Optimizing the Diagnosis, Treatment, and Management of Irritable Bowel Syndrome

February 5, 2015
9:15 AM – 10:30 AM
Fort Lauderdale, FL

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Educational Partner
Miller Medical Communications, LLC.
Session 2: Optimizing the Diagnosis, Treatment, and Management of Irritable Bowel Syndrome

Learning Objectives

1. Diagnose IBS and differentiate from other bowel disorders using established clinical guidelines.
2. Summarize the efficacy and safety of pharmacologic and nonpharmacologic treatment options for IBS.

Faculty

Brooks D. Cash, MD
Professor of Medicine
University of South Alabama
Mobile, Alabama

Brooks D. Cash, MD, is a professor of medicine at the University of South Alabama (USA) in Mobile, Alabama, where he has held a faculty position since 2013. He previously was a professor of medicine at the Uniformed Services University of the Health Sciences in Bethesda, Maryland. He currently serves as the director of the Motility and Physiology Service at the USA Digestive Health Center. Prior to his relocation to USA, Dr Cash served in the United States Navy for 24 years, retiring in 2013 at the rank of Captain as the Deputy Commander for Medicine at Walter Reed National Military Medical Center, Bethesda, Maryland.

Dr Cash received his undergraduate degree in business administration (finance) with honors from The University of Texas at Austin. He earned his medical degree from the Uniformed Services University of Health Sciences and completed his internship, residency, and gastroenterology fellowship at the National Naval Medical Center, also in Bethesda.

Dr Cash is a diplomate of the American Board of Gastroenterology. He is a fellow of the American College of Physicians, American College of Gastroenterology (ACG), American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy. Dr Cash serves on the Rome Foundation Committee for Functional Gastrointestinal Disorders and has authored multiple articles and book chapters on a variety of gastrointestinal topics, including irritable bowel syndrome and chronic constipation, colorectal cancer screening, CT colonography, acid peptic disorders, Barrett esophagus, and evidence-based medicine. He serves as an associate editor for The American Journal of Gastroenterology and is an editorial board member and reviewer for numerous internal medicine and gastroenterology medical journals. Dr Cash most recently served as the Governor of ACG’s Military Region.
Brian E. Lacy, PhD, MD, is professor of medicine at the Geisel School of Medicine at Dartmouth, section chief of the Division of Gastroenterology and Hepatology, and director of the GI Motility Laboratory at the Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire. He received his doctorate in cell biology from Georgetown University in Washington, DC, and his medical degree from the University of Maryland in Baltimore, Maryland. Dr Lacy was a resident in internal medicine at the Dartmouth-Hitchcock Medical Center, where he continued his training as chief resident and then as a fellow in Gastroenterology. He is board certified in Gastroenterology.

Dr Lacy’s clinical and basic science research interests focus on disorders of gastrointestinal motility, with an emphasis on irritable bowel syndrome, dyspepsia, gastroparesis, acid reflux disease, constipation, intestinal pseudo-obstruction, achalasia, and visceral pain. He is the author or co-author of more than 85 peer-reviewed articles and the author or co-author of numerous textbook chapters on gastrointestinal motility disorders and functional bowel disorders. Dr Lacy is a reviewer for a number of scientific journals, and is a member of the American College of Gastroenterology, the American Gastroenterological Association, the American Neurogastroenterology and Motility Society, and the Rome Committee.

Dr Lacy co-authored Healing Heartburn and is the author of Making Sense of IBS: A Physician Answers Your Questions about Irritable Bowel Syndrome, both books for the general public, the first regarding acid reflux disease and the second discussing irritable bowel syndrome. He is the editor and author of 2 books for health care providers titled Curbside Consultation in IBS: 49 Clinical Questions and Functional and Motility Disorders of the Gastrointestinal Tract: A Case Study Approach. Dr Lacy serves as editor-in-chief of the journal Clinical and Translational Gastroenterology.

Faculty Financial Disclosure Statements
The presenting faculty reports the following:
Dr Cash receives Consulting fees from Zx Pharma; Medical Advisory Board fees from Forest, Ironwood, Paion, Salix, and Takeda; Speakers Bureau honorarium from Forest, Ironwood, Salix, and Takeda.
Dr Lacy receives Medical Advisory Board fees from Forest, Furiex, Ironwood, and Salix.

