Practical Approaches Towards Improving Patient Outcomes for Chronic Constipation and Irritable Bowel Syndrome With Constipation (IBS-C) Among Older Adults
Educational Learning Objectives

• Describe the elements of proper diagnosis and follow-up management of chronic constipation (CC) in older adults

• Demonstrate awareness of the prevalence of irritable bowel syndrome-constipation (IBS-C) in older adults and the elements of differential diagnosis from CC

• Discuss how management of CC and IBS-C varies based upon underlying etiologies and across the spectrum of older adults, from the active community dweller to the compromised long term care resident with multiple comorbidities

• List common patient perceptions of constipation and describe how these may impact progress towards practitioners' clinical goals in CC and IBS-C

• Identify patient education and counseling strategies that will allow advanced practice nurses (APN) to collaborate with patients and family members in the successful management of CC and IBS-C in older adults
How Do We Define Constipation?

• The American College of Gastroenterology (ACG) definition of constipation:
  – Unsatisfactory defecation characterized by infrequent stools, difficult stool passage, or both. Difficult stool passage includes straining, a sense of difficulty passing stool, incomplete evacuation, hard/lumpy stools, prolonged time to pass stool, or need for manual maneuvers to pass stool

• The ACG Chronic Constipation Task Force also clarified what is meant by chronic:
  – Chronic constipation is defined as the presence of these symptoms for at least 3 months

GI Symptoms Are Common in the Older Population

- 35% to 40% of geriatric patients will have at least 1 GI symptom in any year
  - Constipation, fecal incontinence, diarrhea, irritable bowel syndrome, reflux disease, and swallowing disorders

- Prevalence rates for constipation in the older adult population range from approximately 19% to 40%
  - Day Hospitals/Living at Home: 25–40%
  - Nursing Homes/Geriatric Hospitals: 60–80%

- Irritable bowel syndrome presents in ~10% of the older population

Overlap Between Common Disorders

Belching
Dyspepsia
IBS
GERD
Chronic Constipation
Constipation
Bloating
Abdominal Pain
Heartburn
Discomfort
Regurgitation

Abdominal Pain: Salient Feature Absent in Chronic Constipation

Presence or absence of abdominal pain is the major differentiating feature

(-) Abdominal Pain
Chronic constipation

(+) Abdominal Pain
IBS with constipation

Prevalence of Functional Gastrointestinal Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Population (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspepsia</td>
<td>40</td>
</tr>
<tr>
<td>Functional Heartburn</td>
<td>25-40</td>
</tr>
<tr>
<td>Chronic Constipation</td>
<td>2-28</td>
</tr>
<tr>
<td>GERD</td>
<td>25</td>
</tr>
<tr>
<td>IBS</td>
<td>3-20</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28</td>
</tr>
<tr>
<td>Migraine</td>
<td>6-18</td>
</tr>
<tr>
<td>Asthma</td>
<td>8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8</td>
</tr>
</tbody>
</table>

References:
**Constipation Increases With Age and Is More Common in Women**

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Study 1 N = 42,375</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>0%</td>
</tr>
<tr>
<td>40-49</td>
<td>2%</td>
</tr>
<tr>
<td>50-59</td>
<td>4%</td>
</tr>
<tr>
<td>60-69</td>
<td>6%</td>
</tr>
<tr>
<td>70-79</td>
<td>8%</td>
</tr>
<tr>
<td>≥80</td>
<td>10%</td>
</tr>
</tbody>
</table>

*Harari, et al.*
*Population: NHIS 1989*
*Criteria: self-report*

**NHIS = National Health Interview Survey**

Study 1 N = 42,375

Study 2 N = 5,430 (Drossman)

Study 3 N = 1,149 (Pare)

Study 4 N = 10,018 (Stewart)

**Sex**

- **Men**
- **Women**

Chronic Constipation Interferes with Daily Lives of the Aging Population

- Impact of chronic constipation on quality of life in Olmsted County, MN, residents aged ≥ 65 years
- Lower score indicates worse quality of life

MOS = medical outcomes survey

Adapted from Talley NJ. Rev Gastroenterol Disord. 2004;4(suppl 2):S3-S10.
Economic Impact of Constipation

- 2.5 million office visits annually
- 92,000 hospital admissions
- 85% are given prescriptions for laxatives or cathartics
- $400 million dollars spent annually for prescription laxatives
- $2253 average cost per long term care resident

