IRRITABLE BOWEL SYNDROME (IBS)
CHRONIC CONSTIPATION
Susan Lucak, MD
IBS: Definitions

- **Functional** disorder = absence of organic abnormalities, i.e. no discernible biochemical or structural changes
- Syndrome **not** Disease
- A complex **biopsychosocial** disorder of unknown cause, characterized by abdominal pain/discomfort and bowel irregularities (C, D, C/D), gut interacts with CNS
IBS: Epidemiology

• Up to **22%** Americans report IBS Sxs
• ~70% IBS patients are **women**
• Age: less than 40
• Not directly lethal, associated with **suicidality** (SI, SA, suicides)
• Impacts on **Quality of Life** (~DM, depression)
• Reduces **productivity** (13.4 v. 4.9 days missed at work)
Pathophysiology of IBS

Proposed Pathophysiology of IBS

- Gastrointestinal (GI) Motor Disturbances
- Visceral Hypersensitivity
- Abnormal Central Processing of Sensations
- Psychological Disturbances

Genetic Factors

Environment

Acute Gastroenteritis

Abuse History

Other Precipitating Factors

Food

Stress

Symptoms

Consultation

Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
IBS: Pathophysiology, Predisposing Factors

**Genetic** Factors
- IBS aggregates in some families
- Gene polymorphisms: 5-HT, IL-10, COMT – pain sensitivity
- Twin studies: monozygotes – increased concordance

**Environmental** Factors – Early Life
- Children of adults with IBS, more health care visits, social learning of illness behavior
- Children with recurrent abdominal pain, higher levels of anxiety + depression, more Sxs

**Abuse** History
- Sexual, physical abuse (30-56% in referral centers in US + Europe, less frequent in primary care centers)
- Childhood abuse (~50%)
- Abuse affects health outcomes (more severe pain, greater impairment in functioning)

**Precipitating** Factors – Adult Life
- Breakup of a relationship
- Stressful life events (war, loss of loved one)
- Chronic life stress (unhappy marriage, war), more severe Sxs
IBS: Pathophysiology, Brain-Gut Interactions + Other Possible Modifying Factors

- Enhanced perception
  - Psychosocial factors
  - Genetic predisposition
  - Infection / inflammation
- 5-HT
- Altered motility
- Visceral hypersensitivity

Adapted from Camilleri et al, Aliment Pharmacol Ther 1997; 11: 3
IBS: Functions of the GI tract - outline

Chemical/physical stimulation in the mucosa releases mediators, stimulate intrinsic neurons in ENS, afferent nerves synapse with:

- **Sensory**: afferent neurons to spinal cord, to brain, descending inhibitory pathways back to ENS
- **Motor**: interneurons in ENS, synapse with motor neurons in ENS, peristalsis (cycles of contraction + relaxation)
- **Secretory**: interneurons, release of mediators stimulate chloride secretion
- **Mediators**: 5-HT, tachykinins, CGRP, enkephalins, Ach, NO, substance P, VIP, cholecystokinin
Some IBS Symptoms May Be Mediated by 5-HT Receptors in the Colon

Adapted with permission from Professor David Grundy, Department of Biomedical Science, The University of Sheffield.
IBS: Brain functional MRI during rectal distention, differential activity in IBS v. C

Active pixels (# per ROI)

IBS Controls

Mertz et. al., Gastroenterology 2000; 118:842
Descending Visceral Pain Pathway

- ACC
- Thalamus
- PAG
- Locus coeruleus
- Caudal raphe nucleus
- Amygdala
- Rostral ventral medulla
- Noradrenergic
- Serotonergic
- Opioidergic
- Colon
Serotonin (5-HT) and motor activity

Proximal contraction

- Oral motor neurons (contraction) ACh / SP
- Interneurons in the myenteric plexus

Distal relaxation

- Caudal motor neurons (relaxation) VIP / NO

Movement of gut content

CGRP

Submucosal IPAN

5-HT (serotonin)

Enterochromaffin cells in GI tract release 5-HT

Adapted from Grider et al, Gastroenterology 1998; 115: 370
Adapted from Gershon, Rev Gastroenterol Disord 2003; 3: S25
Some IBS Symptoms May Be Mediated by 5-HT Receptors in the Colon

Adapted with permission from Professor David Grundy, Department of Biomedical Science, The University of Sheffield.
IBS: Pathophysiology
Secretion via Chloride Channels

IBS: Pathophysiology, Secretion via Chloride Channels (CIC-2)
Pathophysiology of IBS

