

## Early description of symptoms defining IBS

- 1849 – W Cumming

**“The bowels are at one time constipated,  
at another lax, in the same person.  
How the disease has two such different  
symptoms I do not profess to explain...”**

- Historical

- |                             |                   |
|-----------------------------|-------------------|
| – mucous colitis            | – unstable colon  |
| – colonic spasm             | – nervous colon   |
| – neurogenic mucous colitis | – nervous colitis |
| – irritable colon           | – spastic colitis |

- Chronic Relapsing Symptoms

- Long-term (~10 years) followup suggests:  
30% improved  
70% unchanged/worse

W. Cumming, London Medical Gazette, 1849;NS9:969-973.

## Natural History of IBS

- Chronic, relapsing symptoms
- Long-term follow-up suggests that
  - ~ 20% worsened
  - ~ 50% remained unchanged
  - ~ 30% improved

1. El-Serag HB, et al. *Aliment Pharmacol Ther*. 2004;19:861-876.  
2. Engstuber AJ, et al. *Aliment Pharmacol Ther*. 2012;35:308-309.  
3. Garrigue V, et al. *Aliment Pharmacol Ther*. 2007;25:323-332.

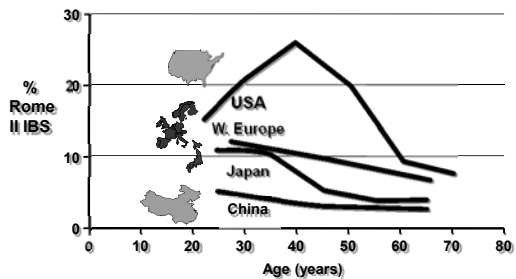
## IBS Symptoms are Common

Prevalence of IBS <sup>1,2</sup>



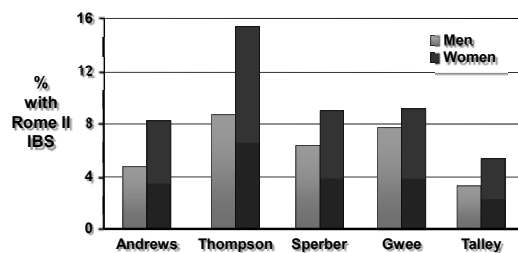
1. Chey WD, et al. *JAMA*. 2015;313:949-958.  
2. Lovell RM, et al. *Clin Gastroenterol Hepatol*. 2012;10:712-721.

## IBS is Particularly Common in Young Adults



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## IBS is More Common in Women



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## IBS Frequently Co-exists with Other Chronic Conditions

### IBS comorbidities include:

- Depression (39%)
- Migraine (37%)
- Anxiety (35%)
- Neuralgia (29%)
- Headache (26%)
- Chronic fatigue (20%)
- Chronic pain (19%)
- Fibromyositis (15%)

Greater  
impairment  
in QoL

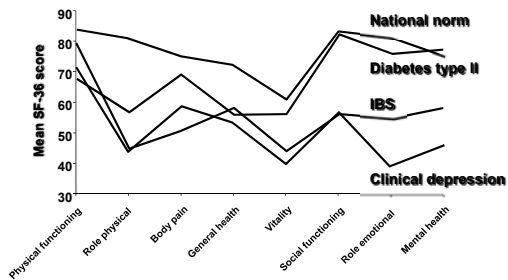
More severe  
IBS symptoms

More anxiety  
and depression

More illness  
related work  
absenteeism

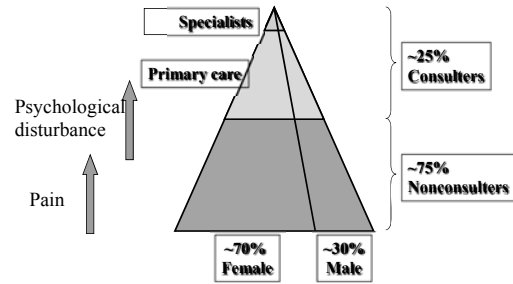
Ladabaum et al. *Gastroenterology* 2007; 132: W1172  
Whitehead et al. *Am J Gastroenterol* 2007; 102: 2767-76  
Vandvik et al. *Aliment Pharmacol Ther* 2004; 20: 1195-203

## IBS Patients have Lower HR-QOL



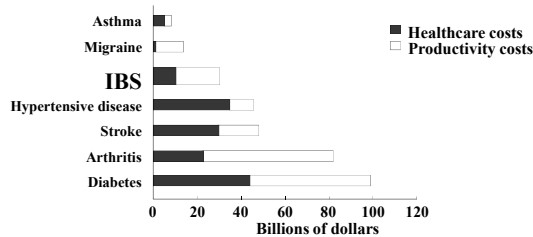
Adapted from Wells et al., *Alimentary Pharmacology Therapeutics*, 1997; 11: 1019-1030.