Economic Burden of Irritable Bowel Syndrome

- IBS care: > $20 billion direct and indirect expenditures
- Patients with IBS consume > 50% more health care costs than matched controls without IBS

Normal Physiology of Defecation

- Increased abdominal pressure or propulsive colorectal contractions
- Relaxation of internal anal sphincter (autonomic)
- Relaxation of external anal sphincter (voluntary)
- Straightening of pelvic musculature (levator ani, puborectalis)

Mediators of Gastrointestinal Function

**Motility**
- Serotonin
- Acetylcholine
- Nitric oxide
- Substance P
- Vasoactive intestinal peptide
- Cholecystokinin
- Corticotropin releasing factor

**Visceral Sensitivity**
- Serotonin
- Tachykinins
- Calcitonin gene-related peptide
- Neurokinin A
- Enkephalins
- Corticotropin releasing factor

**Secretion**
- Serotonin
- Acetylcholine

Rome III Diagnostic Criteria* for Functional Constipation

Chronic constipation must include **2 or more** of the following:

- Straining
- Lumpy or hard stools
- Sensation of incomplete evacuation
- Sensation of anorectal obstruction/blockage
- Manual maneuvers to facilitate defecations
- < 3 defecations per week

• Loose stools are rarely present without the use of laxatives
• Insufficient criteria for irritable bowel syndrome

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

Primary Causes of Chronic Constipation

- Normal-transit constipation
- Slow-transit constipation
- Defecatory dysfunction
- IBS with constipation
Primary Constipation

• **Normal-transit Constipation**
  – Intestinal transit and stool frequency are within the normal range
  – Most frequent type of constipation
Primary Constipation

• Slow-transit Constipation
  – Characterized by prolonged intestinal transit time
  – Altered regulation of enteric nervous system
  – Decreased nitric oxide production
  – Impaired gastrocolic reflex
  – Alteration of neuropeptides (VIP, substance P)
  – Decreased number of interstitial cells of Cajal in the colon
Primary Constipation

- **Defecatory Dysfunction**
  - More common in older women – childbirth trauma
  - Pelvic floor dyssynergia
  - Contributing factors include anal fissures, hemorrhoids, rectocele, rectal prolapse, posterior rectal herniation
  - Excessive perineal descent
  - Pathogenesis may be multifactorial – structural problem
  - Abnormal anorectal manometry and/or defecography

[Role for biofeedback therapy]

Primary Constipation

- Irritable Bowel Syndrome (IBS) with Constipation
  - Alterations in brain-gut axis
  - Stress-related condition
  - Visceral hypersensitivity
  - Abnormal brain activation
  - Altered gastrointestinal motility
  - Role for neurotransmitters, hormones
  - Presence of non-GI symptoms
    - Headache, back pain, fatigue, myalgia, dyspareunia, urinary symptoms, dizziness
Rome III Criteria for IBS-C

Recurrent abdominal pain or discomfort (an uncomfortable sensation not described as pain) at least 3 days per month in the last 3 months associated with 2 or more of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form of stool

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

In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening for patient eligibility

Subtypes of IBS

IBS-C: IBS with constipation
IBS-U: Unsubtyped IBS
IBS-M: IBS mixed
IBS-D: IBS with diarrhea

Combined Risk Factors for Constipation in the Elderly Population

- Reduced fiber intake
- Reduced liquid intake
- Reduced mobility associated with functional decline
- Decreased functional independence
- Pelvic floor dysfunction
- Chronic conditions
  - Parkinson’s disease
  - Dementia
  - Diabetes mellitus
  - Depression
- Polypharmacy (both over the counter and prescription medications, such as NSAIDs, antacids, antihistamines, iron supplements, anticholinergics, opiates, Ca channel blockers, diuretics, antipsychotics, anxiolytics, antidepressants)
Common Changes with Aging that Increase the Risk for Constipation

- Decreased total body water
- Decreased colonic motility*
- Deterioration of nerve function
- Increased pelvic floor descent
- Decreased rectal compliance
- Decreased rectal sensation
- Age-related changes to the internal and external anal sphincter

*Demonstrated in some, but not all studies

Patient Care

- Thorough patient history
- Physical/abdominal/digital rectal exams
- Evaluate symptoms in terms of diagnostic criteria
  - Chronic constipation/IBS-C
- Assessment for red flags/alarm features
  - Need for additional testing
- Treatment/Management plan
Ask the Right Questions

- Define the meaning of “constipation”
- How long have you experienced these symptoms?
- Frequency of bowel movements?
- Abdominal pain?
- Other symptoms?
- What is most distressing symptom?
- Manual maneuvers to assist with defecation?
- Any limitation of daily activities?
- Are you taking any medications?
- What treatment have you tried?
- What investigations have been done?

