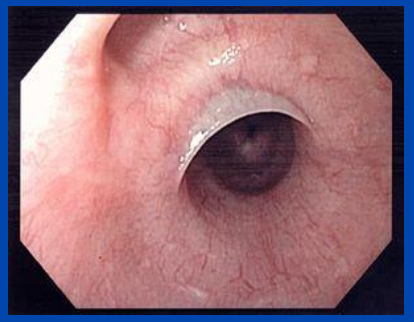
Treat the underlying disorder

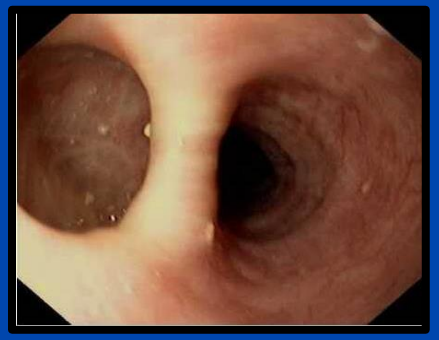
Swallowing rehab and nutrition

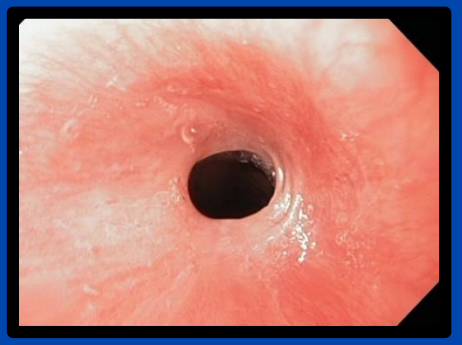
Endoscopic dilation

Cricopharyngeal myotomy

Botulinum injection







Case 1

Tom S is 83 y/o male, experienced a stroke 4 weeks ago.

He complains of dysphagia.

PMHx: GERD, constipation, chronic back pain on opiates, HTN

Current illness: coughing and choking with initial ingestion.

15# weight loss in 3 months. GERD and constipation have

been worse for one month. Dysarthria.

Physical exam: Tongue asymmetry.

CN IX, X, XII affected. Normal lymph.

Plan: Perform videoflouroscopy with barium swallow, manometry.

Consider EGD and colonoscopy if not recent.

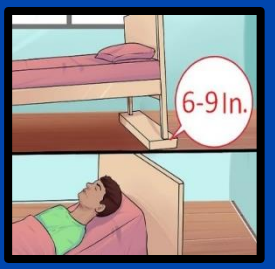
Case 1 (cont)

Primary Goal: Improve food transfer and prevent aspiration

Treat the underlying disorder

Rehabilitation, muscle strengthening, nutrition and diet

GERD management: elevate head of bed, avoid food for 3 hours before reclining, avoid liquids and pills for 1 hour before bed.



Constipation management: laxation agents to reduce straining, promote ease of passage. Avoid opiates

Summary Oropharyngeal Motility

- History and Physical
- Labs and CNS imaging
- If systemic process (CVA, mass): refer, treat
  - Nasopharyngoscopy. Structural evaluation
- Videoflouroscopy and manometry. Severity and mechanism of swallow dysfunction.
- Management. Prevent harm, monitor nutrition and medications, treat GERD and avoid constipation.

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Colon and Anorectal Motility Disorders

Symptoms of Colon and Anorectal Motility Disorders

- Difficult constipation
- Abdominal bloating and distention
- Sense of incomplete evacuation
- Fecal urgency
- No/low urge to go
- Bristol Stool #1-2 > 25% of movements
- Excessive straining

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Case 2

Sarah is a 45 y/o mother of 2. Her complaint is difficult constipation with a recent change in symptoms. She had bowel movements every 2-4 days since high school. For the past year frequency has changed to every 3-14 days with laxatives. Abdominal distention is measurable and bothersome. Fiber makes it worse.

Does she have a motility disorder?

What are the historical clues?

How would you evaluate the cause(s) of constipation?

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Causes of Constipation

Primary

- IBS-C, CIC
- Outlet dysfunction
- Slow transit

Secondary

- Lifestyle – low fiber, low activity
- Iatrogenic – medications
- Psychogenic – eating disorders
- Miscellaneous – travel

Gallegos –Orozco JF. Am J Gastroenterol 2012.

Functional Constipation

IBS-C

•Recurrent **abdominal pain** > 1d/wk in the past 3 mo. Associated with :

1. Improves with defecation
2. change in stool frequency
3. Change in stool appearance

Symptoms present for 6+ mo

CIC

•Criteria include:

- a) straining
- b) lumpy or hard stool
- c) incomplete evacuation
- d) outlet obstruction
- e) manual maneuvers
- f) < 3 movements / week

CIC = chronic idiopathic constipation

Longstreth GF et al. Gastroenterology 2006.

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Bristol Stool Chart

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
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

Causes of Outlet Dysfunction

AKA evacuation disorder, defecation disorder, pelvic floor dysfunction

- Dyssynergy
- Inadequate descent
- Excessive descent
- Rectocele, enterocele, cystocele
- Rectal prolapse
- Obstruction / stricture
- Inadequate propulsive forces

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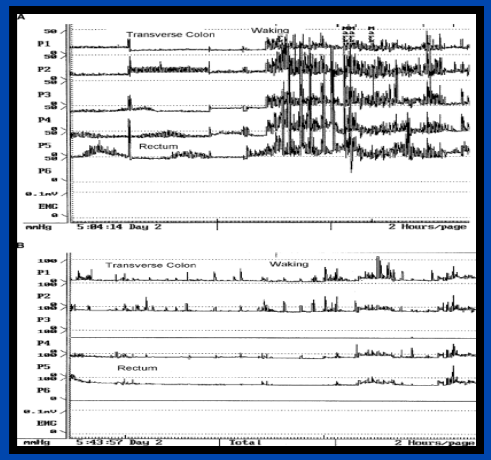
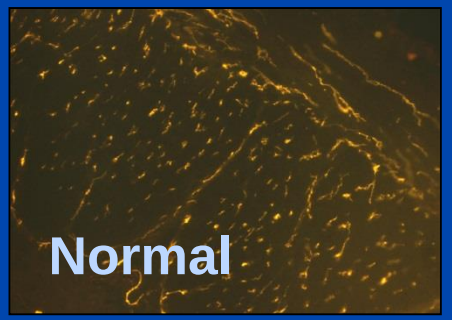
Slow Transit Constipation

- Impaired neurogenic or myogenic response to normal stimuli
  - Decreased numbers of ICC
  - Blunted HAPC response
- More common in young females
- Days or weeks between movements



C-kit immunoreactivity



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Causes of Slow Transit (and intestinal motility disorders generally)

- Autonomic disorders
  - Postural Orthostatic Tachycardia Syndrome
- Connective tissue disorders
  - Scleroderma, Lupus
- Neuromuscular disorders
  - Myopathy, neuropathy
- Post viral, post infectious, post event
- Other

Slow transit can overlap with other causes of constipation

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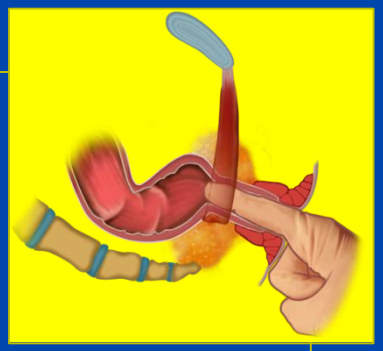
History and anorectal examination

- Duration of symptoms
- BMs /week
- Bristol Stool Scale

- Inspect
- Hemorrhoids
- Descent
- Prolapse
- Sphincter tension
- Fissure



Questions: DO YOU

Completely evacuate, strain, feel the urge, experience soiling or incontinence, use manual maneuvers, have prolapse?