## Who Seeks Medical Care for IBS?

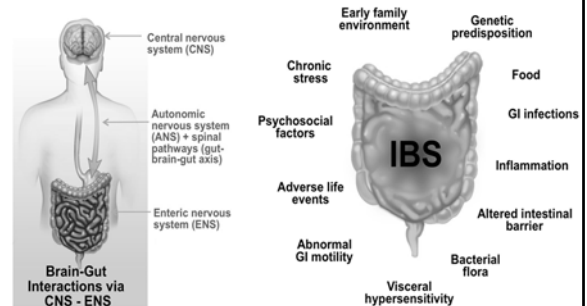


Adapted from Drossman and Thompson, *Ann Intern Med* 1992; 116(pt 1): 1009. Sandler, *Gastroenterology* 1990; 99: 409.

## Economic burden of IBS



## IBS: Pathogenesis/Pathophysiology



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## Clinical Presentation

- 32 year old woman with a 5-10 year h/o frequent attacks of severe, crampy abdominal pain in the LLQ associated with diarrhea (loose/watery stool associated with rectal urgency). Her pain usually improves after BMs. Rarely has constipation.
- She denies wt. loss, BRBPR, nocturnal symptoms, F/H Colon CA or IBD. She work-outs daily, and eats a vegetarian diet. Medications: Vit. D and levothyroxine
- PE: No abdominal scars, masses, or distention. Rectal exam: G-, normal tone, appropriate descent

## History and Physical Examination for Lower GI Symptoms

### History

- Presenting symptoms
- Establish history timeline
- Presence of alarm signals
- Family history: IBS, organic GI disorder
- Diet
- Review current medications

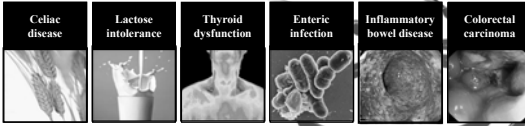
### Examination

- Signs of systemic and local diseases that might cause constipation
- Assess the anorectum and pelvic floor muscles
- Other relevant abnormalities

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## Conditions That Can Mimick IBS



Organic disease in the absence of alarm features is uncommon

### Alarm Features

- Symptom onset > 50 years
- Blood in stools/Fe def anemia
- Weight loss (unintentional)
- FH CRC/IBD
- Nocturnal Symptoms

ACC Task Force on IBS. *Am J Gastroenterol*. 2009;104(suppl 1):S1-S25

## Rome IV Criteria for IBS

Recurrent abdominal pain  
at least 1 day/week in the last 3 months  
associated with 2 or more of the following:

Related to  
defecation

Associated  
with a change  
in frequency of stool

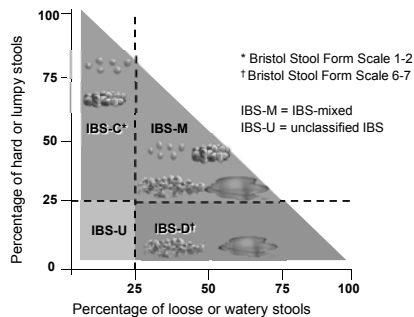
Associated  
with a change  
in form (appearance)  
of stool

\*Criteria fulfilled for the last 3 months with symptom onset  
at least 6 months prior to diagnosis

Lacy B et al. *Gastroenterology*. 2016;150:1393-1407  
Rome Organization. Rome IV Disorders and Criteria.