Common Patient Descriptions of Constipation

Percent of Patients

- Straining: 81%
- Hard or lumpy stools: 72%
- Incomplete emptying: 54%
- Stool cannot be passed: 39%
- Abdominal fullness or bloating: 37%
- < 3 BM per week: 36%
- Need to press on anus: 28%

N = 1149

### The Bristol Stool Form Scale

<table>
<thead>
<tr>
<th>Slow Transit</th>
<th>Fast Transit</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type 1</strong></td>
<td><strong>Type 7</strong></td>
</tr>
<tr>
<td>Separate hard lumps</td>
<td>Watery, no solid pieces</td>
</tr>
<tr>
<td><strong>Type 2</strong></td>
<td></td>
</tr>
<tr>
<td>Sausage-like but lumpy</td>
<td></td>
</tr>
<tr>
<td><strong>Type 3</strong></td>
<td></td>
</tr>
<tr>
<td>Sausage-like but with cracks in the surface</td>
<td></td>
</tr>
<tr>
<td><strong>Type 4</strong></td>
<td></td>
</tr>
<tr>
<td>Smooth and soft</td>
<td></td>
</tr>
<tr>
<td><strong>Type 5</strong></td>
<td></td>
</tr>
<tr>
<td>Soft blobs with clear-cut edges</td>
<td></td>
</tr>
<tr>
<td><strong>Type 6</strong></td>
<td></td>
</tr>
<tr>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
<td></td>
</tr>
</tbody>
</table>

Consider Secondary Causes

**Psychological**
- Depression
- Eating disorders

**Surgical**
- Abdominal/pelvic surgery
- Colonic/anorectal surgery

**Drugs**
- Opiates
- Antidepressants
- Anticholinergics
- Antipsychotics
- Antacids (Al, Ca)
- Ca channel blockers
- Iron supplements

**Lifestyle**
- Inadequate fiber/fluid
- Inactivity

**Metabolic/Endocrine**
- Hypercalcemia
- Hyperparathyroidism
- Diabetes mellitus
- Hypothyroidism
- Hypokalemia
- Uremia
- Addison’s
- Porphyria

**Neurological**
- Parkinson’s
- Multiple sclerosis
- Autonomic neuropathy
- Aganglionosis
  (Hirschsprung’s, Chagas)
- Spinal lesions
- Cerebrovascular disease

**Systemic**
- Amyloidosis
- Scleroderma
- Polymyositis
- Pregnancy

**Gastrointestinal**
- Colorectal: neoplasm, ischemia, volvulus, megacolon, diverticular disease
- Anorectal: prolapse, rectocele, stenosis, megarectum

Digital Rectal Exam

- Place patient in left lateral recumbent position
- Visually inspect the perianal region
  - Fissures, hemorrhoids, masses, skin tags, or evidence of previous surgery, skin lesions
- Stroke the perianal skin to elicit a reflex contraction of the external anal sphincter
- Assess for paradoxical pelvic floor contraction (suggestive of pelvic floor descent)
- Perform a digital assessment
  - Strictures, masses, a rectocele, and hemorrhoids
  - Examine stool for color and consistency
  - Check for occult blood

Any Alarm Symptoms? Are Diagnostic Tests Needed?