Does fiber make it worse?

Do other family members have symptoms?

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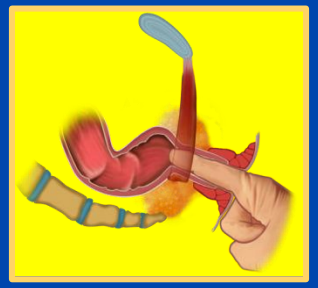
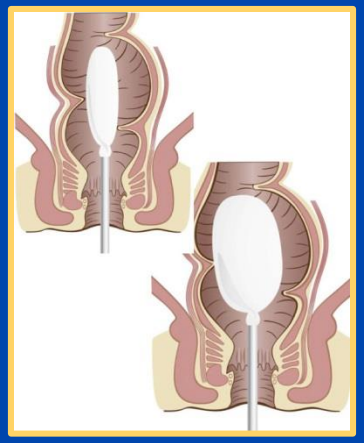
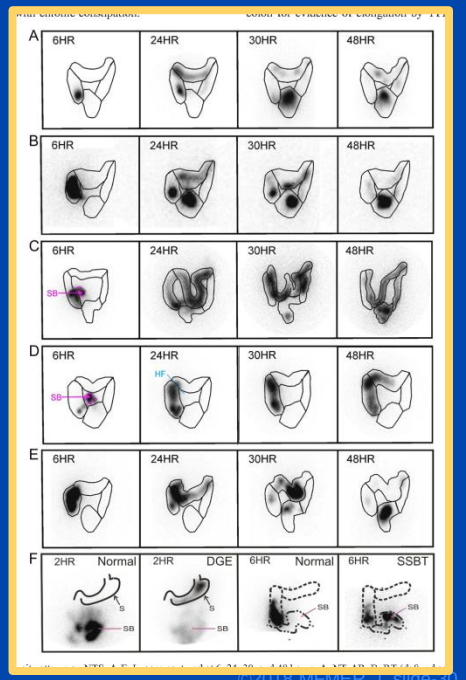
Tests to evaluate cause(s) of constipation

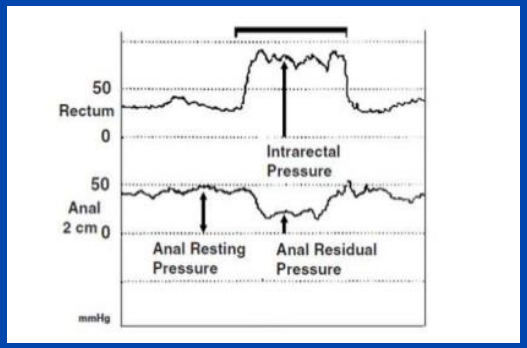
- Anorectal exam
- Anorectal manometry
- Transit
- Defecography



