WELCOME & INTRODUCTIONS

William D. Chey, MD
Housekeeping

- There will be a Q&A session at the end of the program; if you would like to pose a question to the faculty, please write it on one of the cards on your table
- Please silence your cell phones and pagers

Agenda

Incidence and Impact of IBS (subtypes) and CC
William D. Chey (Chair)

Managing IBS-D: Evidence-Based Strategies for Diagnosis and Treatment
Darren M. Brenner

The Diagnostic Dilemma of IBS-C and CC
Brian Lacy

Nuanced Treatment of IBS-C and CC
Amy E. Foxx-Orenstein

Shared Decision Making to Improve Care
All Faculty
Faculty

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Disclosures

**William D. Chey, MD (Chair)**
*Retained Consultant:* AstraZeneca Pharmaceuticals LP; Forest Laboratories, Inc; GlaxoSmithKline; Ironwood Pharmaceuticals; Prometheus Laboratories Inc.; Perrigo Company; Purdue Pharma; Salix Pharmaceuticals, Inc.; Sandhill Scientific; Takeda Pharmaceutical Company Limited

**Darren M. Brenner, MD**
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*Speakers Bureau:* Forest Laboratories, Inc.; Ironwood Pharmaceuticals; Salix Pharmaceuticals, Inc.

**Amy E. Foxx-Orenstein, DO, FACP, FACP**
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**Brian Lacy, MD, PhD**
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Commercial Support

This CME initiative is supported by an educational grant from *Forest Research Institute*, a subsidiary of Forest Laboratories, Inc., and *Ironwood Pharmaceuticals*.

Continuing Medical Education (CME) Information

**Educational Objectives**

Upon proper completion of this activity, participants should be better able to:

- Describe current evidence-based approaches to accurately characterize IBS (subtypes) and CC in order to differentiate them from other medical conditions that present with similar symptoms.
- Formulate individualized treatment plans for patients with IBS (subtypes) and CC based on unique patient characteristics and understanding of current clinical evidence.
- Describe strategies for improving communication and increasing a coordinated approach for care of patients with IBS (subtypes) and CC among a multidisciplinary team of physicians and allied healthcare professionals.
Using the Audience Response Pads

• Each question will be displayed on a slide with an ORANGE title.
• To enter a response, press the button representing your choice when the countdown timer appears.
• You will have 6 seconds to enter a response.
• If you change your mind, just press the new button. The computer will only accept the last response.
• Following the countdown, a graph will appear displaying the distribution of responses.

INCIDENCE AND IMPACT OF IBS (SUBTYPES) AND CC

William D. Chey, MD
**IBS (subtypes) & CC are Common**

<table>
<thead>
<tr>
<th></th>
<th>IBS</th>
<th>CC</th>
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<tbody>
<tr>
<td></td>
<td>≈25-45 million people</td>
<td>≈63 million people</td>
</tr>
<tr>
<td></td>
<td>• 10%-15% of US population¹</td>
<td>• ≥20% of US population²</td>
</tr>
<tr>
<td>Demographics³,⁴</td>
<td>• All ages (most common &lt;50 y)</td>
<td>Demographics</td>
</tr>
<tr>
<td></td>
<td>• Peak incidence early adult to 34 y</td>
<td>• Elderly (=40% ≥65 y)⁵</td>
</tr>
<tr>
<td></td>
<td>• Female &gt; male</td>
<td>• Female &gt; male⁶</td>
</tr>
<tr>
<td>Up to 3.5 million physician visits/y⁷</td>
<td>Up to 3.5 million physician visits/y⁷</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≈63 million people</td>
<td>≈2.5 million physician visits/y⁸</td>
</tr>
</tbody>
</table>

CC, chronic constipation; IBS, irritable bowel syndrome


**IBS & CC are Costly**

**Direct Cost of IBS**
- Annual cost per patient: $5049¹
- 50% higher costs vs matched controls²

**Indirect Cost of IBS¹**
- Absenteeism
- Impaired productivity

**Direct Cost of CC**
- Annual cost per patient: $7522¹
- >2x cost of controls over 15-y period²

**Indirect Cost of CC³-⁵**
- Compared with matched controls, those with CC report
  - Significantly reduced HRQoL and work productivity
  - Significantly greater use of healthcare resources (office and ED visits, hospitalizations)
  - More missed workdays