- Hematochezia
- Family history of colon cancer
- Family history of inflammatory bowel disease
- Anemia
- Positive fecal occult blood test
- “Unexplained” weight loss ≥ 10 pounds
- Severe, persistent constipation that is unresponsive to treatment
- New-onset constipation in an elderly patient
ACG Task Force Recommendations on Diagnostic Testing

- ACG task force does not recommend diagnostic testing in patients without alarm signs or symptoms
  - **BUT** routine colon cancer screening recommended for all patients aged ≥ 50 years (African Americans aged ≥ 45 years)
- Diagnostic studies are indicated in patients with alarm signs or symptoms
- Thyroid function tests
- Measurements of
  - Calcium
  - Electrolytes

# Diagnostic Tests That May Be Performed After a Referral

<table>
<thead>
<tr>
<th>Test</th>
<th>Use</th>
</tr>
</thead>
</table>
| Anorectal manometry     | Assesses the internal and external anal sphincters, pelvic floor, and associated nerves  
                          | Screening test of choice for dyssynergic defecation                  |
| Balloon expulsion       | Detects defecatory disorders                                           
                          | Simple, office-based screening test                                   |
| Defecography            | Detects structural abnormalities of the rectum                       
                          | Operator dependent, poor reliability, not widely available            |
| Colonic transit study   | Measures rate at which fecal mass moves through colon                 |
| Colonoscopy             | Provides a visual diagnosis while performing biopsies with detection and removal of polyps |

## Differentiating Between Occasional and Chronic Constipation

<table>
<thead>
<tr>
<th>Occasional Constipation</th>
<th>Chronic Constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrequent</td>
<td>Present for <strong>at least 3 months</strong> and may persist for years</td>
</tr>
<tr>
<td>Occasional or short-term condition that may temporarily interrupt usual routine</td>
<td>Long-term condition that may dominate personal and work life</td>
</tr>
<tr>
<td>May be brought on by patient’s behavior, change in diet, lack of exercise, illness, or medication</td>
<td>Not only related to patient’s behavior, change in diet, lack of exercise, or medication</td>
</tr>
<tr>
<td>May be relieved by diet, exercise, and over-the-counter (OTC) medication</td>
<td>May need medical attention and prescription medication</td>
</tr>
</tbody>
</table>
# Lifestyle Modifications

<table>
<thead>
<tr>
<th>Modification</th>
<th>Targeted Mechanism</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase fluid intake</td>
<td>Increase stool volume by augmenting luminal fluid</td>
<td>Limited; majority of fluid is absorbed before reaching the colon and is expelled via urine</td>
</tr>
<tr>
<td>Increase exercise</td>
<td>Improve motility by decreasing transit time through the GI tract</td>
<td>Moderate; some evidence suggests this is beneficial; however, not sufficient to treat</td>
</tr>
<tr>
<td>Increase dietary fiber</td>
<td>Increase water and bulk stool volume</td>
<td>Limited benefit compared with placebo</td>
</tr>
</tbody>
</table>

## Treating Constipation With Laxatives

<table>
<thead>
<tr>
<th>Laxative</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulking Agents</td>
<td>Absorbs liquids in the intestines and swells to form a soft, bulky stool; the increase in fecal bulk is associated with accelerated luminal propulsion.</td>
</tr>
<tr>
<td>Osmotic Laxatives</td>
<td>Draws water into the bowel from surrounding body tissues providing a soft stool mass and improved propulsion [saline, poorly absorbed mono- and disaccharides, polyethylene glycol].</td>
</tr>
<tr>
<td>Stimulant Laxatives</td>
<td>Cause rhythmic muscle contractions in the intestines, increase intestinal motility and secretions.</td>
</tr>
<tr>
<td>Lubricants</td>
<td>Coats the bowel and the stool mass with a waterproof film; stool remains soft and its passage is made easier.</td>
</tr>
<tr>
<td>Stool Softeners</td>
<td>Helps liquids mix into the stool and prevent dry, hard stool masses; has been said not to cause a bowel movement but instead allows the patient to have a bowel movement without straining.</td>
</tr>
<tr>
<td>Combinations</td>
<td>Combinations containing more than 1 type of laxative; for example, a product may contain both a stool softener and a stimulant laxative.</td>
</tr>
</tbody>
</table>