Education Partner Financial Disclosure Statement
The content collaborators at Miller Medical Communications, LLC, report the following:
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Suggested Reading List


9:15 – 10:30am

Optimizing the Diagnosis, Treatment, and Management of Irritable Bowel Syndrome

SPEAKERS
Brooks D. Cash, MD
Brian E. Lacy, PhD, MD

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► Dr. Lacy receives Medical Advisory Board fees from Forest, Furiex, Ironwood, and Salix

Off-Label/Investigational Discussion
► In accordance with pmICME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives
After participating in this educational activity the participant should be able to:

• Diagnose IBS and differentiate from other bowel disorders using established clinical guidelines
• Summarize the efficacy and safety of pharmacologic and nonpharmacologic treatment options for IBS
• Implement patient-specific methods for managing IBS symptoms and improving function and quality of life

Drug List

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<tr>
<th>Generic Name</th>
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<tr>
<td>Alosetron</td>
<td>Lotronex</td>
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<td>Amitriptyline</td>
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<td>PEG 3350+E</td>
<td>Final, Singerol, Target</td>
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<td>Elliptix</td>
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Prevalence and Impact of IBS

• Worldwide prevalence: 7% to 10%
• 1.5 times more prevalent in women
• More commonly diagnosed in patients <50 years of age
• More common in lower socioeconomic groups
• Patients with IBS have more physician visits, hospitalizations, missed workdays, prescriptions, and diagnostic tests than those without

IBS=irritable bowel syndrome.
Rome III Criteria for IBS

Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months associated with 2 of the following:

- Improvement with defecation
- Onset associated with a change in frequency of stool
- Onset associated with a change in form of stool

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

Additional IBS "testing," including routine laboratory tests and colonoscopy, unnecessary unless alarm features present


What brings patients to your office?

- Abdominal pain – 29% state this is the predominant symptom
- Misinformation
  - 15% believe IBS will turn into cancer
  - 30% believe IBS increases risk for IBD
  - 17% believe IBS will lead to malnutrition
- Lack of information
  - Prevalent physician belief IBS due to anxiety (80.5%) or depression (63.2%)
  - Only 2/3 of patients recognize that IBS does not shorten life expectancy

IBD=Inflammatory Bowel Disease.


Case 1

- 35-year-old woman presents with a 2-year history of constipation alternating with diarrhea
- She reports generalized abdominal pain on days with diarrhea
  - pain is relieved with bowel movements
- Denies rectal bleeding, nocturnal symptoms, weight loss, family history of organic gastrointestinal diseases
- She also suffers from migraine headaches

Case 1 (continued)

- Employed as an elementary school teacher
  - Her GI symptoms have caused her to call in sick 3 times over the past 6 months
- She has tried over-the-counter laxatives, antidiarrheal agents, and probiotics without success
- Her physical examination is unremarkable

GI=gastrointestinal.

Proposed Pathophysiology of IBS

- Enteric nervous system dysfunction
- Gastrointestinal dysmotility
- Visceral hypersensitivity
- Disordered CNS pain processing
- Post-infectious
- Small intestinal bacterial overgrowth
- Dysbiosis
- Food intolerance
- Genetics
- Mast cell dysfunction
- Somatization

CNS=central nervous system.

Differential Diagnosis of IBS With Constipation

- Gastrointestinal
  - Colorectal cancer
  - Diverticular disease
- Gynecologic
  - Ovarian cancer
  - Endometriosis
- Drugs
  - Opiates
  - Anticholinergics
  - Antidepressants
- Metabolic/Endocrine
  - Hypothyroidism
  - Diabetes
- Neurologic
  - Parkinson disease
  - Multiple sclerosis
  - Autonomic neuropathy
- Other
  - Amyloidosis
  - Scleroderma

Differential Diagnosis of IBS With Diarrhea

- Dietary factors
  - Lactose
  - Gluten
  - Other FODMAPs
- Drugs
  - Antidepressants
  - Anticholinergics
  - Opiates
- Infection
  - Giardiasis
  - Amebiasis
  - Campylobacter
- Malabsorption
  - Celiac disease
  - Other

Diagnostic Paradigm for IBS

- IBS is a syndrome—a collection of symptoms
- Diagnosis possible via a thorough history of symptoms and physical examination
  - Because symptoms are non-specific, must consider alternative organic diagnoses
  - Serious organic illnesses typically produce alarm symptoms (eg, bleeding, weight loss, etc)

Is a Positive Diagnosis Really Possible?