ED, emergency department; HRQoL, health-related quality of life

The Patient-Physician Encounter: 
**Patient Perspective**

- Embarrassing symptoms
  - Significant interference with daily life
- Perceived lack of validation, empathy, and understanding of the nature of symptoms
  - Clinicians may underestimate symptom occurrence, severity, and impact on QoL
- Minimization/dismissal of symptoms
  - “Don’t worry, it’s nothing serious”
  - “It’s a nuisance, but it won’t kill you”
  - “You’ll have to learn to live with it”
  - “It’s all in your head”


The Patient-Physician Encounter: 
**Physician Perspective**

- No reliable biomarker or universal pathophysiology
- Diverse symptoms (GI and non-GI) frequently complicated by psychosocial comorbidities
  - Difficult to quantify objectively
- Many organic conditions can masquerade as IBS or CC
- Treatments offer marginal therapeutic gain and can cause potential harms

GI, gastrointestinal
Key Takeaways

• IBS and CC are
  – Common
  – Costly
  – Significant

• IBS and CC have overlapping symptoms that can cause challenges for patients and providers

• A trusting patient-provider relationship and evidence-based management recommendations can improve outcomes

MANAGING IBS-D:
EVIDENCE-BASED STRATEGIES FOR DIAGNOSIS AND TREATMENT

Darren M. Brenner, MD
Rome III Diagnostic Criterion for IBS*

• Recurrent abdominal pain or discomfort† ≥3 d/mo in the last 3 mo 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 (appearance) of stool

*Criterion fulfilled for ≥3 mo with symptom onset ≥6 mo prior to diagnosis
†Discomfort means an uncomfortable sensation not described as pain


Bristol Stool Form Scale

| 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 (passed easily) |
| Type 6 | Fluffy pieces with ragged edges, a mushy stool |
| Type 7 | Watery, no solid pieces, entirely liquid |

IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; IBS-M, mixed IBS (also referred to as IBS-A [alternating])


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ARS Question 1

Which of the following conditions must be considered in the differential diagnosis of IBS-D?

A. Gluten sensitivity
B. Celiac disease
C. Fibromyalgia
D. A and B
E. B and C

Food for Thought...

• What is the diagnostic overlap between celiac disease and IBS-D?
• Who should be tested for comorbid celiac disease?
• What is the role of a gluten-free diet in IBS-D patients who do NOT have celiac disease?
• What is the role of antibiotics for the treatment of IBS-D?
Prevalence of Biopsy-Proven Celiac Disease in Patients with IBS-D

Pooled OR for Biopsy-Proven Celiac Disease in Patients Meeting Diagnostic Criteria for IBS vs Controls\(^1\)

<table>
<thead>
<tr>
<th>Study</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanders DS et al. Lancet 2001;358(9292):1504-1508</td>
<td>7.29 (1.65, 66.52)</td>
</tr>
<tr>
<td>Sanders DS et al. Eur J Gastroenterol Hepatol. 2003;15(4):407-413.</td>
<td>4.49 (0.97, 17.03)</td>
</tr>
<tr>
<td>Shahbazkani B et al. Aliment Pharmacol Ther. 2003;18(2):231-235.</td>
<td>28.23 (1.90, 578.67)</td>
</tr>
<tr>
<td>Chey WD et al. Gastroenterol. 2007;132(suppl 1):A147.</td>
<td>1.52 (0.22, 16.93)</td>
</tr>
<tr>
<td>Ozdil K et al. Dig Dis Sci. 2008;53(7):1852-1855.</td>
<td>0.67 (0.00, 26.11)</td>
</tr>
<tr>
<td>Combined (random)</td>
<td>4.34 (1.78, 10.58)</td>
</tr>
</tbody>
</table>

CI, confidence interval; OR, odds ratio


Cost-Effectiveness of CS Testing vs Empiric Therapy for IBS-D

- CS testing costs additional $11,000 per additional symptom improvement compared to empiric therapy
- Incremental cost declines rapidly as baseline prevalence of underlying CS increases
  - Reaches $0.00 when CS prevalence is 8%

CS, celiac sprue

Irritable Bowel Syndrome and Chronic Constipation: Digesting Recent Advances and Current Thinking

ACG Recommendations on CS Testing in Patients with IBS-D

- "Routine serologic screening for [CS] should be pursued in patients with IBS-D and IBS-M (Grade 1B)"
- ACG lists IBS among conditions in which CS occurs more frequently than in the general population and/or for whom GFD may be beneficial

ACG, American College of Gastroenterology; GFD, gluten-free diet


Celiac Prevalence in IBS-D: Overestimated?