# Laxatives

<table>
<thead>
<tr>
<th>Laxative Type</th>
<th>Generic Name</th>
<th>Brand Name(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bulk-forming</strong></td>
<td>Methylcellulose</td>
<td>Citruce®</td>
</tr>
<tr>
<td></td>
<td>Polycarbophil</td>
<td>FiberCon®, Fiber-Lax®</td>
</tr>
<tr>
<td></td>
<td>Psyllium</td>
<td>Metamucil®, Konsyl®</td>
</tr>
<tr>
<td><strong>Lubricating</strong></td>
<td>Glycerin</td>
<td>Glycerin suppository (generic)</td>
</tr>
<tr>
<td></td>
<td>Mineral oil</td>
<td>Mineral oil (generic)</td>
</tr>
<tr>
<td></td>
<td>Magnesium hydroxide (milk of magnesia) and mineral oil</td>
<td>Phillips® M-O</td>
</tr>
<tr>
<td><strong>Stool Softeners</strong></td>
<td>Docusate sodium</td>
<td>Colace®, Dulcolax® Stool Softener, Phillips’ Liqui-Gels®</td>
</tr>
<tr>
<td><strong>Saline</strong></td>
<td>Magnesium hydroxide (milk of magnesia)</td>
<td>Ex-Lax® Milk of Magnesia Laxative/Antacid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phillips® Chewable Tablets</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phillips® Milk of Magnesia</td>
</tr>
<tr>
<td><strong>Stimulant</strong></td>
<td>Bisacodyl</td>
<td>Ex-Lax Ultra, Dulcolax Bowel Prep Kit</td>
</tr>
<tr>
<td></td>
<td>Sodium bicarbonate and potassium bitartrate</td>
<td>Ceo-Two Evacuant®</td>
</tr>
<tr>
<td></td>
<td>Sennosides</td>
<td>Ex-Lax® Laxative Pills</td>
</tr>
<tr>
<td></td>
<td>Castor oil</td>
<td>Purge®</td>
</tr>
<tr>
<td></td>
<td>Senna</td>
<td>Senokot®</td>
</tr>
<tr>
<td><strong>Osmotic</strong></td>
<td>Polyethylene glycol 3350</td>
<td>GlycoLax®, MiraLAX®</td>
</tr>
<tr>
<td></td>
<td>Lactulose</td>
<td>Kristalose®</td>
</tr>
</tbody>
</table>
## Bulk Laxatives: Review of Efficacy

<table>
<thead>
<tr>
<th>Laxative</th>
<th>Studies</th>
<th>Evidence</th>
<th>Summary and Recommendation</th>
</tr>
</thead>
</table>
| **Psyllium** | • 5 RCTs:  
  – 3 placebo controlled  
  – 1 well designed | • 2 trials: greater stool frequency, better stool consistency, and greater ease of defecation  
  • 1 trial: no improvement | Psyllium appears to improve stool frequency and consistency  
 GRADE B |
| **Bran** | • 3 RCTs:  
  – 1 placebo controlled  
  – All poorly designed | • Stool frequency was significantly greater with bran than placebo if placebo was given first, but not if bran was given first | Insufficient data to make a recommendation |
# Stool Softeners and Stimulant Laxatives: Review of Efficacy

<table>
<thead>
<tr>
<th>Laxative</th>
<th>Studies</th>
<th>Evidence</th>
<th>Summary and Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Docusate</strong></td>
<td>• 4 RCTs:</td>
<td>• 1 trial: greater stool frequency</td>
<td>Insufficient data to make recommendation</td>
</tr>
<tr>
<td></td>
<td>– 2 placebo controlled</td>
<td>• 1 trial: greater stool frequency and global symptom assessment</td>
<td>Docusate may be inferior to psyllium in increasing stool frequency</td>
</tr>
<tr>
<td></td>
<td>– 3 well designed</td>
<td>• 2 trials: no improvement (1 vs placebo, 1 vs psyllium)</td>
<td></td>
</tr>
<tr>
<td><strong>Stimulant laxatives</strong></td>
<td>• 4 RCTs:</td>
<td>• In 3 studies, no difference between stimulant laxative and control in stool frequency or consistency</td>
<td>Not possible to make a recommendation about efficacy</td>
</tr>
<tr>
<td></td>
<td>– None placebo controlled</td>
<td>• 1 trial: less efficacy compared with lactulose at increasing stool frequency</td>
<td></td>
</tr>
<tr>
<td></td>
<td>– Low-quality study design</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RCT = randomized controlled trial