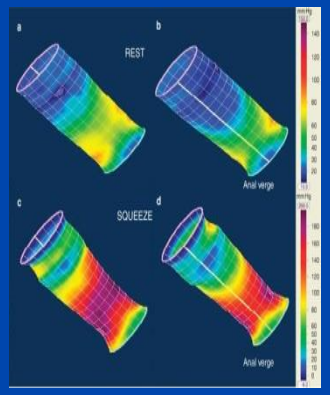


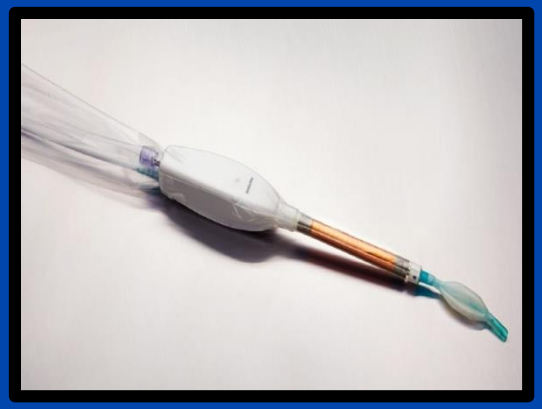


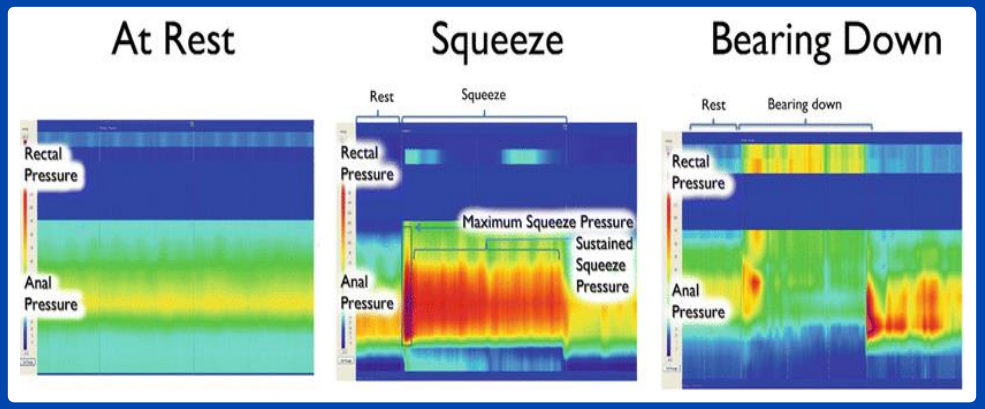
Perfusion manometry



Manometric probe



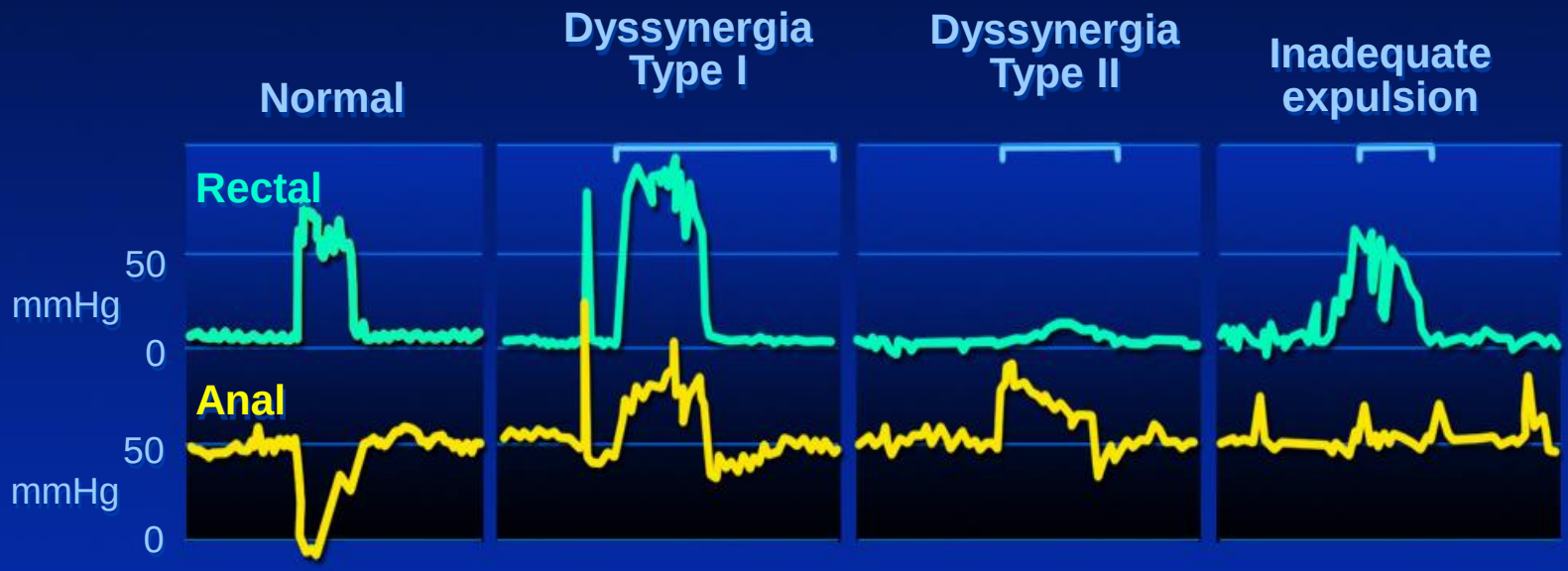




Normal ranges must be established in each laboratory for each technique used

Anorectal Manometry Test	Indication	Interpretation
Resting pressure	Assess IAS	Decreased= weak or disrupted IAS Increased=smooth or striated m spasm
Squeeze pressure	Assess EAS	Decreased = weak EAS or noncompliant patient
Rectoanal inhibitory reflex	Screen Hirschsprung's Disease	Present= NO Hirschsprung's Absent = Possible Hirschsprung's or tonic contraction
Cough reflex	Screen for malingering or damage to sacral arc	Cough response **>** voluntary squeeze=probable noncompliant patient Cough response **<** voluntary squeeze=probable defect in sacral arc
Anocutaneous reflex	Screen for damage to sacral arc	Similar to cough reflex, but lacks sensitivity and specificity

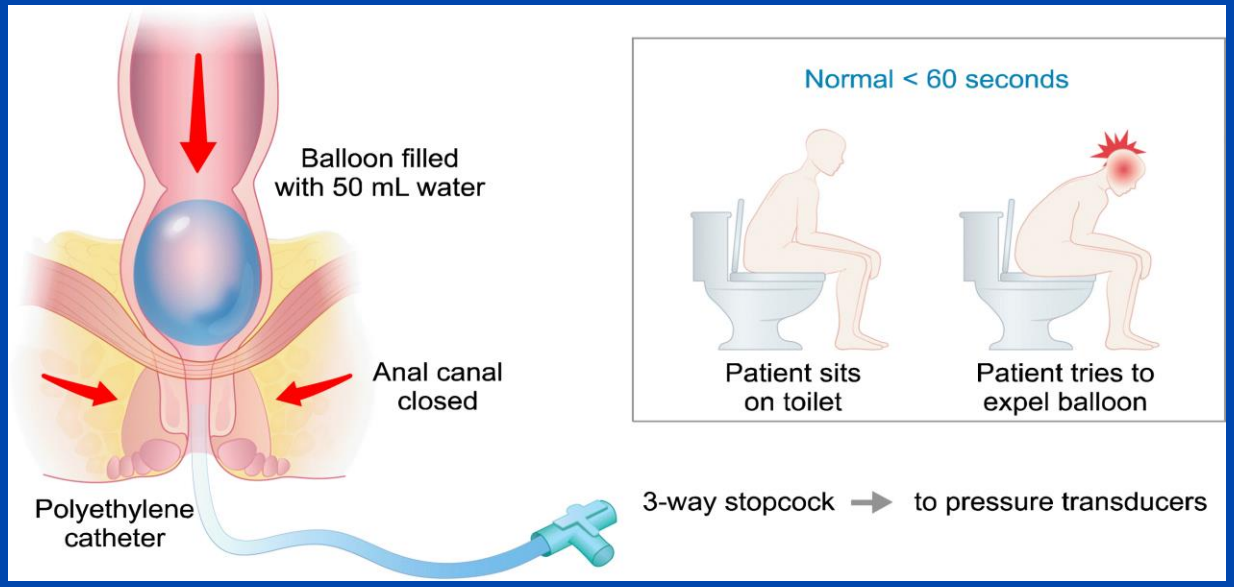
Anorectal Manometry: Dyssynergy



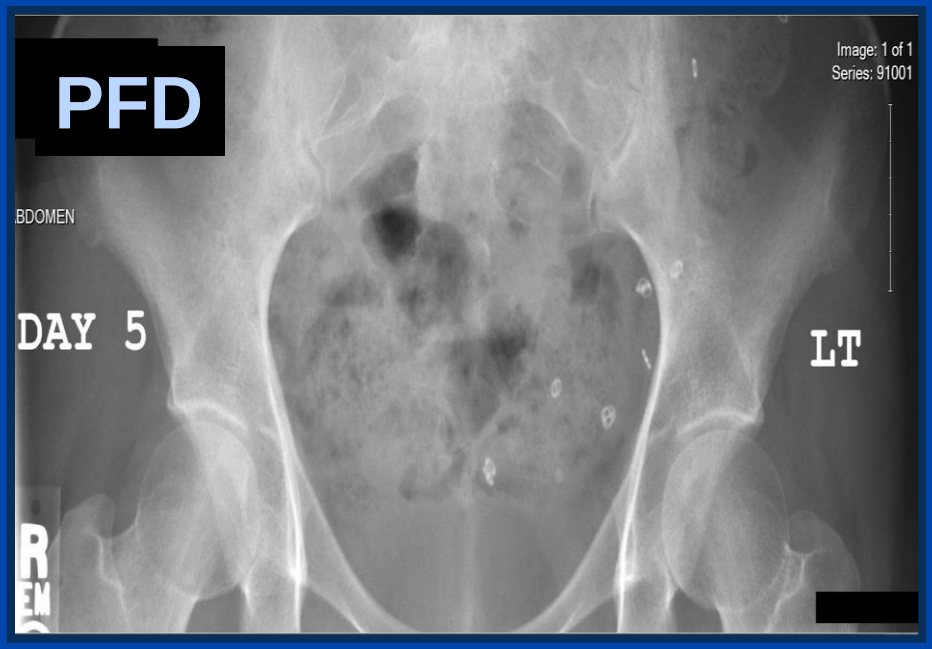
Remes-Troche JM et al. Curr Gastroenterol Rep 2006;
Surrenti E, et al. Am J Gastroenterol 1995

Balloon Expulsion Test

Establish the time required to achieve evacuation.