<table>
<thead>
<tr>
<th>Test</th>
<th>Suspected IBS (n=492) n (%)</th>
<th>Healthy Controls (n=458) n (%)</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy-proven celiac disease</td>
<td>2 (0.41)</td>
<td>2 (0.44)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Any abnormal celiac disease test</td>
<td>36 (7.32)</td>
<td>22 (4.8)</td>
<td>.25</td>
<td>1.49 (0.76, 2.90)</td>
</tr>
<tr>
<td>AGA IgG</td>
<td>24 (4.88)</td>
<td>14 (3.06)</td>
<td>.70</td>
<td>1.19 (0.50, 2.79)</td>
</tr>
<tr>
<td>AGA IgA</td>
<td>8 (1.63)</td>
<td>8 (1.75)</td>
<td>.54</td>
<td>1.41 (0.47, 4.22)</td>
</tr>
<tr>
<td>EMA</td>
<td>3 (0.61)</td>
<td>2 (0.44)</td>
<td>.66</td>
<td>1.65 (0.17, 15.42)</td>
</tr>
<tr>
<td>TTG IgA</td>
<td>6 (1.22)</td>
<td>2 (0.44)</td>
<td>.15</td>
<td>3.87 (0.61, 24.74)</td>
</tr>
<tr>
<td>DQ2</td>
<td>164 (33.33)</td>
<td>180 (39.30)</td>
<td>.004</td>
<td>0.61 (0.44, 0.86)</td>
</tr>
<tr>
<td>DQ8</td>
<td>81 (16.46)</td>
<td>83 (18.12)</td>
<td>.54</td>
<td>1.14 (0.76, 1.70)</td>
</tr>
</tbody>
</table>

Gluten sensitivity may be more common than biopsy-proven CD compared to controls

Nonceliac Patients with IBS-D May Benefit from GFD

- Randomized controlled trials of IBS-D patients without celiac disease randomized to receive either GCD or GFD

  - Compared with GCD, GFD significantly improved
    - Symptom control
    - Bloating
    - Pain
    - Fatigue
    - Stool frequency and consistency

FODMAP, Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols; GCD, gluten-containing diet


Dietary Considerations in IBS

**Low FODMAP™ Diet: Evolution of Evidence in IBS-D**

### Double-blind, placebo-controlled rechallenge study*

(N=25)
Fructose and fructans specifically induced symptoms that mimicked IBS-D

### Observational cohort studies

Consistent response of 75% of patients across all symptoms

### Comparative studies

Low FODMAP vs standard diet associated with significantly better response across all functional GI symptoms

### RCTs

(N=30)
2-day intervention of low vs high FODMAP diet; significantly >IBS symptoms with high FODMAP diet

*In response to challenge studies showing that fructose, fructans, sorbitol, mannitol, lactose, fructose, and sorbitol induce symptoms in patients with IBS versus healthy controls


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**Low FODMAP™ Diet in Patients with Gluten Sensitivity**

Irritable Bowel Syndrome and Chronic Constipation: Digesting Recent Advances and Current Thinking

High/Low Gluten Diet: Impact on Symptom Severity

- No statistically significant changes in abdominal pain, tiredness, or nausea
- VAS, Visual Analogue Scale


Nocebo response

- Order of dietary interventions associated with degree of symptomatic response
- First intervention significantly induced greater symptomatic changes than subsequent challenges, regardless of what it contained

Evidence-Based Summary of Medical Therapies for IBS-D Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Global Sx</th>
<th>Pain</th>
<th>Bloating</th>
<th>Stool Frequency</th>
<th>Stool Consistency</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alosetron</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2A/1B</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>1B</td>
</tr>
<tr>
<td>Loperamide</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
<td>2C</td>
</tr>
<tr>
<td>Antispasmodics</td>
<td>±</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>2C</td>
</tr>
<tr>
<td>Probiotics</td>
<td>+</td>
<td></td>
<td>(Bifidobacteria; some combos)</td>
<td>+</td>
<td></td>
<td>2C</td>
</tr>
<tr>
<td>Fiber (psyllium)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Insufficient evidence</td>
</tr>
</tbody>
</table>