Proposed Pathophysiology of IBS

- Gastrointestinal (GI) Motor Disturbances
- Visceral Hypersensitivity
- Abnormal Central Processing of Sensations
- Psychological Disturbances

Genetic Factors
Environment
Acute Gastroenteritis
Abuse History
Other Precipitating Factors
Symptoms
Food
Stress
Consultation

Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
Gut Flora in IBS

- Postinfectious IBS (PI-IBS)
- SIBO
Normal Intestinal Microflora

- 10 trillion nonpathogenic bacteria in the GI tract (1-2 kg)
- Exert protective function by creating a barrier against pathogenic by producing various anti-microbial factors
- Influence the development and function of the mucosal immune system

<table>
<thead>
<tr>
<th>Most common bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaerobic genera</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Bifidobacterium</td>
</tr>
<tr>
<td>Clostridium</td>
</tr>
<tr>
<td>Bacteroides</td>
</tr>
<tr>
<td>Eubacterium</td>
</tr>
</tbody>
</table>

Risk of PI-IBS Increases 7-fold After Infectious Gastroenteritis*

*Systematic review of 8 studies involving 588,061 subjects; follow-up ranged from 3 to 12 months.

Increased Inflammatory Cells Found in PI-IBS Rectal Biopsies

**Enteroendocrine Cells**

<table>
<thead>
<tr>
<th></th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Control</th>
<th>PI-IBS‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteroendocrine Cell Counts/100 Epithelial Cells</td>
<td><img src="chart1.png" alt="Graph" /></td>
<td><img src="chart1.png" alt="Graph" /></td>
<td><img src="chart1.png" alt="Graph" /></td>
<td><img src="chart1.png" alt="Graph" /></td>
<td><img src="chart1.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

**CD8 Lymphocyte Counts**

<table>
<thead>
<tr>
<th></th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Control</th>
<th>PI-IBS‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraepithelial CD8 Lymphocytes/100 Epithelial Cells</td>
<td><img src="chart2.png" alt="Graph" /></td>
<td><img src="chart2.png" alt="Graph" /></td>
<td><img src="chart2.png" alt="Graph" /></td>
<td><img src="chart2.png" alt="Graph" /></td>
<td><img src="chart2.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

*P<.001 vs controls; †Significantly elevated compared with controls.
‡Experienced gastroenteritis in previous 8 to 12 months.

Factors Predicting GI Symptoms in Post-infectious IBS

**Factors Predicting GI Symptoms**

- Psychologic distress
- Females
- Younger age
- Duration of diarrhea
- Duration of abdominal pain

*Neal R, BMJ, 1997; 314:779*
*Gwee et al, Gut 1999; 44:400*
Prevalence of SIBO in IBS in Case-control Studies

### Case-control Studies (Age-Sex Matched)

<table>
<thead>
<tr>
<th>Study</th>
<th>Sugar</th>
<th>Patients (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grover 2008</td>
<td>Sucrose</td>
<td>158</td>
<td>34</td>
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<tr>
<td>Parodi 2009</td>
<td>Glucose</td>
<td>70</td>
<td>130</td>
</tr>
<tr>
<td>Lupascu 2005</td>
<td>Lactulose</td>
<td>102</td>
<td>65</td>
</tr>
<tr>
<td>Pimentel 2003</td>
<td>Control</td>
<td>15</td>
<td>111</td>
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<tr>
<td>Bratten 2008</td>
<td></td>
<td>40</td>
<td>224</td>
</tr>
<tr>
<td>Walters 2005</td>
<td></td>
<td>20</td>
<td>39</td>
</tr>
</tbody>
</table>

### References

Elevated Serum But Low to Normal Mucosal Cytokines in IBS

Serum\(^1,2\)  
**IL-6**

\[
\begin{array}{c|c|c}
\text{IL-6 (pg/mL)} & \text{IBS} & \text{Controls} \\
100 & 100,000 & 10,000 \\
10 & 1000 & 100 \\
1 & 1 & \\
0 & 0 & \\
\end{array}
\]

\[P \leq 0.0017\]

Colonic Mucosa\(^3,4\)  
**IL-6**

\[
\begin{array}{c|c|c|c}
\text{Log}_{10}(\text{IL-6} \text{ pg/mL}) & \text{IBS} & \text{Control} & \text{IBD} \\
1 & 100,000 & 10,000 & 1000 \\
1 & 1000 & 100 & 1 \\
\end{array}
\]

\[P \leq 0.0017\]

Mast Cells Are Increased and Are Closer to Nerve Fibers in Colonic Mucosa in IBS

HC=healthy controls
Mast Cell Mediators Excite Visceral Sensory Neurons

HC=healthy controls; *vs buffer; †IBS vs HC.