- 302 Danish patients aged 18-50 years referred from primary care. No alarm features.
  - Randomized to:
    - Exclusionary strategy: Blood work, stool samples, lower endoscopy with biopsy
    - Positive strategy: CBC and CRP only
    - Followed for 3 years
    - No difference in any outcome measure (symptoms, HRQOL, use of health care resources, etc)
  - No cases of IBD, CRC, or celiac disease identified
  - Exclusionary strategy more expensive
    - Direct costs: $863 greater
    - Mean total costs: $1955 greater
  - Patients believed IBS diagnosis was more common in a subset of patients with IBS-D who were 254 years (2.3%)

Positive IBS Diagnosis May Reduce Diagnostic Testing and Resource Utilization

Clinicians who believed IBS was a diagnosis of exclusion ordered 1.6 times more tests and spent $165 more on diagnostic tests per patient (P<.0002)

Yield of Colonoscopy in IBS

<table>
<thead>
<tr>
<th>Lesion</th>
<th>IBS Patients 446 (%)</th>
<th>Controls 453 (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenomas</td>
<td>36 (1.6)</td>
<td>118 (2.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Hyperplastic polyps</td>
<td>35 (0.8)</td>
<td>51 (1.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Cloecal adenocarcinoma</td>
<td>0 (0.0)</td>
<td>1 (0.0)</td>
<td>NS</td>
</tr>
<tr>
<td>IBD</td>
<td>2 (0.5)</td>
<td>0 (0.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Microscopic colitis</td>
<td>7 (1.6)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Microscopic colitis was more common in a subset of patients with IBS-D who were 254 years (2.3%).

Note: N/A = not applicable; NS = not significant

Radiological Imaging in IBS
A Systematic Review

- There is a paucity of evidence guiding radiologic imaging in IBS
- Imaging study should be influenced by predominant symptoms
- Data suggest very low yield of CT and US
- Definitive recommendations must await further research

US-ultrasonography.

What Can You Miss?

Chronic Abdominal Wall Pain Syndrome

- Up to 10% of chronic idiopathic abdominal pain
  - Entrapment of anterior cutaneous branch of thoracic intercostal nerve
  - Sharply localized pain and superficial tenderness
  - + Carnett sign: accentuated localized tenderness with abdominal wall tensing
  - Reassurance and avoidance of precipitating causes often sufficient
  - Anesthetic/corticosteroid injection effective in ≈ 75%
    - Also serves as diagnostic confirmation


Primary Bile Acid Diarrhea (PBAD)

- 2% of the adult population; 25% of those diagnosed with IBS-D
- Tests that directly assess bile acid malabsorption (SeHCAT, 14C-glycocholate breath tests, serum C4, fecal bile acids) either not available in United States or not validated
- Therapeutic trial only option
  - Bile acid sequestrants

SeHCAT = Selenium homotaurocholic acid test.

IBD

- Crohn's disease, ulcerative colitis, undifferentiated IBD
- IBS symptoms ARE common in IBD patients in "remission"
  - 35% overall; higher in Crohn's disease
- Opinion divided as to what they mean
  - Unrecognized (latent) IBD
  - Real or coincident IBS, linked to psychosocial issues

IBD study.