Rifaximin Significantly Relieves Global Symptoms & Bloating

**Systematic Review and Meta-analysis of Rifaximin vs Placebo**
(N=1803)

- **Global symptom improvement**: Rifaximin 42.2% vs Placebo 32.4%
- **Bloating**: Rifaximin 41.6% vs Placebo 31.7%

- *Therapeutic gain=9.8%
- †Therapeutic gain=9.9%


TARGET 1 and TARGET 2: Loss of Efficacy Over Time

- Two identical phase 3, double-blind, placebo-controlled trials
- Randomized to rifaximin 550 mg or placebo, TID x 2 wk

Success Rate of Rifaximin Retreatment

<table>
<thead>
<tr>
<th>Subjects Responding, %</th>
<th>1st RTX</th>
<th>2nd RTX</th>
<th>3rd RTX</th>
<th>4th RTX</th>
<th>5th RTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Treatment (RTX)</td>
<td>83.5</td>
<td>95.5</td>
<td>94.5</td>
<td>85.4</td>
<td>75</td>
</tr>
</tbody>
</table>


Panel Discussion
THE DIAGNOSTIC DILEMMA OF IBS-C AND CC

Brian Lacy, MD

Food for Thought...

- IBS-C and CC: 1 disease or 2?
IBS-C & CC

- Classically thought of as 2 separate disorders
  - Implies that pathophysiology is different
  - By extension, if pathophysiology is different, treatments should be different
- Research studies distinguish the 2
- Distinct Rome III definitions

Rome III Diagnostic Criterion for IBS*

Recurrent abdominal pain or discomfort* ≥3 d/mo in last 3 mo associated with ≥2 of the following
- Improvement with defecation
- Onset associated with change in frequency of stool
- Onset associated with change in form (appearance) of stool

≥1 of following symptoms ≥25% of occasions for subgroup identification
- Abnormal stool frequency (<3/wk)
- Abnormal stool form (lumpy/hard)
- Abnormal stool passage (straining, incomplete evacuation)
- Bloating/feeling of abdominal distension
- Passage of mucous
- Frequent, loose stools

*Criterion fulfilled for ≥3 mo with symptom onset ≥6 mo prior to diagnosis
Discomfort means an uncomfortable sensation not described as pain

Rome III Diagnostic Criteria for Functional Constipation*

- ≥2 symptoms present ≥25% of the time
- **Patients cannot meet criteria for IBS**
  - Straining
  - Hard stool or scybala
  - Sensation of incomplete evacuation
  - Sense of anorectal obstruction/blockade
  - Manual maneuvers (digital disimpaction)
  - < 3 BMs/wk

*Criteria fulfilled for ≥3 mo with symptom onset ≥6 mo prior to diagnosis
BM, bowel movement


Pathophysiology of IBS at a Glance

5-HT, serotonin; CRF, corticotropin-releasing factor; SIBO, small intestinal bacterial overgrowth
Lin HC. *JAMA.* 2004;292:852-858.
Irritable Bowel Syndrome and Chronic Constipation: Digesting Recent Advances and Current Thinking

Primary Causes of Constipation

- **Defecation disorders**: 13%–28%
- **Slow transit constipation**: 11%–13%
- **Functional constipation (IBS-C and CC)**: 59%–71%

Primary Causes of Constipation

<table>
<thead>
<tr>
<th>Cause</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defecation disorders</td>
<td>13%–28%</td>
</tr>
<tr>
<td>Slow transit constipation</td>
<td>11%–13%</td>
</tr>
<tr>
<td>Functional constipation (IBS-C</td>
<td>59%–71%</td>
</tr>
<tr>
<td>and CC)</td>
<td></td>
</tr>
</tbody>
</table>

**Schiller LR. Aliment Pharmacol Ther. 2001;15(6):749-763.**


IBS & CC: More Than Stool Symptoms

Symptoms in IBS Patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>88%</td>
</tr>
<tr>
<td>Bloating</td>
<td>80%</td>
</tr>
<tr>
<td>Trapped gas</td>
<td>66%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>60%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>59%</td>
</tr>
<tr>
<td>Clothing...</td>
<td>58%</td>
</tr>
<tr>
<td>Constipation</td>
<td>53%</td>
</tr>
<tr>
<td>GERD</td>
<td>47%</td>
</tr>
</tbody>
</table>