IBS: Pathophysiology
The Role of Inflammation and Altered Gut Flora - Summary

• Infectious gastroenteritis significantly increases the risk of developing IBS
  — Severity of gastroenteritis symptoms and are predictive for PI-IBS
  — Stress and other psychological factors are associated with PI-IBS

• Gut microflora may play a role in IBS (SIBO)

• The role of inflammation is an emerging area of research in IBS
IBS: DIAGNOSIS
Rome III Diagnostic Criteria

• Recurrent abdominal pain or discomfort for ≥3 days per month in the last 3 months associated with ≥2 of the following:
  – Improvement with defecation
  – Onset associated with a change in stool frequency
  – Onset associated with a change in stool form (appearance)

• Diagnostic criteria fulfilled for the last 3 months with symptom onset ≥6 months prior to diagnosis

Longstreth GF et al. Gastroenterology. 2006;130:1480-1491.
IBS Subtypes Based on Bowel Form

IBS-C: Hard/lumpy stools ≥25%  
Loose/watery stools <25%

Type 1*: Separate hard lumps like nuts (difficult to pass)
Type 2*: Sausage shaped but lumpy

IBS-D: Hard/lumpy stools <25%  
Loose/watery stools ≥25%

Type 6*: Fluffy pieces with ragged edges, a mushy stool
Type 7*: Watery, no solid pieces, entirely liquid

IBS-M: Hard/lumpy stools ≥25%  
Loose/watery stools ≥25%

IBS-U: Hard/lumpy stools ≥25%  
Loose/watery stools <25%

*Bristol Stool Form Scale
IBS-C=constipation-predominant IBS; IBS-D=diarrhea-predominant IBS; IBS-M=mixed IBS; IBS-U=unsubtyped IBS.
Diagnostic Investigation Recommended in Patients With Alarm Features

- Onset of symptoms after age 50
- GI bleeding
- Nocturnal diarrhea
- Weight loss
- Iron-deficiency anemia
- Family history of organic GI disease (colorectal cancer, inflammatory bowel disease [IBD], celiac sprue)

Diagnosis of IBS: Summary

• Patients with typical symptoms and no alarm features can be confidently diagnosed with IBS

• Patients with alarm features such as anemia, weight loss, a family history of colorectal cancer, IBD, or celiac disease, or symptom onset after age 50 warrant a more detailed evaluation (colon cancer screening)

• Patients with IBS-D or M should be screened for celiac sprue

• When patients with IBS-D undergo colonoscopy, random biopsies should be obtained to rule out microscopic colitis
IBS: Therapeutic Strategies

CNS=central nervous system; ANS=autonomic nervous system; CRF=corticotrophin-releasing factor; NK=neurokinin.
Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
IBS: PERIPHERAL MANAGEMENT
Pharmacologic RxIs Directed at Dominant Sxs

Diarrhea
- Loperamide
- Diphenoxylate
- Alosetron

Constipation
- Fiber
- Osmotic and stimulant laxatives
- Lubiprostone

Abdominal pain/ discomfort
- Antispasmodics
- Antidepressants
- Alosetron
- Lubiprostone

Bloating
- Antibiotics
- Probiotics

Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
## Evidence-based Summary of Medical Therapies for IBS-D Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Global Symptoms</th>
<th>Pain</th>
<th>Bloating</th>
<th>Stool Frequency</th>
<th>Stool Consistency</th>
<th>Recommendation</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber (psyllium)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loperamide</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>Antispasmodics</td>
<td>±</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>Alosetron</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>2/1</td>
<td>A/B</td>
</tr>
<tr>
<td>Rifaximin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>Probiotics (bifidobacteria/some combos)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>C</td>
</tr>
</tbody>
</table>

*Recommendations – based on the balance of benefits, risks, burdens, and sometimes cost: Grade 1=strong, Grade 2=weak; Assessment of Quality of evidence – according to the quality of study design, consistency of results among studies, directness and applicability of study endpoints: Grade A=high, Grade B=moderate, Grade C=low*


Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
## Evidence-based Summary of Medical Therapies for IBS-C Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Global Symptoms</th>
<th>Pain</th>
<th>Bloating</th>
<th>Stool Frequency</th>
<th>Stool Consistency</th>
<th>Grading Recommendations</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiber (psyllium)</td>
<td></td>
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<td>+</td>
<td>+</td>
<td>2</td>
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<tr>
<td>Laxatives (PEG)</td>
<td></td>
<td></td>
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<td>+</td>
<td></td>
<td>2</td>
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<tr>
<td>Lubiprostone</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>B</td>
</tr>
<tr>
<td>Tegaserod†</td>
<td>+</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>2</td>
<td>A</td>
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</tbody>
</table>

*Recommendations – based on the balance of benefits, risks, burdens, and sometimes cost: Grade 1=strong, Grade 2=weak; Assessment of Quality of evidence – according to the quality of study design, consistency of results among studies, directness and applicability of study endpoints: Grade A=high, Grade B=moderate, Grade C=low

† Available only under Emergency IND program. PEG=polyethylene glycol.

Adapted from ACG Task Force on IBS. *Am J Gastroenterol.* 2009;104(suppl 1):S1-S35.
Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
Lubiprostone activates ClC-2
Stimulates Gut Secretion
AMITIZA™ (lubiprostone) Activates CIC-2 Chloride Channels

- Specific chloride channel-2 (CIC-2) activator
- Promotes fluid secretion
- Enhances intestinal fluid secretion to facilitate increased motility
- Dose for IBS-C: 8μg PO BID with meals

IBS: Treatment with Antibiotics

Rifaximin = non-absorbable ABX derived from rifamycin
- < 0.4% systemic absorption
- Delivered in high concentrations to GI tract
- Inhibits RNA synthesis of targets microorganisms
  - In-vitro activity against Gm+ and Gm- aerobic and anaerobic bacteria
- Improves IBS Sxs for up to 10 weeks beyond RX
- Improves gas-related Sxs (bloating, flatulence) in pts without SIBO
Probiotics - Definitions

**Probiotics**: live, viable microorganisms that when ingested in adequate amounts, exert a health benefit on the host\(^1\)

**Single-organism probiotics\(^1\)\(^-\)\(^3\)**
- *E. coli* 1917 *Nissle*
- *L. salivarius* UCC4331
- *L. reuteri*
- *L. casei*
- *L. plantarus* 299v
- *L. rhamnosus* GG
- *B. infantis* 35624
- *B. animalis* DN-173010
- *Saccharomyces boulardii*

**Composite probiotics\(^1\)\(^-\)\(^3\)**
- VSL #3 (*Bifidobacterium, Lactobacillus, Streptococcus salivarius thermophilus*)
- Lacteol Fort (*L.acidophilus* LB, lactose monohydrate, calcium carbohydrate, silicic acid, talc, magnesium stearate, anhydrous lactose)

**Prebiotics**: food ingredients that influence the composition of the commensal flora\(^2\)

**Symbiotics**: combination of probiotic and prebiotic\(^2\)

---

Potential Mechanisms of Probiotics in IBS

• Displace gas-producing, bile salt-deconjugating bacterial species
  – Inhibit pathogenic bacterial adherence

• Immunomodulatory properties

• Acidification of the colon by nutrient fermentation

• Secretion of bacteriocins that inhibit pathogenic bacteria

• Enhance epithelial barrier function

Bifidobacterium infantis Affects Cytokine Levels in IBS

*P* = .001.

**B infantis** Improves IBS Symptoms But Insufficient Evidence for Other Probiotics

- 4648 probiotics in IBS citations retrieved
- 21 probiotic studies assessed
- 16 RCTs included

RCTs
- Adults with IBS defined by Manning or Rome II criteria
- Single or combination probiotic vs placebo
- Improvement in IBS symptoms and/or decrease in frequency of AEs reported

No other probiotic showed significant improvement in IBS symptoms in appropriately designed RCTs (7 RCTs with isolated *Lactobacillus* species)

*B infantis* 35624 demonstrated efficacy in 2 appropriately designed RCTs

RCTs=randomized, controlled trials.