7

## IBS Subtypes Based on Stool Consistency



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

## Diagnostic Testing for Patients with Suspected IBS and Alarm Features

All IBS Subtypes

CBC

Age-appropriate CRC screening

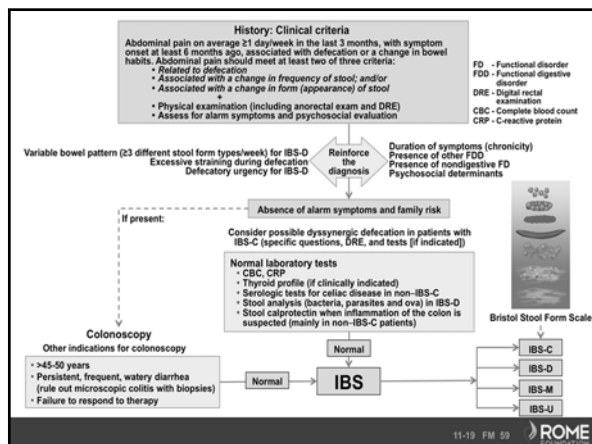
IBS-C  
Consider assessment of pelvic  
floor function if medically  
refractory

IBS-D  
CRP and/or fecal calprotectin  
IgA TitG ± quantitative IgA  
When colonoscopy performed, obtain random  
biopsies  
Assess for bile acid malabsorption (serum C<sub>4</sub>)  
For IBS-M consider abdominal x-ray to evaluate for  
stool accumulation

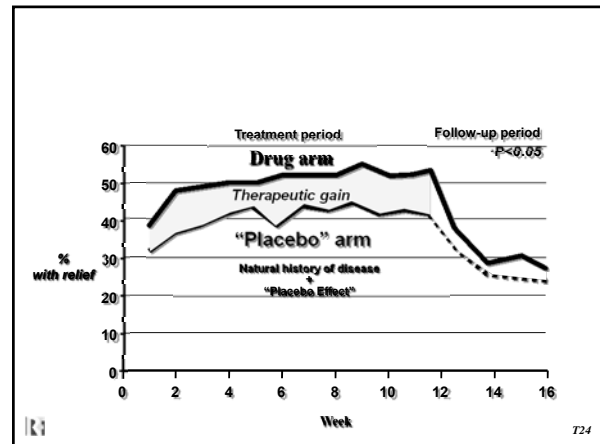
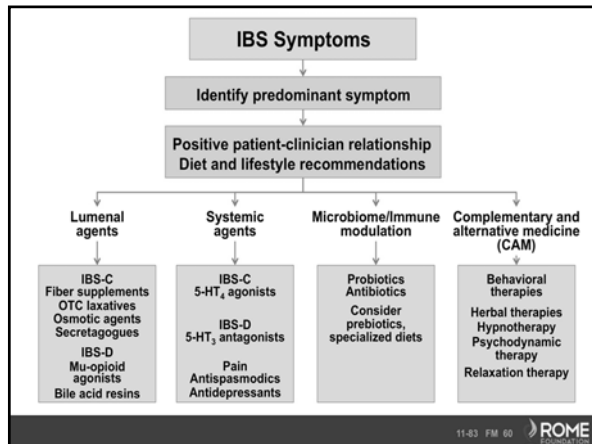
Role of SIBO breath testing, anti-vinculin/anti-Cdtb (IBScheck®) is unclear

Lactose breath testing may be appropriate when lactose free diet is not definitive

CBC, complete blood count; CRC, colorectal screening; CRP, C-reactive protein; TitG, tissue transglutaminase.  
Chey WD et al. *JAMA*. 2015;313(9):949-958.



## Treatments for IBS



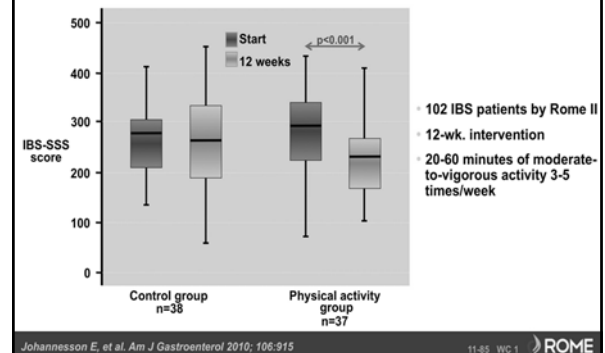
## Dietary and Lifestyle Considerations

- Up to 75% of IBS patients associate symptom onset or worsening with eating a meal
- Maintaining a brief diary of dietary intake and symptoms may help determine if a correlation exists between food and IBS symptoms. Common triggers include:
  - Fatty/greasy food
  - Poorly absorbed carbohydrates
  - Gas-producing foods
  - Soluble fiber

FODMAPs=fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; RCT=randomized, controlled trial.