Transit – Sitz mark



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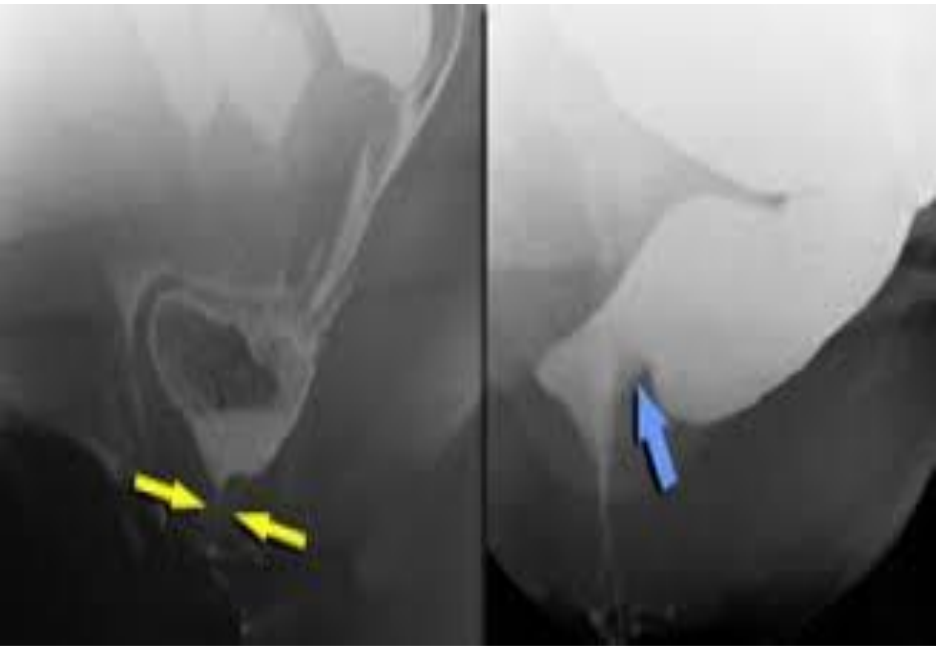
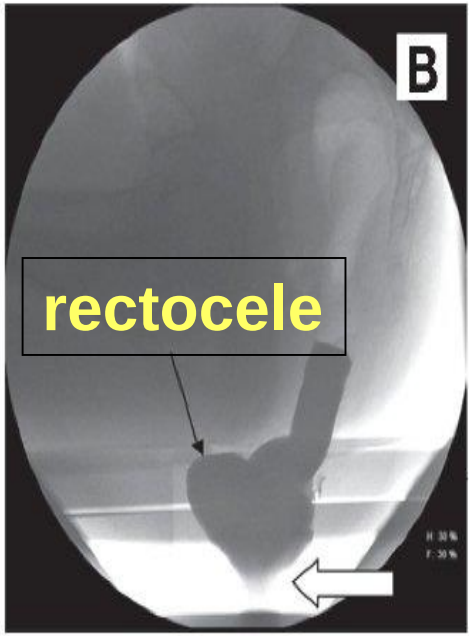
Defecography: Outlet Dysfunction Suspected



dyssynergy



excessive perineal descent

Treatment for colon and anorectal motility dysfunction

One billion dollars spent on constipation management US

*800 million on prescriptions

Many effective non-pharmacologic and pharmacologic treatments for constipation

Healthcare goal: Improve the primary symptom

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Gallegos –Orozco JF, Foxx-Orenstein AE. AJG 2012.

First Line Approach
Improve effective emptying

- ↑ Physical activity
- Avoid constipating drugs
- Hydrate
- 20-30 grams of fiber daily

High fiber can worsen STC and severe PFD. Add slowly, reevaluate, consider testing.

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Bowel Management Techniques

- Impro
- Maxi king, eating, ca
- Resp
- Eleva

Biofeedback for Dyssynergy (and IBS-C)

Biofeedback is the treatment for dyssynergia

- Prospective study in patients with dyssynergic defecation (N=50) plus IBS-C (n=29)
  - Similar response to biofeedback in dyssynergic and IBS-C groups (55% vs 67%, *P* >0.05)
  - **IBS-C symptoms improved in 41% patients who had successful response to biofeedback**

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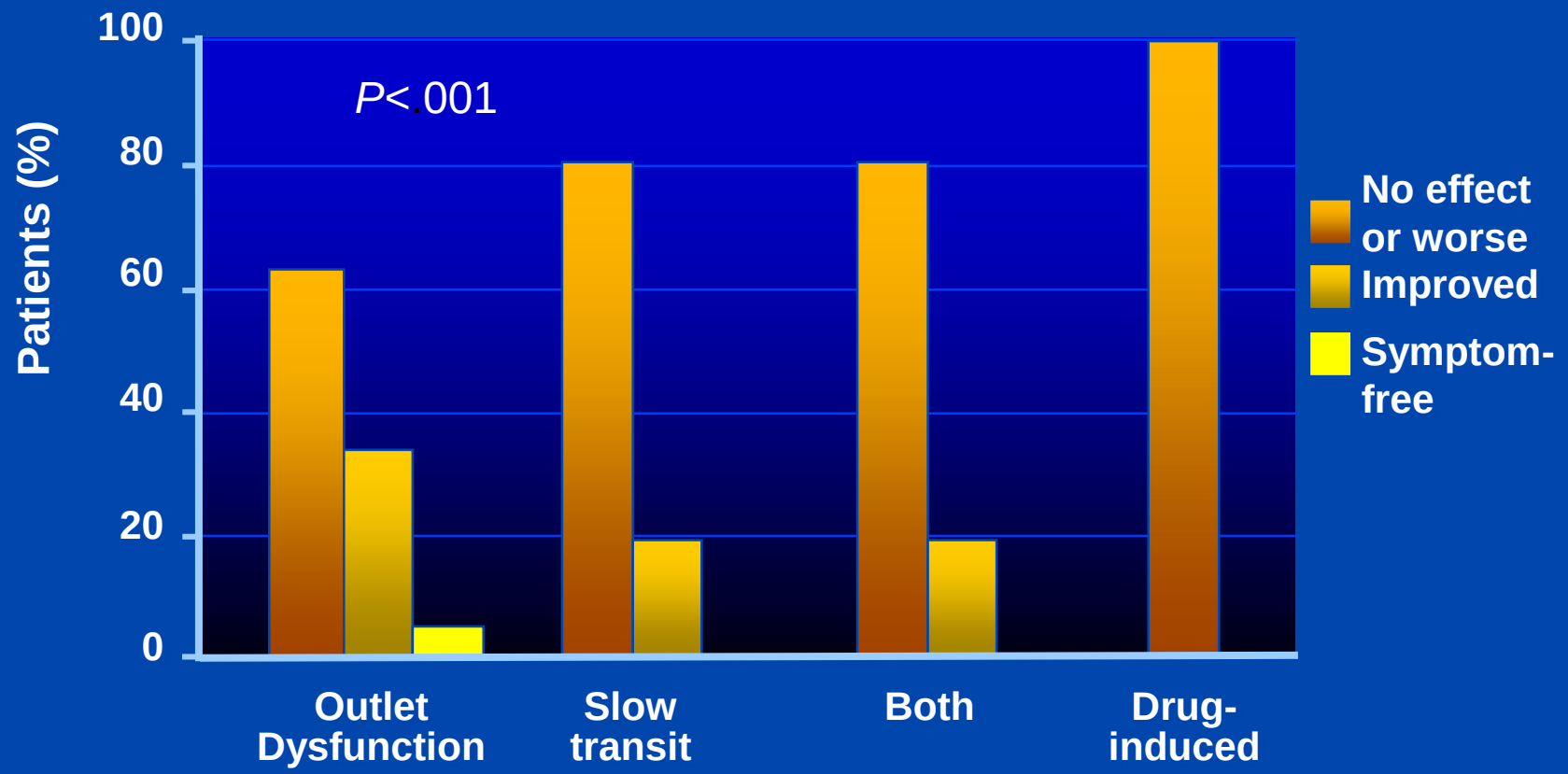
Patcharatrakul T et al. J Clin Gastroenterol. 2011