Antibiotics and Probiotics for IBS: Unanswered Questions/Issues

<table>
<thead>
<tr>
<th></th>
<th>Antibiotics</th>
<th>Probiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal dose, and duration of therapy</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Long-term safety and effectiveness (eg, durability of response)</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Potential contribution of widespread use to bacterial resistance</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Benefits and timing of sequential strategies (eg, probiotic use after antibiotics)</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Lack of quality control ensuring purity, viability, and safety</td>
<td></td>
<td>?</td>
</tr>
</tbody>
</table>

Peripheral Mgmt of IBS Symptoms: Summary

• Current therapeutic strategies are largely directed against predominant symptoms

• Evidence-based treatments
  – IBS-D: TCAs, alosetron, non-absorbable ABX,
  – IBS-C: lubiprostone, SSRIs

• Rifaximin appears effective for global improvement of IBS symptoms

• Many probiotics studied in IBS
  – Efficacy demonstrated with B.infantis
    (More data needed to determine the role + characterize optimal RX)

* Restricted use through the alosetron prescribing program; †Available only under an Emergency IND program.
Central Management of IBS Symptoms
IBS Conceptual Model

Early Life
- Genetics
- Environment

Psychosocial Factors
- Life stress
- Psychologic state
- Coping
- Social support

Physiology
- Motility
- Sensation

CNS

ENS

IBS
- Symptom experience
- Behavior

Outcome
- Medications
- MD visits
- Daily function
- Quality of life

Antidepressants: Mechanism of Action

Antidepressant action

Visceral analgesia

Changes in motility

Smooth muscle relaxation (TCA)

TCA=tricyclic antidepressant.
Adapted from Rome Foundation Functional GI Disorders Specialty Modules.
### Efficacy of TCAs in Relieving Global IBS Symptoms*

<table>
<thead>
<tr>
<th>Study (yr, drug dose)</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (Random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heefner (1978, desipramine 150 qd)</td>
<td>10/22</td>
<td>12/22</td>
<td></td>
</tr>
<tr>
<td>Myren (1982, trimipramine 50 qd)</td>
<td>5/30</td>
<td>10/31</td>
<td></td>
</tr>
<tr>
<td>Nigam (1984. amitriptyline 12.5 qd)</td>
<td>14/21</td>
<td>21/21</td>
<td></td>
</tr>
<tr>
<td>Boerner (1988, doxepin 50 qd)</td>
<td>16/42</td>
<td>19/41</td>
<td></td>
</tr>
<tr>
<td>Bergmann (1991, trimipramine 50 qd)</td>
<td>5/19</td>
<td>14/16</td>
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<tr>
<td>Vij (1991, doxepin 75 qd)</td>
<td>14/25</td>
<td>20/25</td>
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<tr>
<td>Drossman (2003, desipramine 50-150 qd)</td>
<td>60/115</td>
<td>26/57</td>
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<tr>
<td>Talley (2008, imipramine 50 qd)</td>
<td>0/18</td>
<td>5/16</td>
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<tr>
<td>Vahedi (2008, amitriptyline 10 qd)</td>
<td>8/27</td>
<td>16/27</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>319</strong></td>
<td><strong>256</strong></td>
<td><strong>RR=0.68</strong></td>
</tr>
</tbody>
</table>

*(95% CI=0.56-0.83)  NNT=4

*Significant heterogeneity among studies may limit conclusions.
Study duration ranged from 4 weeks to 3 months.
Efficacy of SSRIs in Relieving Global IBS Symptoms*

<table>
<thead>
<tr>
<th>Study (yr, drug dose)</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (Random)95% CI</th>
</tr>
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<tbody>
<tr>
<td>Kuiken (2003, fluoxetine 20 qd)</td>
<td>9/19</td>
<td>12/21</td>
<td></td>
</tr>
<tr>
<td>Tabas (2004, paroxetine 10-40 qd)</td>
<td>25/44</td>
<td>36/46</td>
<td></td>
</tr>
<tr>
<td>Vahedi (2005, fluoxetine 20 qd)</td>
<td>6/22</td>
<td>19/22</td>
<td>RR=0.62 (95% CI=0.45-0.87) NNT=3.5</td>
</tr>
<tr>
<td>Talley (2008, citalopram 40 qd)</td>
<td>5/17</td>
<td>5/16</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>113</td>
<td>117</td>
<td></td>
</tr>
</tbody>
</table>

*Significant heterogeneity among studies may limit conclusions.
Study duration ranged from 6 weeks to 12 weeks.