- Moayyedi P, et al. *Clin Transl Gastroenterol*. 2015;6:e107.
- Savary SC, Liorio A. *Gastroenterol Clin North Am*. 2003;32:507-529.
- ALXG Trial Force on IBS. *Am J Gastroenterol*. 2009;104(suppl 1):S1-S13.
- Johannesson E, et al. *Am J Gastroenterol*. 2011;106:915-922.

## Impact of Physical Activity on IBS and IBS Severity Scoring System – IBS Score



## Diets in IBS

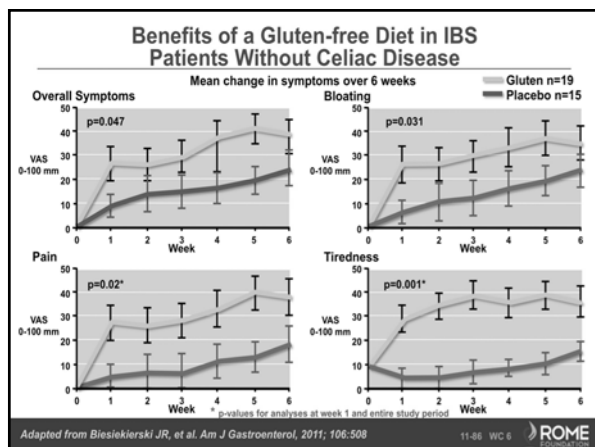
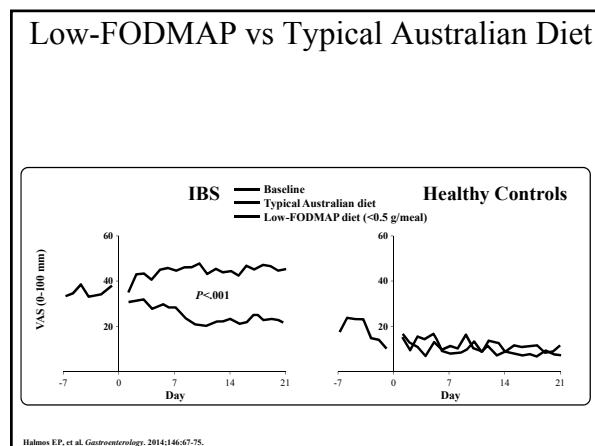
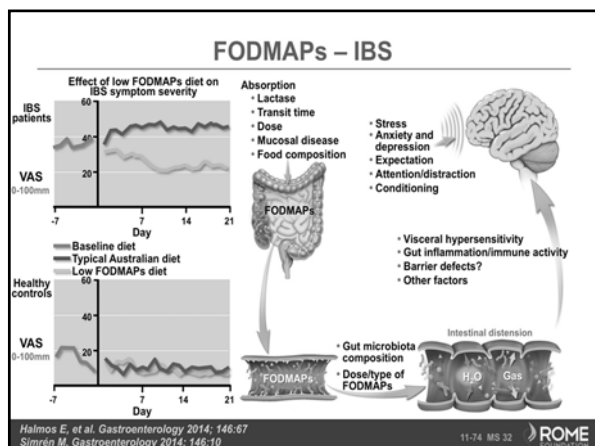
- Pros:**
  - Non-pharmacological
  - Most provide symptom relief, at least short term
- Cons:**
  - No standard diet
  - Difficult and expensive to follow
  - Nutrition consult often necessary
  - Long term impact on health is unclear
  - Well conducted controlled trials are lacking
    - Many claim efficacy, few have proof

## The FODMAP Diet

Eliminate foods containing FODMAPs<sup>1-3</sup>

Excess Fructose	Lactose	Fructans	Galactans	Polyols
fruit apple, mango, pear, cherries, watermelon sweeteners sugar, high-fructose corn syrup other honey, asparagus	milk milk from cows, goats, or sheep custard, ice cream, yogurt cheeses soft unripened cheeses (eg, cottage cheese, ricotta)	vegetables onion, leek, garlic, shallots, artichokes, asparagus, peas, beetroot, chicory cereals wheat, barley, rye	legumes baked beans, chickpeas, kidney beans, lentils	fruit apple, pear, apricot, cherries, peaches, nectarines, plums, watermelon vegetables cauliflower, mushrooms sweeteners sorbitol, mannitol, xylitol, chewing gum

- Shepherd SJ, et al. *Am J Gastroenterol*. 2013;108:707-717.
- Shepherd SJ, Gibson PR. *J Am Diet Assoc*. 2006;106:1631-1639.
- Balett JS, Gibson PR. *Ther Adv Gastroenterol*. 2012;5:261-268.