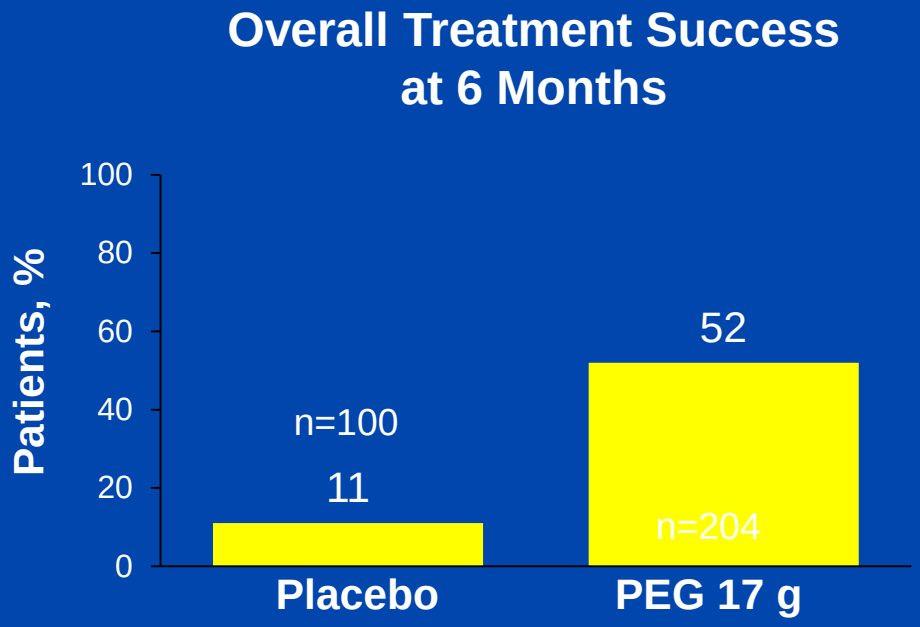
Effect of Fiber on Constipation Subtypes



30mg/d of *Plantago ovata* seeds in 3 divided doses

Voderholzer WA et al. Am J Gastroenterol; 1997

Polyethylene Glycol (PEG) for CIC (not IBS?)

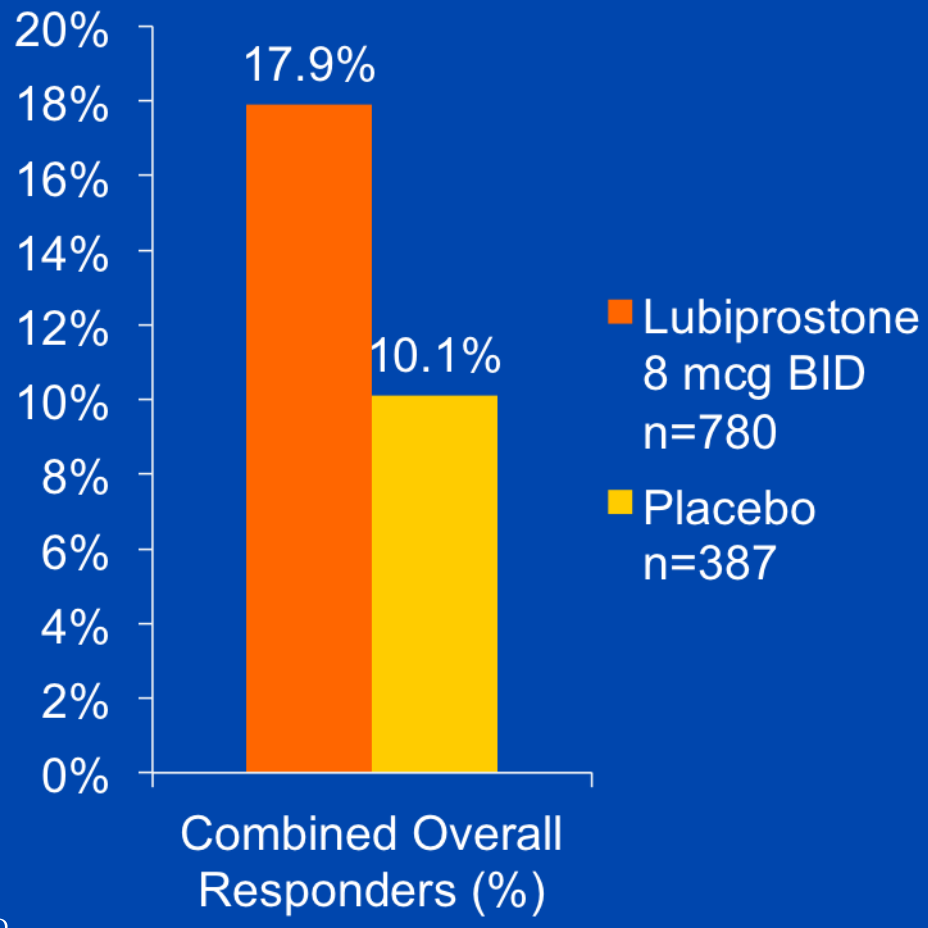


Significant Improvement in Secondary Endpoints (*P*<0.001)

CSBM
Straining
Incomplete defecation
Hard stools
≥3 BMs/week
Global Satisfaction

DiPalma J et al. Am J Gastroenterol 2007

Lubiprostone for IBS-C:

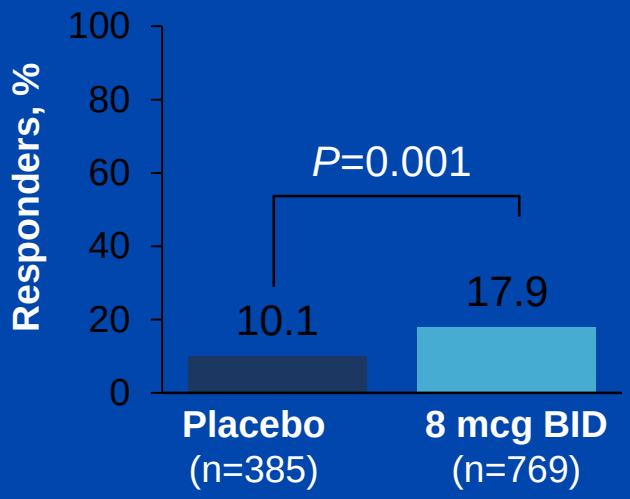


- 12-wk treatment period
- Overall responder= monthly responder ≥2-3 mo
- Monthly responder= at least moderate relief 2-4 wk *or* significant relief >2-4 wk