Diverticular Disease

- "Post-diverticulitis IBS"
  - 224 subjects at Los Angeles Veterans Administration medical center who had an episode of diverticulitis and followed for 6-3 years
  - Almost 5 times more likely to be diagnosed with IBS later
- Symptomatic uncomplicated diverticular disease (SUDD)
  - 229 treated with mesalamine vs L casei alone vs placebo for 10 days per month for 12 months
  - Higher remission rates in treatment groups
  - Symptomatic diverticulitis in 6 week and 1 year in probiotic group
  - 345 patients with uncomplicated diverticulitis
    - Mesalamine 3 g daily vs placebo for 48 weeks
    - 1% recurrence-free at 48 weeks: 68% mesalamine, 74% placebo

IBS study.
Celiac Disease

- General Practice Research Database in the United Kingdom
- Celiac patients were 3 times more likely to have a prior diagnosis of IBS, even for 20 years previously
- 38% of celiac disease patients have IBS symptoms; especially if non-adherent with gluten free diet
- Should you screen for celiac disease?
  - YES
  - NO


Between Celiac Disease and IBS: The "No Man's Land" of Gluten Sensitivity

- Is it IBS, Celiac Disease or Something in Between?

ACG Recommendations: Evaluation of IBS With No Alarm Features

- Routine laboratory tests: CBC, CMP, TSH, stool O&P, abdominal imaging → not recommended
- Serologic testing for celiac disease (IBS-D/M) → strongly consider
- Lactose breath testing → selected cases
- Colonoscopy → recommended if 50 years of age, with biopsies in refractory IBS-D (to exclude microscopic colitis)

ACG Recommendations: Evaluation of IBS With No Alarm Features

- Only 1% to 3% with IBS diagnosed with an alternative organic GI disorder after 30 years of follow-up
- Long-term follow-up: 2% to 18% worse, 30% to 50% of patients unchanged
- Prior surgery (1 study), higher somatic scores (1 study), higher baseline anxiety (2 studies), depression (1 study) predicted worse symptoms during long-term follow-up
- Short duration and constipation: better outcome

Natural History of IBS Meta-analysis

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- Short duration and constipation: better outcome
Identify IBS symptoms, presence of alarm features

Meet criteria, no alarm features → make diagnosis of IBS

Does not meet criteria, has alarm features → look for alternative diagnosis

Symptomatic treatment for predominant symptoms

Assess response to treatment

Good response → continue Rx

Poor response → reassess

Management of IBS: Symptom-Based Approach

Case Study #2

EM, a 33-year-old woman, presents with an 8-year history of abdominal pain and altered bowel habits
- Crampy left lower quadrant pain
- Pain peaks just before bowel movement
- Pain is relieved by defecation
- Bowel movements are frequently urgent and vary in consistency from loose to semi-formed
- Frequency of bowel movements varies from once daily to 4 times per day

Case Study #2 (cont’d)

- Other symptoms: occasional episodes of reflux and bloating
- Weight has remained stable; no history of anemia or rectal bleeding
- Previous evaluation included colonoscopy with biopsies (negative), endoscopy with biopsies (negative), and abdominal sonogram (negative)
- Patient has tried lactose-free diet, increased dietary fiber, dicyclomine, and hyoscyamine, all without benefit
- Physical examination is unremarkable

IBS: What Do Your Patients Want?

- They want you to listen
  - Understand their history (symptoms, work, home)
- Education about their condition
  - Address questions or concerns
  - Address uncertainty of IBS
- Reassurance
- A positive diagnosis
  - Review results with patients
- Symptom improvement

Treatment Options for IBS

Review results with patients
- Psychological treatments
- Goal: improved function
- Continuing care
  - Follow-up visit
  - Manage stress
  - Drug therapy
  - Diet, lifestyle advice
  - Positive diagnosis
  - Explain, reassure

Treatment Depends on Severity of IBS

Brian E. Lacy, PhD, MD
Professor of Medicine
Geisel School of Medicine at Dartmouth
Chief, Section of Gastroenterology & Hepatology
Dartmouth-Hitchcock Medical Center
Lebanon, New Hampshire
**IBS Pharmacologic Therapies by Symptom**

- **Abdominal pain/Discomfort**
  - Antispasmodics
  - Antidepressants (TCAs and SSRIs)
  - Alosetron (5HT3 antagonist)

- **Bloating/Distension**
  - Fiber
  - MOM/PEG solution
  - Lopinopride (chloride channel activator)
  - Linaclotide (guanylate cyclase C agonist)

- **Diarrhea**
  - Loperamide
  - Diphenoxylate–atropine
  - Cholestyramine
  - Alosetron
  - Rifaximin