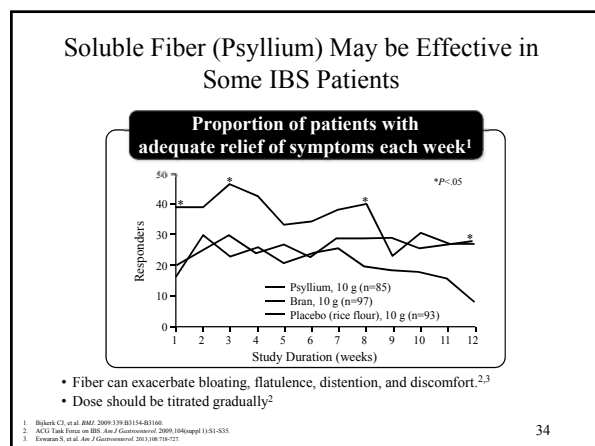
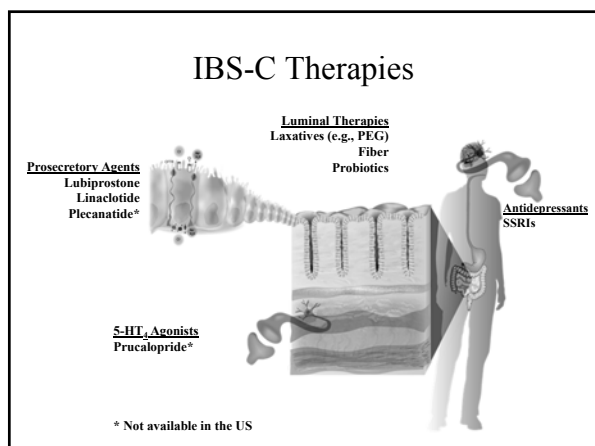


### Psychological Therapy for IBS

Therapy	Trials	N	RR (95% CI)	NNT (95% CI)
<b>Cognitive behavioral therapy (CBT)</b>	9	610	0.60 (0.44-0.83)	3 (2-6)
Relaxation training or therapy	6	255	0.77 (0.57-1.04)	—
<b>Hypnotherapy</b>	5	278	0.74 (0.63-0.87)	4 (3-8)
<b>Multi-component psychological therapy</b>	5	335	0.72 (0.62-0.83)	4 (3-7)
Self-administered, minimal-contact CBT	3	144	0.53 (0.17-1.66)	—
CBT via Internet	2	140	0.75 (0.48-1.17)	—
Dynamic psychotherapy	2	273	0.60 (0.39-0.93)	3.5 (2-25)
Stress management	2	98	0.63 (0.19-2.08)	—
Multi-component therapy via telephone	1	126	0.78 (0.64-0.93)	—
Mindfulness meditation training	1	75	0.57 (0.32-1.01)	—
<b>Total</b>	36	2334	0.68 (0.61-0.76)	32

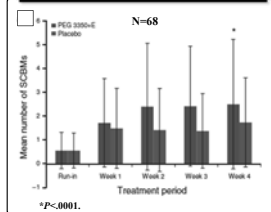
CI=confidence interval; NNT=number needed to treat; RR=risk ratio; — not provided.

Ford AC, et al. *Am J Gastroenterol*. 2014 Sep;109:1358-1365.

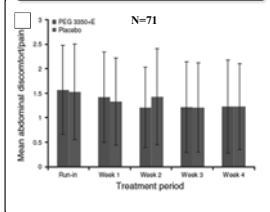


## Polyethylene Glycol (PEG) Does Not Improve Abdominal Symptoms in IBS-C

### Spontaneous Complete Bowel Movements (SCBMs)



### Abdominal Discomfort/Pain



- Between 1 and 3 sachets of PEG 3350 + E (13.8 g per day) or matching placebo were administered
- Patients adjusted the dose based on stool consistency

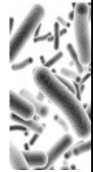
Chapman RW, et al. *Am J Gastroenterol*. 2013;108(9):1508-1515.