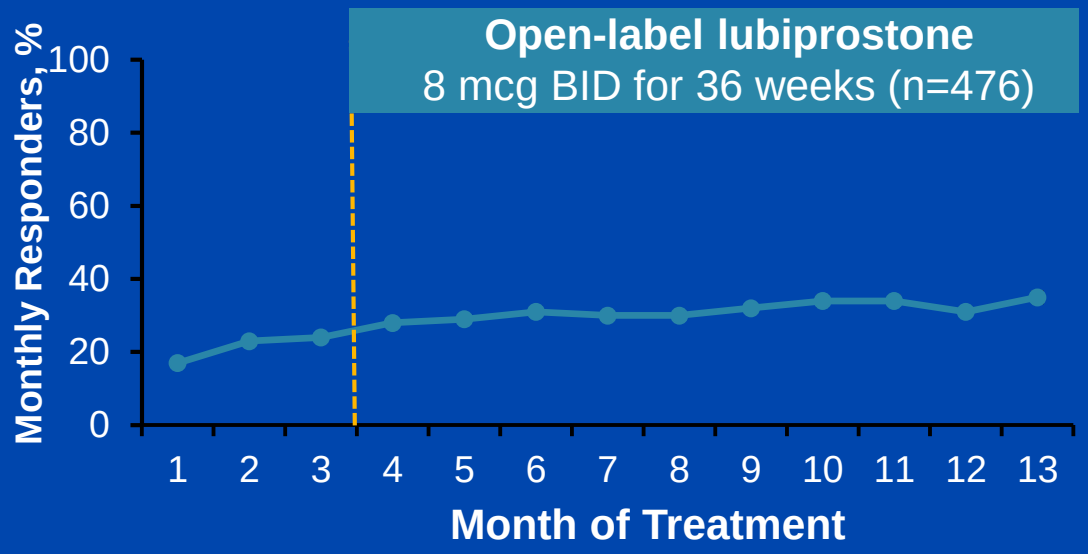
Drossman DA et al. Aliment Pharmacol Ther. 2009

Lubiprostone for IBS-C (and OIC)

Overall Responders at 12 Weeks*[1]



Monthly Responder Rates in Randomized Withdrawal/Extension Studies[2]



Lubiprostone improves abdominal pain and bloating

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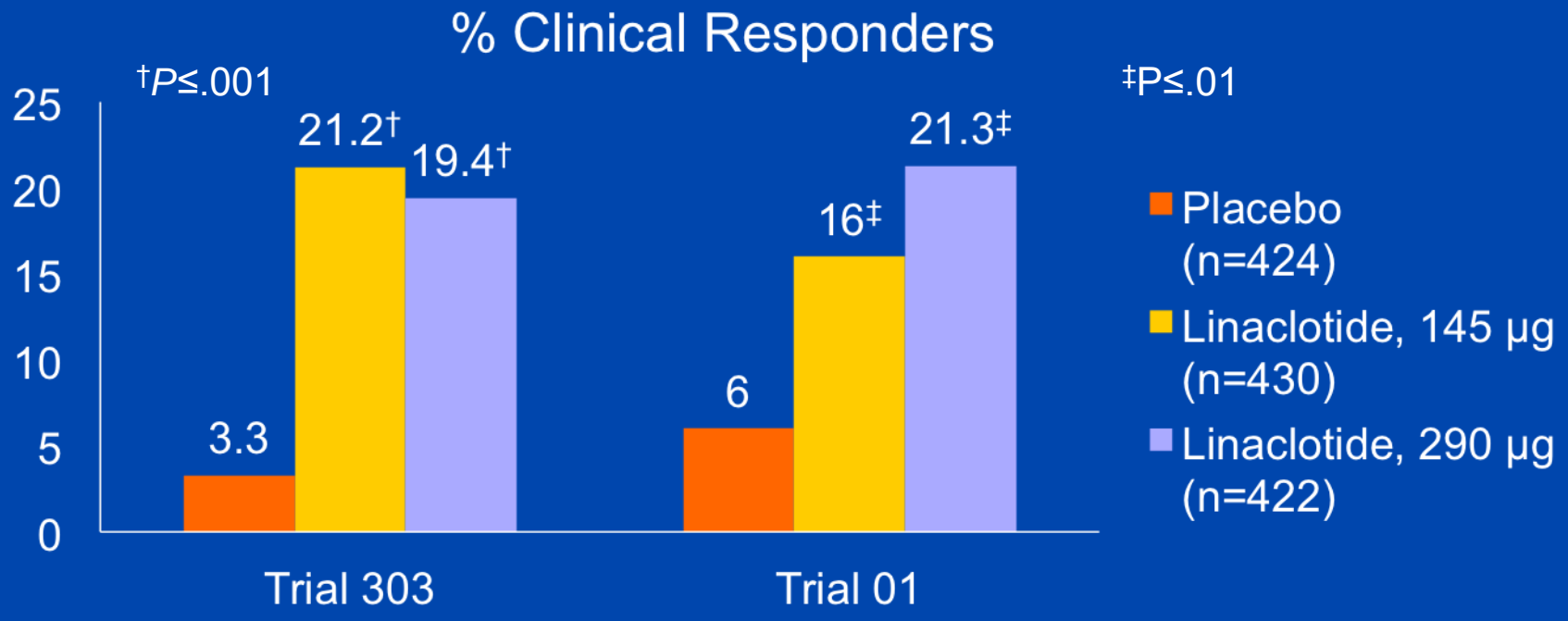
Drossman DA et al. Aliment Pharmacol Ther. 2009;29:329
Chey WD et al. Aliment Pharmacol Ther. 2012; 35:587

Linaclotide for Chronic Constipation:



Responder: >3 CSBM/wk and > 1 CSBM/wk for 9 out of 12 wks

Lembo AJ, et al. N Engl J Med. 2011

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Lubiprostone In The Clinic

Dosage for CIC
24 mcg BID

Dosage for IBS-C
8 mcg BID

Adverse Events in IBS-C and CIC Trials

Adverse Events	IBS-C		CIC	
	PBO n=435	LUB 8 mcg BID n=1011	PBO n=316	LUB 24 mcg BID n=1113
	%			
Nausea	4	8	3	29
Diarrhea	4	7	1	12
Abdominal pain	5	5	3	8
Abdominal distension	2	3	2	6

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ACG Systematic Review of Efficacy of Linaclotide in CIC

3

Clinical trials

1,582

Patients treated

0.84

(0.80-0.87)