- **Constipation**
  - Fiber
  - MOM/PEG solution
  - Lopinopride (chloride channel activator)
  - Linaclotide (guanylate cyclase C agonist)

*These agents are not currently FDA approved for IBS.*

**IBS-D Treatment Options**

- Diet
- Antidiarrheal agents
- Probiotics
- Antibiotics
- Smooth muscle antispasmodics
- 5-HT3 antagonists
- Antidepressants (TCAs and SSRIs)

**IBS and Dietary Treatment Options**

- Low carbohydrate
- Low fructose/fructan
- Low gluten
- Low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyol)

**IBS and Low Gluten**

- R, DB, PC, rechallenge study
- 34 IBS patients (Rome III); celiac excluded
- Prior improvement in Sx on gluten-free diet
- 16 g of nonfermentable gluten/d vs 16 g of gluten
- Primary end point: adequate symptom relief
- Gluten-group had less improvement in Sx than those on gluten-free (68% vs 40%; P=.001)

**What Are FODMAPs?**

<table>
<thead>
<tr>
<th>Fermentable Oligo, Di-, Monosaccharides And Polys</th>
<th>Excess Fructose</th>
<th>Fructans</th>
<th>Sorbitol</th>
<th>Raffinose</th>
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</thead>
<tbody>
<tr>
<td>Honey, apples, pears, peaches, mangos, fruit juice, dried fruit</td>
<td>Wheat (large amounts), rye (large amounts), onions, leeks, zucchini</td>
<td>Apricots, peaches, artificial sweeteners, artificially sweetened gums</td>
<td>Lentils, cabbage, Brussels sprouts, asparagus, green beans, legumes</td>
<td></td>
</tr>
</tbody>
</table>

**IBS and Low-FODMAP Diet: Or, what is there left to eat?**

- Lean proteins
- Gluten-free breads, rolls, pasta
- Rice, corn, oat products
- Quinoa
- Safe fruits and vegetables:
  - Snow peas, bok choy, mandarin oranges
**IBS: Prospective Study to Evaluate Low-FODMAP diet**

- 82 consecutive IBS patients (NICE criteria)
- Detailed symptom and dietary evaluation
- 9-month evaluation — performed in United Kingdom
- Individual symptoms and global IBS symptoms measured
- 39 in the standard diet group
- 42 in the low-FODMAP diet group

**Improvements in IBS Symptom Scores: Low FODMAP vs Control Diet**

- Graph showing patients with improved symptom response:
  - Standard Diet vs Low FODMAP Diet
  - Differences in symptom scores
  - *P ≤ .001
  - † *P < .05

**IBS and Low-FODMAP Diet: Some Problems Exist**

- What is the cut-off for FODMAP content?
- Resources differ on low-FODMAP diets
- Total meal FODMAPs should be counted, not individual FODMAP

**Loperamide for IBS-D**

- Low doses 2 mg once or twice daily may be effective to decrease stool frequency, improve stool consistency
- 2 randomized controlled trials in IBS (N=42) show efficacy for diarrhea
- No impact on symptoms of abdominal discomfort, bloating, or global IBS
- Adverse Effects: dizziness, abdominal pain/bloat, constipation, dry mouth, fatigue

**Probiotics for IBS**

- Lactobacilli – anaerobic, gram (+) rods
  - casei
  - plantarum
  - acidophilus
  - reuteri
- Bifidobacteria – anaerobic, gram (+) rods
- VSL #3 (8 separate organisms: 3 bifidobacteria, 1 Streptococcus, 4 lactobacilli)
- Enterococcus
- Streptococcus salivarius
- Saccharomyces

**Probiotics: Mechanisms of Action**

- Competitive inhibition
- Barrier protection
- Immune effects
- Anti-inflammatory effects
- Production of various substances (enzymes, SCFA, bactericidal agents)
- Ability to alter local pH and physiology
- Provides nutrition to colonocytes

SCFA = short-chain fatty acid.
**Bifidobacterium infantis** 35624 for IBS Global Assessment of Relief

![Graph showing relief of symptoms](image)