E=electrolytes.

35

## Probiotics General Considerations

- Probiotics are 'live microorganisms which when administered in adequate amounts confer a health benefit on the host'
- Traditionally in foods (e.g., kefir and yogurt), recently sold separately
- Least regulated product consumers use in their bodies (considered a medical food or dietary supplement not a drug)
- Many effects are strain specific, yet only genus and species appear on the label



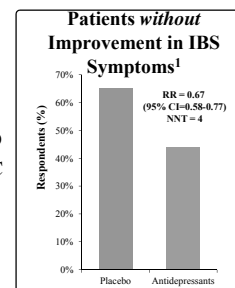
Ford AC, et al. *Am J Gastroenterol*. 2014;109:1547-1561.

## Probiotics in IBS

- Probiotics appear to improve global symptoms, bloating, and flatulence
- Recommendations regarding individual species, preparations, or strains cannot be made
- NNT of 7 (95 % CI 4 – 12.5)
  - Subanalysis showed only combination probiotics, *Lactobacillus plantarum* DSM 9843 and *E. coli* DSM17252, to be effective

## Antidepressants Can Improve IBS Symptoms

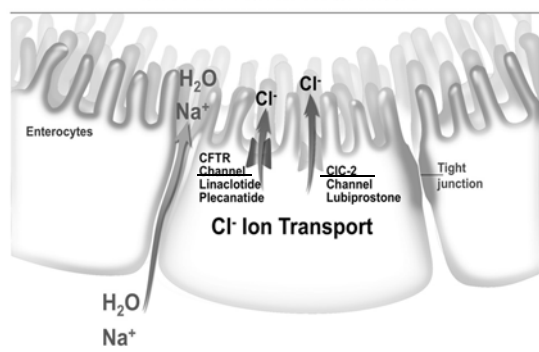
- Effective at reducing IBS symptoms and abdominal pain<sup>1</sup>
- Adverse effect profiles may guide use in IBS subtypes<sup>2</sup>
- TCAs best for patients with IBS-D
- SSRIs best for patients with IBS-C



RR=relative risk; SSRI=selective serotonin-reuptake inhibitor; TCA=tricyclic antidepressant.

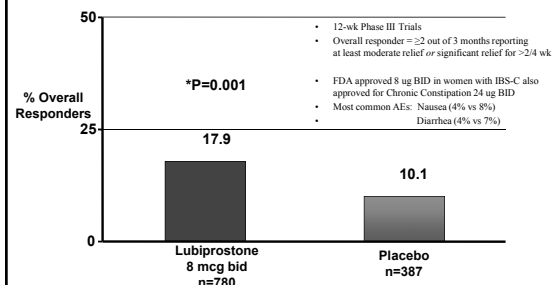
- Ford AC, et al. *Am J Gastroenterol*. 2014;109:1350-1365.
- Chey WD, et al. *JAMA*. 2015;313:949-958.

## Intestinal Chloride Channels



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## Lubiprostone for IBS-C: Data from 2 Phase III Trials



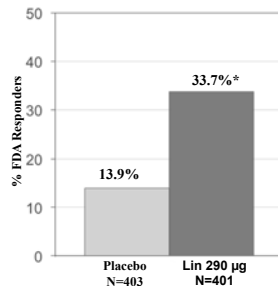
Grossman DA et al. *Aliment Pharmacol Ther*. 2009;29:329-341.

## Linacotide, a Guanylate Cyclase C Agonist

FDA Approved dose 290 ug QD for IBS-C (men and women)  
Also approved for Chronic constipation 145 ug QD

≥30% abdominal pain reduction  
+ increase ≥1 CSBM from  
baseline; in the same week for  
50% of weeks (i.e, 6 out of 12  
weeks)

Most common AEs:  
Diarrhea (3% vs 20%)  
Abdominal pain (5% vs. 7%)



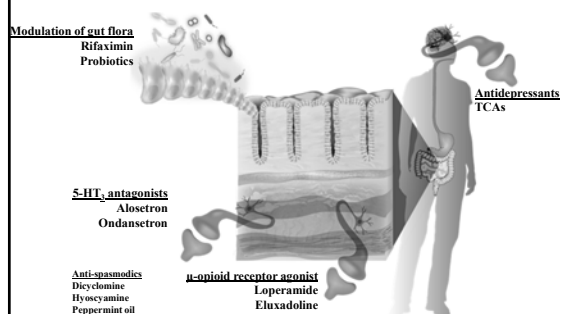
Chey WD et al. AJG 2013.