Symptom Scores in CC Patients vs Healthy Controls

- **Incomplete evacuation**: Healthy controls (n=23) = 0, CC patients (n=11) = 2
- **Straining**: Healthy controls (n=23) = 0.5, CC patients (n=11) = 3
- **Abdominal pain**: Healthy controls (n=23) = 1, CC patients (n=11) = 2
- **Depression**: Healthy controls (n=23) = 0, CC patients (n=11) = 2.5
- **Anxiety**: Healthy controls (n=23) = 1, CC patients (n=11) = 5

*Community survey of >40,000 adults in 8 countries

Irritable Bowel Syndrome and Chronic Constipation: Digesting Recent Advances and Current Thinking

In Clinical Practice, IBS-C & CC Often Overlap

- Symptom-based criteria for IBS-C and CC overlap
  - Abdominal pain/discomfort and gas/bloating creates spectrum between IBS-C and CC


In Clinical Practice, Patients Move From Group to Group

IBS-M\(^{1-3}\) 19\%–49\%

IBS-C\(^{1-3}\) 19\%–44\%

IBS-D\(^{1,2}\) 15\%–36\%

Proportions of patients in each subgroup stable over time, but...\(^4\):
- 75\% will experience change in subgroup over time

IBS-M, IBS-mixed (also referred to as IBS-A [alternating])

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Food for Thought...

• Does making an accurate diagnosis of IBS-C and CC really matter?

Why Distinguish IBS-C from CC?

• Differentiation may help identify distinct comorbid disorders
• An accurate diagnosis may help explain the natural history
• Distinguishing IBS-C from CC may clarify treatment options
ARS Question 2

Recent clinical trials show that, compared with patients who have IBS-C, patients with chronic idiopathic constipation have:

A. Comparable incidence of abdominal pain symptoms
B. Similarly delayed colonic transit times
C. Greater visceral sensitivity
D. All of the above

Inability of Rome Criteria to Distinguish IBS-C from CC

Overlap between IBS-C and CC when Rome III requirement that CC cannot be diagnosed in a patient who meets criteria for IBS is suspended

- IBS-C patients had significantly greater frequency of abdominal pain/discomfort
  - Yet, 44.8% of CC patients reported experiencing abdominal pain/discomfort within past 3 mo

BSI, Brief Symptom Inventory of psychological distress;
PAC-QOL, Patient Assessment of Constipation Quality of Life

Patients with IBS-C & CC vs HVs

- If the Rome III requirement that patients meeting criteria for IBS cannot be diagnosed with CC was suspended, 86% (20 of 23) of IBS-C patients would meet criteria for CC
  - Similarly delayed colonic and right segmental transit vs HVs
  - Significantly increased abdominal and BM symptoms vs HVs

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Transit Times (mean; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonic transit times ($P&lt;.001$)</td>
<td></td>
</tr>
<tr>
<td>HV</td>
<td>38 h; 6-66 h</td>
</tr>
<tr>
<td>IBS-C</td>
<td>64 h; 24-72 h</td>
</tr>
<tr>
<td>CC</td>
<td>71 h; 13-72 h</td>
</tr>
<tr>
<td>Right colonic transit times ($P&lt;.001$)</td>
<td></td>
</tr>
<tr>
<td>HV</td>
<td>5 h; 0-25 h</td>
</tr>
<tr>
<td>IBS-C</td>
<td>17 h; 3-35 h</td>
</tr>
<tr>
<td>CC</td>
<td>21 h; 8-51 h</td>
</tr>
</tbody>
</table>

*HV, healthy volunteer

Patients with IBS-C & CC vs HVs: Sensory Thresholds

- IBS-C patients tend to reside at sensitive end of visceral sensitivity spectrum vs CC patients
  - Hypersensitivity: 30% vs 0%, respectively
  - Hyposensitivity: 4% vs 27%, respectively

*SCompared with CC patients, $P<.05$
The Bottom Line: Treat the Predominant Symptom

- CC: constipation
- IBS-C: abdominal pain or constipation or gas/bloating
- Recognize that patients will shift groups over time
  - Should not be considered a warning sign
  - It’s the natural history and is expected
- Therefore, treatments will need to shift over time

Summary

- Use Rome III criteria as diagnostic tool
- IBS-C and CC exist on a continuum
  - They don’t exist in isolation
- Expect movement between groups
- Treat the predominant symptom
PANEL DISCUSSION

NUANCED TREATMENT OF IBS-C AND CC

Amy E. Foxx-Orenstein, DO, FACG, FACP
ARS Question 3

Which of the following psychological treatment(s) has/have been shown to improve symptoms of IBS?