RR symptoms

Linaclotide is superior to placebo for the treatment of CIC

Recommendation

Strong

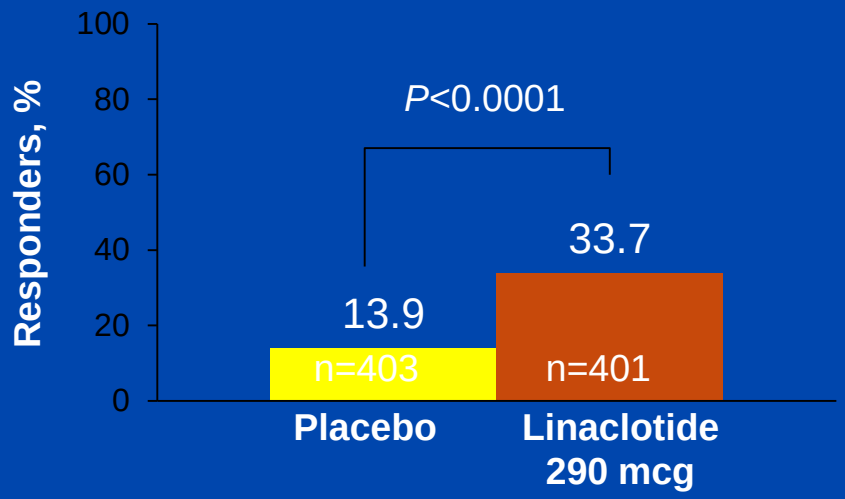
Quality of evidence

High

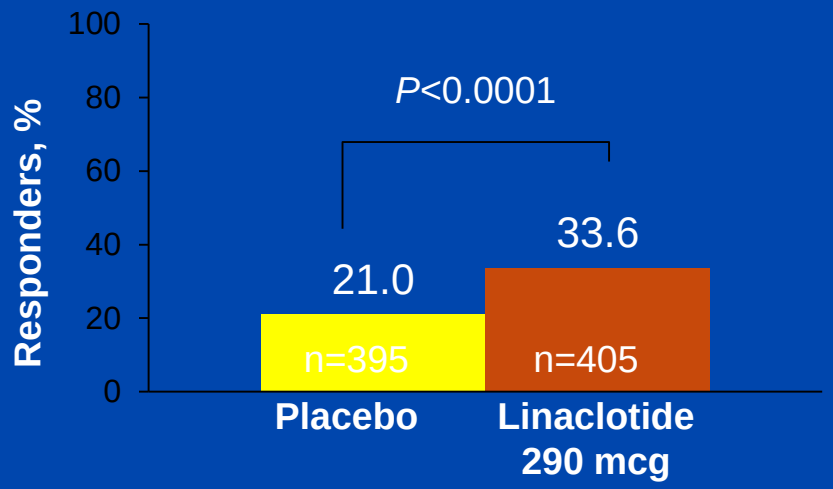
Ford AC et al. Amer J Gastroenterol 2014

Linaclotide Improves Abdominal Pain and Bloating Symptoms In IBS-C

FDA Composite Endpoint (primary endpoint) in Linaclotide Pivotal Trials



PAIN



Bloating

Chey W et al. Am J Gastroenterol. 2012;107:1714

Linaclotide Adverse Events

Adverse Events in IBS-C and CIC Trials

	IBS-C		CIC	
	PBO n=798	LIN 290 mcg n=807	PBO n=423	LIN 145 mcg n=430
Adverse Event	%			
Diarrhea	3	20	5	16
Abdominal pain†	5	7	6	7
Flatulence	2	4	5	6
Abdominal distension	1	2	2	3

If severe diarrhea occurs, dosing should be suspended and the patient rehydrated.

Linaclotide prescribing information 2017

Linaclotide in the Clinic

Dosage for CIC
72 mcg or 145 mcg once daily

Dosage for IBS-C
290 mcg once daily

Administration

- Take on empty stomach ≥30 minutes before first meal of the day
- Can mix with water or applesauce for dose reduction or patients with difficulty swallowing
- Not approved for patients <18 years of age

Linaclotide prescribing information 2017

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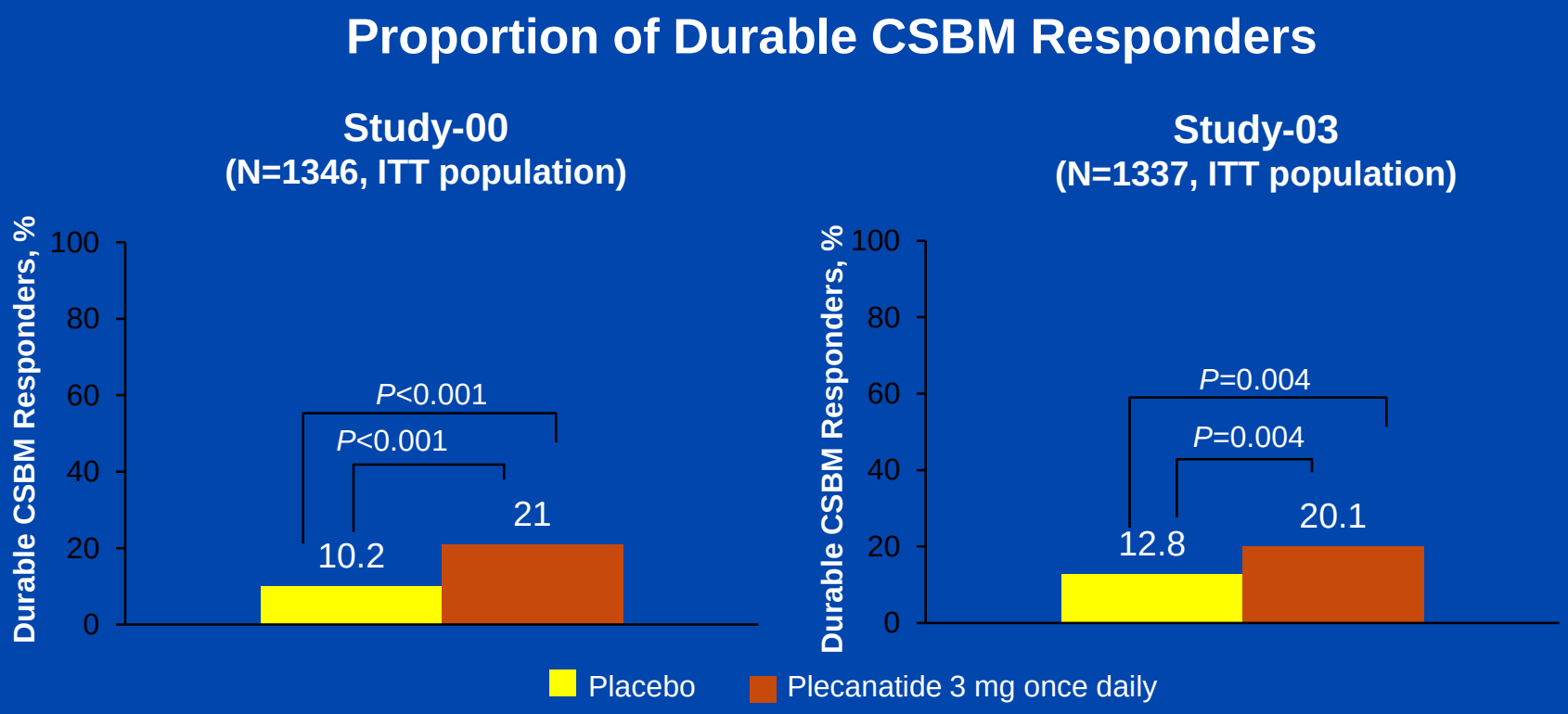
Plecanatide for CIC
Phase III trial durable CSBM results



CSBM = complete spontaneous bowel movement

Miner PB et al. Am J Gastroenterol. 2017;112:613
DeMicco M et al. Ther Adv Gastroenterol. 2017;10:837