**Rifaximin: The Most Extensively Studied Antibiotic for IBS**

- Gut-directed antibiotic
- Not systemically absorbed
- Doses studied for IBS: 400 mg bid to 550 mg tid
- Generally well tolerated
- Adverse effects include headache, abdominal pain, and upper respiratory tract infection

**Rifaximin Trials: Global Relief of IBS Without Constipation**

- Two phase 3 randomized controlled trials; N=1260 patients
- Rifaximin 550 mg tid x 2 weeks; patients followed additional 10 weeks
- 40.7% vs 31.7% with adequate relief of global symptoms (P=0.002)

**Antispasmodics for IBS**

- 23 randomized controlled trials comparing 12 different antispasmodics vs placebo (N=2154 patients)
- Significant heterogeneity among studies
- Only 2 agents available in United States
- Hyoscyamine and dicyclomine
- Appear most useful for abdominal pain
- In meta-analysis, symptoms persist in 39% of patients receiving antispasmodics vs 56% of placebo-treated patients (RR: 0.68; 95% CI: 0.57-0.81)
- NNT=5

**Alosetron: Therapeutic Gain for IBS-D**

<table>
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<tr>
<th>Study</th>
<th>N</th>
<th>Female, %</th>
<th>Response: Alosetron, %</th>
<th>Response: Placebo, %</th>
<th>Therapeutic Gain, %</th>
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*Comparison randomized double-blind placebo.

**Alosetron for IBS-D**

- Female patients with chronic, severe IBS-D who failed other treatments
- Dose: 0.5-1.0 mg od to bid
- Patient education regarding possible serious adverse effects of severe constipation or ischemic colitis
- 0.95 cases of ischemic colitis/1000 patient-years
- 0.36 cases of severe constipation/1000 patient-years
- If ischemic colitis occurs, it is usually within the first month of therapy
- Prescribing program mandated by FDA
- Requires patient to sign attestation form
**Global Relief of IBS Symptoms With TCAs/SSRIs**

- **TCAs: 11 studies (N=416 drug vs 328 placebo)**
  - Imipramine, desipramine, amitriptyline, doxepin; doses 10-120 mg
  - Meta-analysis favors treatment: NNT=4

- **SSRIs: 7 studies (N=136 drug vs 180 control)**
  - Fluoxetine, paroxetine, citalopram; dose 10-40 mg
  - Meta-analysis favors treatment: NNT=4

TCAs have more analgesic properties and SSRI efficacy is most likely in patients with significant anxiety/depression.

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**Case Study #3**

- **MH is a 40-year-old woman with a 6-year history of constipation symptoms sent for a second opinion**
  - She describes hard stool with straining and feelings of incomplete evacuation
  - She has lower abdominal pain, which transiently improves after having a bowel movement
  - Symptoms are present more days than not
  - She frequently feels bloated and describes herself as looking “5 months pregnant”
  - She is not anemic; her weight has been stable

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**Case Study #3 (cont’d)**

- **All: none**
- **Medications: OC**
- **PMH: migraine HA; interstitial cystitis**
- **PSH: appendectomy as a child**
- **PE: BMI = 26; mild tenderness in left lower quadrant; otherwise normal**

**Question:** What’s the diagnosis and what treatment options are available?

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**IBS-C Treatment Options**

- **Diet**
- **Bulking agents**
- **Probiotics**
- **Osmotic agents**
- **Secretagogues**
  - Chloride channel activators (lubiprostone)
  - Guanylate cyclase activators (linaclotide)
- **CAM**

CAM = complementary and alternative medicines.

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**Psyllium Can Improve IBS Symptoms**

- Randomized, placebo-controlled trial (N=275 patients with IBS; 53%-58% were IBS-C)
- Psyllium (50 gm) vs bran (50 gm) vs placebo
- Primary End Point: adequate symptom relief 2 weeks in previous month, analyzed after 1, 2, and 3 months

**RESULTS**

- Higher % responders in psyllium vs placebo group during first month (57% vs 33%)
- Higher % responders through 2 months of treatment (59% vs 41%), but no difference at 3 months
- High dropout rate in the bran group because of worsening of IBS
- No significant improvement was noted in measurement of abdominal pain relief