## ACG Task Force Recommendations for IBS-C

	Recommendation	Quality	Comments
Diets	Weak	Very low	Likely to relate to only some pts
Fiber	Weak	Moderate	Psyllium may be more effective than insoluble fiber
Probiotics	Weak	Very low	Likely only some pts will respond
Polyethylene glycol	Weak	Very Low	No evidence that PEG improves overall symptoms and pain in IBS
Lubiprostone	Strong	Moderate	Cost
Linacotide	Strong	High	Cost

Ford et al., AJG, 2014

## IBS-D Therapies



## Loperamide for IBS with Diarrhea

- Only antidiarrheal studied in IBS
- Three RCTs of low-intermediate quality
- Decreased stool frequency and improved stool consistency but not abdominal pain or global IBS symptoms
- Most appropriate for patients with diarrhea-predominant symptoms



Brandt LJ et al. Am J Gastroenterol 2002; 97: suppl:S7

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## Antispasmodics in IBS Limited Evidence

- Most are anticholinergics – reduce bowel constriction
  - Side effects include dry mouth, constipation, urinary retention, blurred vision
  - Examples include: Dicyclomine, Hyoscyamine, Peppermint oil
- Limited evidence: low quality studies, single center, small n's
- Enteric coated peppermint oil (200 mg) appears to be more effective than placebo
  - Delayed release peppermint oil available in the US

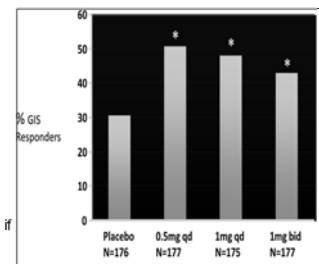
## Alosetron, a 5-HT<sub>3</sub> antagonist, Improves Global Symptoms in Women with Severe IBS-D

### Safety Profile of Alosetron

- Black-box warning: serious GI effects
- Ischemic colitis
  - 2 per 1000 pts over 3 months
  - 3 per 1000 pts over 6 months
- Constipation
  - Alosetron (1 mg bid) = 29%
  - Placebo = 6%