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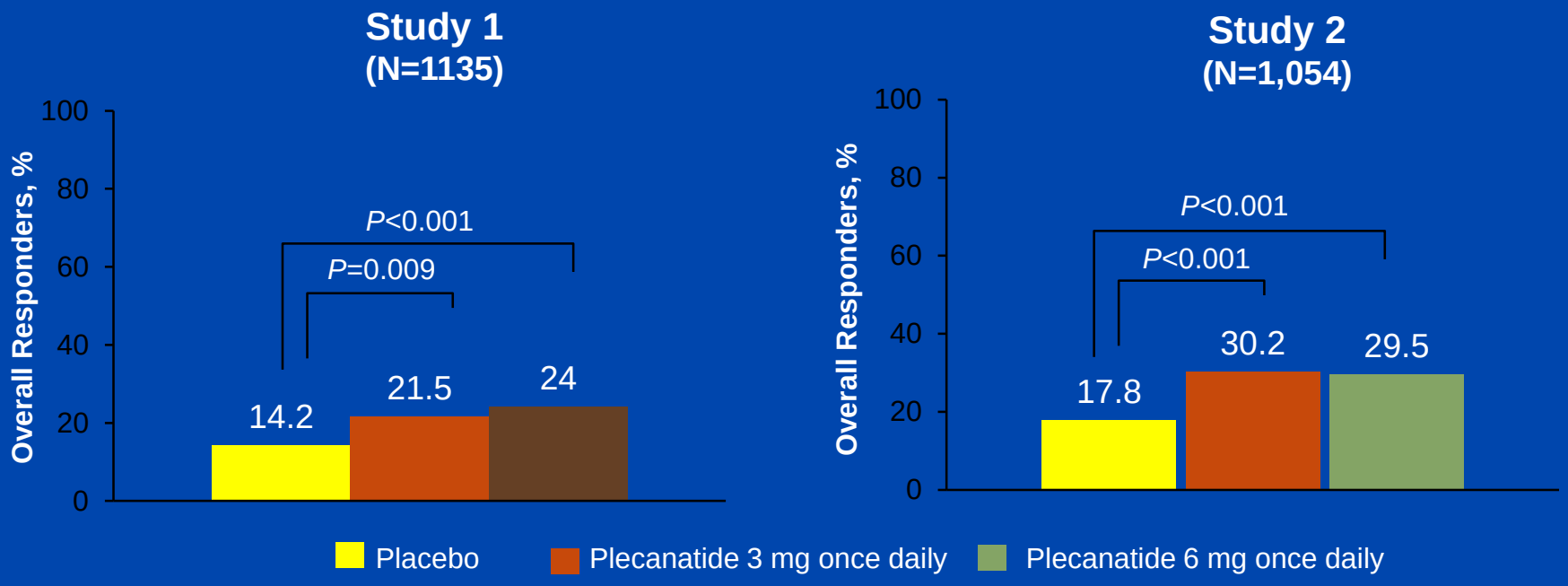
Plecanatide for IBS-C:
Phase III Trial Efficacy Results

Overall Responders During 12 Weeks



Brenner DM et al. Am J Gastroenterol. 2018;113(5):735-745.

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Plecanatide In The Clinic

Dosage for CIC and IBS-C
3 mg once daily

Adverse Events

Adverse Events	CIC		IBS-C	
	Placebo n=870	Plecanatide 3 mg n=863	Placebo n=726	Plecanatide 3 mg n=723
	%		%	
Diarrhea	1	5	1	4.3
Severe diarrhea	0.3	0.6	0.1	1
Discontinuation due to diarrhea	0.5	2	0	1.2

Diarrhea occurred within the first 3 days of treatment. If severe diarrhea occurs, stop therapy, rehydrate.

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Slow Transit Constipation Treatment

Medical

- Nonabsorbed substances
- Stimulants
- Secretory (lubiprostone and linaclotide)
- Pyridostigmine
  - 180 ER 1 qd
  - 30-60 mg tid
  - 60mg/5ml tid 15-30 minutes ac
- Low fiber, low residue diet

Surgical Colectomy

- Medically refractory patients with poor QOL

Locke G, et al. Gastroenterol 2000;
Nyam DC, et al. Colon Rectum 1997

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Opioid Induced Constipation (OIC)

- Bowel regimens are not particularly effective.
- Conventional laxatives may be helpful but have limited efficacy

TREATMENT: stop the opiate

PAMORA – peripherally acting opioid receptor antagonist

- Methylnaltrexone bromide: 8 mg sq once daily
- Naloxegol: 25 mg or 12.5 daily.
- Oxycodone/naloxone combination: to deter misuse
- Lubiprostone: 24 mg bid

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Summary of Colon and Anorectal Motility Disorders

- History and physical to determine factors contributing to symptoms
- Limited testing: anorectal manometry, defecography, transit studies
- Management:
  - Bowel management techniques
  - Biofeedback for outlet dysfunction (and IBS)
  - Time laxative use to augment bowel activity triggers
    - early evening to promote AM evacuation
    - before meals
  - Aim for daily – every other day bowel elimination

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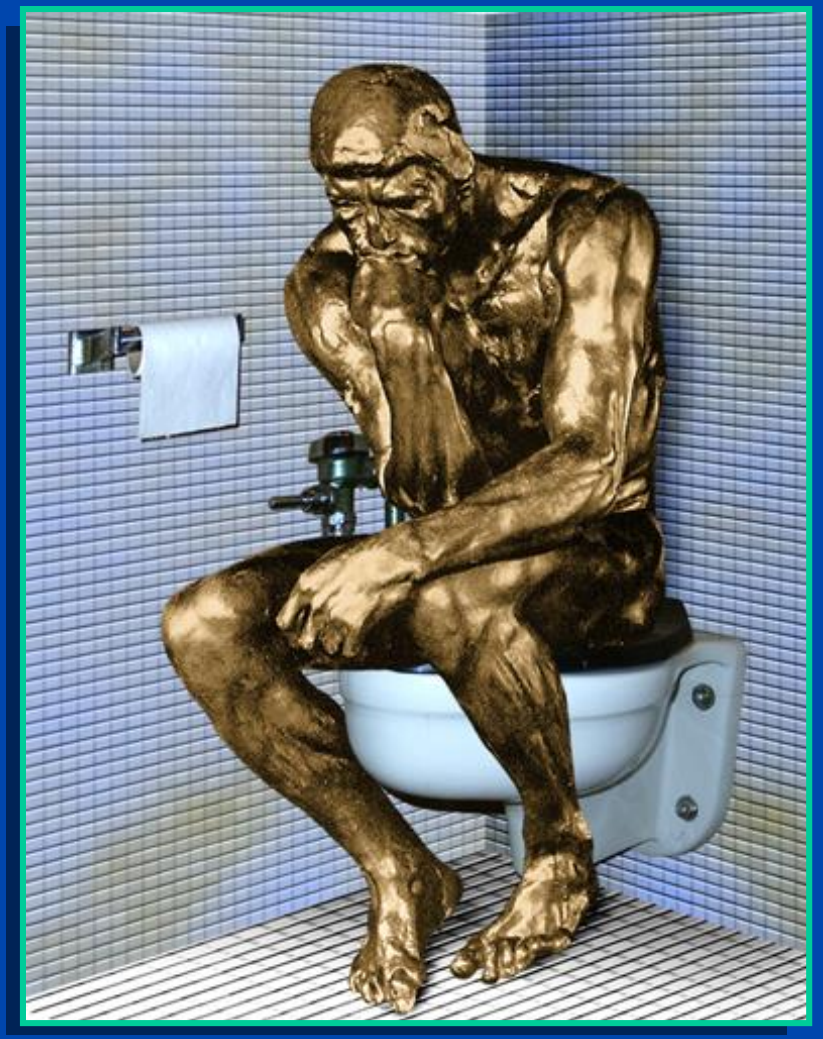
Thank you!



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