A. Cognitive behavioral therapy
B. Hypnotherapy
C. Acupuncture
D. A and B
E. A, B, and C

Biofeedback in IBS-C

- Prospective study in patients with dyssynergic defecation (N=50) plus IBS-C (n=29)
  - Similar responses to biofeedback in dyssynergic and IBS-C groups (55% vs 67%, P >0.05)
  - **IBS-C symptoms disappeared in 41% patients who had pre-treatment IBS-C symptoms**
    - Symptom resolution more common in biofeedback responders vs nonresponders (P<.05)
- Conclusion: assessment of pelvic floor function (and therapy to address it) may be useful in select patients with IBS-C

Other Mind-Body Therapies That Significantly Improve IBS

- **CBT**
  - Improves GI symptoms, psychological distress, QoL\(^1\) \(^3\)

- **Mindfulness Training**
  - Reduces overall IBS severity at 3 mo\(^4\)

- **Psychological Therapy**
  - Improves IBS vs usual care (49% vs 28%); 20 studies, N=1278\(^5\)

- **Hypnotherapy**
  - Reduces symptoms of moderate-to-severe and refractory IBS\(^6\) \(^8\)

- **Exercise**
  - Improves symptom severity; less likely to have symptoms worsen\(^9\)

---

**CC Therapies: Graded Recommendations**

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
<th>Level C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisacodyl</td>
<td>Bran</td>
<td>Milk of magnesia</td>
</tr>
<tr>
<td>Lactulose</td>
<td>Docusate sodium</td>
<td></td>
</tr>
<tr>
<td>Lubiprostone</td>
<td>Methylcellulose</td>
<td></td>
</tr>
<tr>
<td>PEG</td>
<td>Polycarbophil</td>
<td></td>
</tr>
<tr>
<td>Psyllium</td>
<td>Sorbitol</td>
<td></td>
</tr>
<tr>
<td>Senna</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: Linaclotide was not included in this review.*

Food for Thought...

- Are all fiber products equal in reducing symptoms of IBS-C and CC?

### Overall Forest Plot of Fiber Studies

<table>
<thead>
<tr>
<th>Random</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bran (subtotal)</td>
<td>114</td>
<td>107</td>
<td>31.75</td>
<td>1.02</td>
<td>(0.82, 1.27)</td>
</tr>
<tr>
<td>Ispaghula (subtotal)</td>
<td>161</td>
<td>160</td>
<td>65.24</td>
<td>0.78</td>
<td>(0.63, 0.96)</td>
</tr>
<tr>
<td>Fiber* (subtotal)</td>
<td>25</td>
<td>24</td>
<td>3.00</td>
<td>1.37</td>
<td>(0.62, 3.01)</td>
</tr>
<tr>
<td>Total</td>
<td>300</td>
<td>291</td>
<td>100.00</td>
<td>0.87</td>
<td>(0.76, 1.00)</td>
</tr>
</tbody>
</table>

*Unspecified
Psyllium vs Bran vs Placebo for IBS-C

Responders, %

Month 1 Month 2 Month 3

Psyllium Bran Placebo

* Adequate symptom relief for ≥2 of previous 4 wk

PEG 3350 & Electrolytes for IBS-C

- RCT of PEG 3350 + E (n=68) vs placebo (n=71)
- Primary endpoint
  - No. SBMs/d in Wk 4
- PEG 3350 + E significantly improved no. SBMs/d, stool consistency, and straining vs placebo (P<.0001)
  - PEG 3350 + E significantly improved abdominal pain from baseline (P<.005)
  - Not observed with placebo

No. SBMs (weekly mean)

PEG 3350 + E Placebo

Baseline Wk 4

1.28 1.37

4.4 3.11

P<.0001

SBM, spontaneous bowel movement
Sodium Picosulfate for CC

• Patients with CC (N=367) randomized to SPS or placebo
• Primary outcome:
  – Mean complete SBMs/wk over 4 wk

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>4 Wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPS</td>
<td>0.9 ± 0.1</td>
<td>3.4 ± 0.2</td>
</tr>
<tr>
<td>Placebo</td>
<td>1.1 ± 0.1</td>
<td>1.7 ± 0.1</td>
</tr>
<tr>
<td>P value</td>
<td>—</td>
<td>P&lt;.0001</td>
</tr>
</tbody>
</table>

• Overall PAC-QoL score improved
• Conclusion: SPS effective, safe, well-tolerated in CC

PAC-QoL, Patient Assessment of Constipation Quality of Life; SPS, sodium picosulfate


ARS Question 4

Which of the following does not have a specific indication for IBS-C and chronic idiopathic constipation?