### Prescribing Program

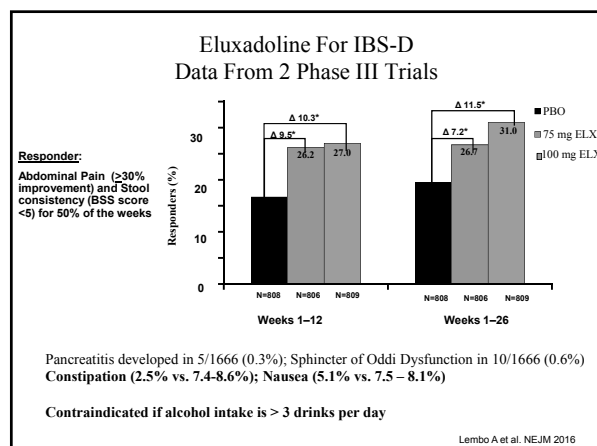
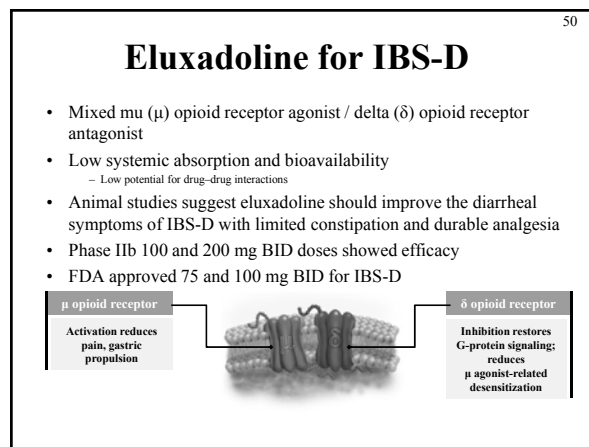
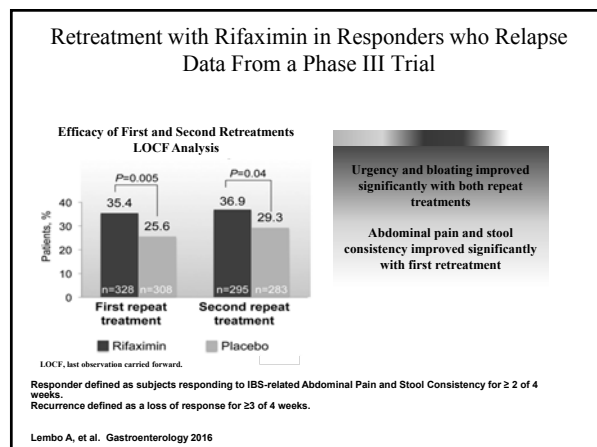
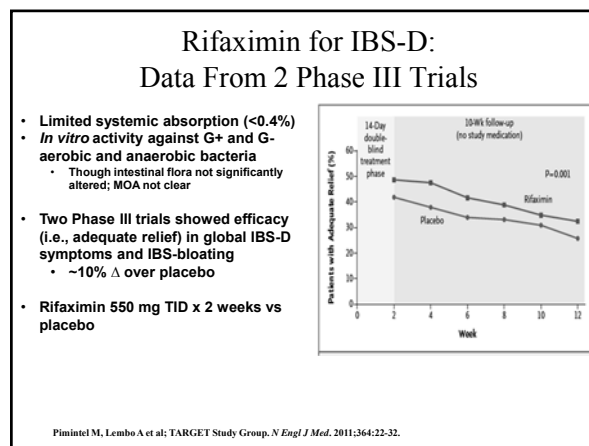
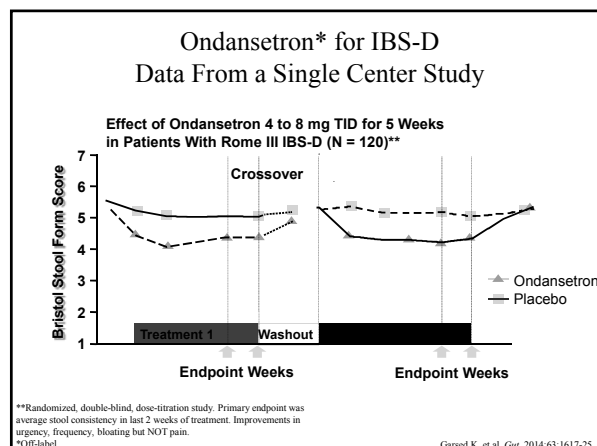
- 0.5 mg BID, increase 1 mg BID if tolerated



\*P<0.02 vs placebo  
Assessment at 12 weeks  
GIS = Global Improvement Scale

Alosetron [package insert]; 2016

Krause R et al. Am J Gastroenterol 2007; 102:1709



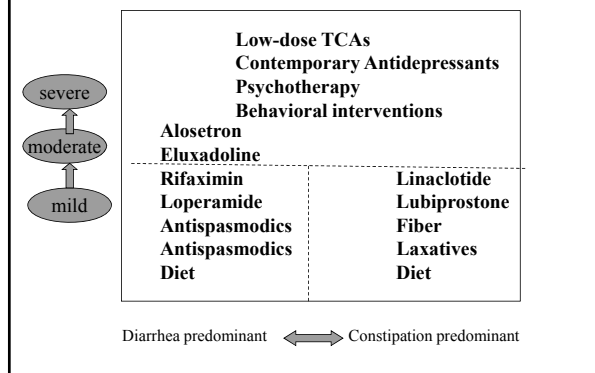
### ACG Task Force Recommendations for IBS-D

	Recommendation	Quality	Comments
Diets	Weak	Very low	Likely to relate to only some pts
Prebiotics	Insufficient Evidence		
Probiotics	Weak	Very low	Likely only some pts will respond
Rifaximin	Weak	Moderate	Cost
Antispasmodics	Weak	Low	Likely to be effective only short-term
Loperamide	Strong	Very low	Improves bowel function with limited effects on pain
Antidepressants	Weak	High	Associate with AE with a NNH of 9
Alosetron	Weak	Moderate	Ischemic colitis, restricted to women

Ford et al. *AJG*. 2014



## Summary Treatment Options in IBS



## Summary: Graded Treatment Response for IBS