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**Bulking Agents for IBS-C: Systematic Review and Meta-analysis**

<table>
<thead>
<tr>
<th></th>
<th>RCTs</th>
<th>N</th>
<th>Response*</th>
<th>RR of Unimproved Symptoms (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fiber</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>14</td>
<td>906</td>
<td>48%</td>
<td>43%</td>
<td>0.87 (0.76-1.0)</td>
</tr>
<tr>
<td>Ipapagula</td>
<td>6</td>
<td>324</td>
<td>48%</td>
<td>36%</td>
<td>0.78 (0.63-0.96)</td>
</tr>
<tr>
<td>Bran</td>
<td>5</td>
<td>223</td>
<td>46%</td>
<td>46%</td>
<td>1.16 (0.82-1.67)</td>
</tr>
</tbody>
</table>

*Improved or resolved symptoms.

- Insoluble fiber was not more effective and sometimes worsened symptoms
- Soluble fiber improved global symptoms
- 4 out of 5 bran studies of poor quality

RCTs = randomized controlled trials.

**Bifidobacterium animalis: DN-173 010 for IBS-C**

- Probiotic (n=135)
- Placebo (n=132)

Stool frequency increased in patients with <3 bowel movements/week

![Graph showing stool frequency increase](image)

**Osmotic Agents: PEG for IBS-C**

- Prospective, multi-center, R, DB, PC
- Rome III criteria
- 239 patients (mean age=41 years; 83% women)
- 18-day study; 13.8 gm/sachet
- 3-3 sachets/d vs placebo
- Primary End Point: mean # of SBM/d
- Results: at week 4, 4, 4 SBM/wk vs 3.1 SBM/wk (PEG vs placebo; P<.0001)

SBM=spontaneous bowel movement.

**PEG 3350+E Improves SBMs in IBS-C**

- Placebo (n=75)
- PEG 3350+E (n=68)

![Graph showing improvement in SBMs](image)

**Overall Responder Rates† to Lubiprostone in IBS-C Patients**

![Graph showing responder rates](image)

**Effect of Lubiprostone on IBS-C: Patients With Follow-up Over 52 Weeks**

- Summary of SBM Frequency
- Abdominal Pain/Discomfort

![Graph showing changes in SBM frequency](image)

**Efficacy of Linaclotide in Patients With IBS-C**

- Treatment Period
- RW Period

![Graph showing efficacy of linaclotide](image)
### Linacotide Phase 3 IBS-C Trial: Abdominal Pain Over 26 Weeks

![Graph showing change in worst abdominal pain over 26 weeks.](image)

ITT population, observed cases, LS-mean presented. P-values based on ANCOVA at each week. Bars represent 95% CI.

P = .0007 for week 1
P < .0001 for weeks 2-26

### Psychological Therapies for IBS

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Trials</th>
<th>N</th>
<th>RR (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive behavior therapy</td>
<td>9</td>
<td>610</td>
<td>0.60 (0.44-0.89)</td>
<td>3 (2-6)</td>
</tr>
<tr>
<td>Relaxation training</td>
<td>6</td>
<td>255</td>
<td>0.77 (0.57-1.04)</td>
<td></td>
</tr>
<tr>
<td>Dynamic psychotherapy</td>
<td>2</td>
<td>273</td>
<td>0.60 (0.39-0.95)</td>
<td>3.5 (2.05)</td>
</tr>
<tr>
<td>Hypnotherapy</td>
<td>5</td>
<td>278</td>
<td>0.74 (0.63-0.87)</td>
<td>4 (3.0)</td>
</tr>
</tbody>
</table>


### Emerging Therapies for IBS

- Eluxadoline (for IBS-D)
- Elobixibat (for IBS-C)
- Plecanatide (for IBS-C)
- Prucalopride (for IBS-C)
- FMT – fecal microbiota transplant

### Summary: IBS Treatment Options

- Every patient is different
- Identify the predominant symptom
- “Curing” is not possible – set expectations
- Fiber is not a magical cure for all IBS patients
- Dietary interventions may help – but use an evidence-based approach
- Consider medications that improve global symptoms – this may reduce polypharmacy


dirty text