A. Lubiprostone
B. Linaclotide
C. PEG 3350
D. All of the above are indicated for both IBS-C and chronic idiopathic constipation
Food for Thought...

- What is the role of medical therapy in treating patients with IBS-C and CC?

Evidence-Based Summary of Medical Therapies for IBS-C & CC Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Global Symptoms</th>
<th>Abdominal Pain</th>
<th>Bloating</th>
<th>Stool Frequency</th>
<th>Stool Consistency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants (SSRIs, TCAs)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fiber (psyllium)</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Laxatives (PEG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Lubiprostone</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Linaclotide</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Chey WS et al. Gut and Liver. 2011;5:253-266. 2011 © Copyright by Gut and Liver. All rights reserved.
Brandt LG et al, for the ACG Task Force on IBS. Am J Gastroenterol. 2009;104(suppl 1):S1-S35.
Lubiprostone for IBS-C: Data from Two Phase 3 Trials

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


Long-term Efficacy of Lubiprostone: Monthly Responder Rates

Incidence of Nausea with Lubiprostone

- CC: 24 mcg BID with food
- IBS-C: 8 mcg BID with food

Linaclotide for IBS-C: Adequate Symptom Relief ≥13/26 Wk

Adequate Relief: IBS Symptoms, %

- Linaclotide 290 mcg (n=401): 49.1%
- Placebo (n=403): 25.1%

Most common AE: diarrhea (19.7% vs 2.5%)

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Irritable Bowel Syndrome and Chronic Constipation:
Digesting Recent Advances and Current Thinking

Linaclotide Phase 3 IBS-C Trial: Abdominal Pain

% Change, Worst Abdominal Pain Over 26 Wk

![Graph showing % change in worst abdominal pain over 26 weeks.]

ANCOVA, analysis of covariance

Symbiotic for CC

- 14-day crossover trial of each:
  - **Symbiotic**: yogurt with 10(8) UFC/g of *B animalis* and fructoligosaccharide
  - **Control**: lacteous dessert without probiotics
- Symbiotic significantly improved stool frequency, stool consistency, straining, and pain with defecation

Food for Thought...

• What IBS-C and CC treatments are on the horizon?

Emerging Therapies

• Prucalopride
  — 5-HT₄ receptor agonist

• Chenodeoxycholate
  — Primary bile acid synthesized from cholesterol

• Elobixibat
  — First-in-class ileal bile acid
Summary

- Range of prescription and nonprescription treatments of IBS-C and CC
- High degree of interpatient variability
  - Evaluation and treatment is tailored to subtype and to individual patient
- Trials of treatments singly or in combination may be necessary to identify regimens that provide maximum efficacy and minimal side effects
- Physician–patient relationship is key

Panel Discussion
Clinician/Patient Disconnect?

Irritable Bowel Syndrome and Chronic Constipation:
Digesting Recent Advances and Current Thinking

SHARED DECISION-MAKING TO IMPROVE CARE

William D. Chey, MD

Constipated??
She is moving her bowels every day...

I can’t deal with the straining and hard stools anymore...

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What Do Patients Want? (Expectations vs Reality)

The ideal office visit provides an accepting and supportive environment


ARS Question 5

Which of the following are important strategies for improving the care of patients with IBS-C or CC?

A. Establish a strong and positive physician-patient relationship
B. Assess severity and treat the predominant symptom
C. Perform a thorough work-up including imaging tests to confirm diagnosis
D. A and B
E. B and C

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Improving Communication & Care

- Empathic listening, explanations, and reassurance
- Make sure you understand the symptoms
- Get a feel for the patient’s QoL
- Emphasize the basics (diet, sleep, exercise)
- Assess severity and treat predominant symptom(s)
- Set follow-up
- Create a healthcare team: nurse, physician assistant, dietician, psychologist, psychotherapist
- Provide educational materials or give out online resource sites (ACG + AGA websites: www.iffgd.org, www.ibsgroup.org)
THANK YOU!