IBS—Psychological Treatments

- **Cognitive–behavior therapy (CBT)**
  - Uses diaries and exercises to reframe maladaptive thoughts and increase control over symptoms

- **Interpersonal psychodynamic therapy (“talk therapy”)**
  - Identify and address difficulties in relationships

- **Hypnotherapy (HT)**
  - Suggestion used to reduce gut sensations

- **Relaxation training (stress reduction)**
  - Uses imagery and relaxation techniques to reduce autonomic arousal and stimulate muscular relaxation

# Psychosocial Therapies Are More Effective Than Usual Care at Relieving Global IBS Symptoms

<table>
<thead>
<tr>
<th>Treatment Modality</th>
<th>Studies (n)</th>
<th>N</th>
<th>RR (95% CI)</th>
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<td>Controls</td>
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<td>Cognitive behavioral therapy (CBT)</td>
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<td>Multicomponent psychological therapy</td>
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<tr>
<td>Dynamic psychotherapy</td>
<td>2</td>
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<td>135</td>
</tr>
</tbody>
</table>

Summary: Central Management of IBS

• Psychototropic agents and psychological/behavioral therapies can effectively relieve IBS symptoms.
• Antidepressants (TCAs, SSRIs) exert their beneficial effects in IBS via central and peripheral actions, which can be independent of their effect on mood.
• Efficacious psychological therapies for IBS include cognitive behavioral therapy, hypnosis, psychotherapy and stress management.
IBS: CONCLUSIONS

• IBS is a complex biopsychosocial disorder
• Pathophysiologic mechanisms include an interplay between genetic, early life, environmental factors with gut physiology (hypersensitivity, dysmotility) and different central processing + psych. co-morbidities
• Low-grade inflammation + altered gut flora may play a role in pathophysiology of IBS
• Current pharmacotherapies are largely directed at the predominant symptoms (peripherally directed Rxs)
• Non-absorbable ABX + B. infantis PBX appear effective for global improvement in IBS symptoms
• Centrally directed Rxs may reduce global IBS symptoms + improve well-being in selected patients
CHRONIC CONSTIPATION

• PRIMARY (IDIOPATHIC)
  – SLOW TRANSIT
  – PELVIC FLOOR DYSSYNERGIA

• SECONDARY
  – RELATED TO A VARIETY OF CAUSES
Prevalence and incidence of constipation in the US

- Prevalence:
  - estimated 55 million Americans (prevalence 28%)\(^1\)
    - men 12\(^2\)
    - women 16\(^2\)
    - elderly individuals 40\(^3\)
- Onset rate 40 / 1000 person-years\(^4\)

\(^1\)Locke et al, Gastroenterology 2000; 119: 1766
\(^2\)Stewart et al, Am J Gastroenterol 1999; 94(12): 3530
\(^3\)Talley et al, Am J Gastroenterol 1996; 91: 19
Overlap in IBS-C and CC – The ROME III criteria

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

**IBS**
- Recurrent abdominal pain / discomfort* at least 3 days/month in the last 3 months associated with two or more:
  - Improvement with defecation
  - Onset associated with a change in frequency of stool
  - Onset associated with a change in form (appearance) of stool

* Uncomfortable sensation, not described as pain

**CC**
- Must include two or more of the following (>25% of defecations):
  - Hard or lumpy stool
  - Straining
  - Incomplete evacuation
  - Sensation of anorectal obstruction / blockage
  - Manual maneuvers
  - <3 defecations / week
- Loose stools rarely present without laxative use
- Insufficient criteria for IBS

Longstreth et al. Gastroenterology 2006;130(5):1480–91
Functional subtypes of idiopathic constipation

- Slow transit constipation 47%
- Dyssynergic defecation 59%
- Irritable bowel syndrome 58%

- Slow-transit and IBS-C overlap in half of each group

Mertz et al, Am J Gastroenterol 1999; 94: 609
Measurement of colonic transit: Distribution of radiographic markers

A  Normal
≤5 markers remain

B  Slow-transit
Rings are scattered throughout the colon

C  Functional outlet obstruction
Rings are gathered in the rectosigmoid

Faigel et al, Clin Cornerstone 2002; 4: 11
Manometry in patients with dyssynergia

Normal

Rectal

Anal

Dyssynergic defecation

Rectal

Anal

Pathophysiologic-based treatment approach for chronic constipation

- **Slow transit constipation**
  - PEG compounds
  - Lubiprostone

- **IBS-C / Constipation overlap**
  - Lubiprostone (PEG compounds)

- **Dyssynergia**
  - Biofeedback therapy
CHRONIC CONSTIPATION: CONCLUSIONS

• Determine if CC is primary or secondary
• Differentiate between CC and IBS-C (Rome III)
• Sitzmark study + anorectal motility studies can distinguish between STC (slow-transit) v. PFD (dyssynergic or pelvic floor dyssynergia)
• STC responds to laxatives + prokinetic meds
• PFD treated with meds as STC + biofeedback