## Osmotic Laxatives: Review of Efficacy

<table>
<thead>
<tr>
<th>Laxative</th>
<th>Studies</th>
<th>Evidence</th>
<th>Summary and Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactulose</td>
<td>• 3 RCTs:</td>
<td>• All trials favor lactulose</td>
<td>Effective at improving stool frequency and stool consistency</td>
</tr>
<tr>
<td></td>
<td>– All placebo controlled</td>
<td>• Significantly improved stool consistency</td>
<td><strong>GRADE A</strong></td>
</tr>
<tr>
<td></td>
<td>– 2 well designed</td>
<td>• Mean number of BM/day significantly greater vs placebo</td>
<td></td>
</tr>
<tr>
<td>Polyethylene Glycol (PEG)</td>
<td>• 5 placebo-controlled RCTs</td>
<td>• Increased stool frequency and improvement in stool consistency vs. placebo</td>
<td>Effective at improving stool frequency and stool consistency</td>
</tr>
<tr>
<td></td>
<td>• 2 RCTs comparing PEG and lactulose</td>
<td>• Stool frequency greater, straining less often, overall effectiveness higher vs. lactulose</td>
<td><strong>GRADE A</strong></td>
</tr>
</tbody>
</table>

PEG 3350 – 12-Month Study

An Open-Label, Single Treatment Multi-Centre Study of 311 Patients (117 aged 65 and older)

PEG 3350 was determined safe and effective for treating constipation in adult older patients for periods up to 12 months, with no signs of tachyphylaxis.

Adverse Effects of Laxatives

• Bulking agents
  – Bloating
  – Severe adverse events: esophageal and colonic obstruction, anaphylactic reactions

• Osmotic laxatives
  – Possible electrolyte abnormalities, hypovolemia
  – Diarrhea (2% to 40% of PEG-treated patients)
  – Excessive stool frequency, nausea, abdominal bloating, cramping, flatulence

• Stimulant laxatives
  – Abdominal discomfort, electrolyte imbalances, allergic reactions, hepatotoxicity

Dangers of Saline Laxatives in the Elderly

- Oral sodium phosphate products [Visicol®, OsmoPrep®, Fleet* Phospho-soda] for bowel cleansing
- Black box warning for Visicol®, OsmoPrep®
- Acute phosphate nephropathy
- Patients with identifiable risk factors
  - Age > 55
  - Baseline kidney disease
  - Hypovolemic, reduced intravascular volume
  - Bowel obstruction, active colitis
  - Using medications that affect renal perfusion or function

*Withdrawn from the market
Are Patients Satisfied With Laxatives and Fiber?

- Ineffective Relief of Constipation
  - OTC laxatives: 44%
  - Prescription laxatives: 60%
  - Fiber: 66%

- Ineffective Relief of Multiple Symptoms
  - OTC laxatives: 50%
  - Prescription laxatives: 50%
  - Fiber: 71%

- Lack of Predictability
  - OTC laxatives: 50%
  - Prescription laxatives: 75%
  - Fiber: 79%

- Ineffective Relief of Bloating
  - OTC laxatives: 67%
  - Prescription laxatives: 52%
  - Fiber: 80%

Lubiprostone: A Chloride Channel Activator

- Gastrointestinal-targeted bicyclic functional fatty acid
- Activates ClC-2 chloride channels
  - Movement of Cl⁻, Na⁺, H₂O follow
  - Increased luminal fluid secretion
  - Shortened colonic transit time

- Indicated for:
  - Treatment of chronic idiopathic constipation (24 µg BID) in the adult population including age > 65 years (FDA approval 2006)
  - Treatment of irritable bowel syndrome with constipation (8 µg BID) in women ≥ 18 years (FDA approval 2008)
Lubiprostone: Stool Frequency in Patients Over 65 with Chronic Constipation

N = 57 (patients aged ≥ 65 years vs placebo)

*P ≤ 0.03
†P < 0.0001

SBM = spontaneous bowel movement

Safety Profile of Lubiprostone

- Well tolerated in 4 week and 6-12 month trials
- Nausea, diarrhea, and headache
- No clinically significant changes in serum electrolyte levels
- Low likelihood of drug-drug interactions
  - Non-absorbed; works intraluminally and does not result in measurable blood levels

Directed testing
Refer to a specialist as needed

Alarm Symptoms

No Alarm Symptoms

Lifestyle, OTC, stimulant laxative

Trial of lactulose or PEG 3350

No response
+ Response

Trial of lubiprostone

No response
+ Response

Bleeding, anemia, weight loss, sudden change in stool caliber, abdominal pain

OTC = over-the-counter therapies (probiotics, herbal medications, stool softeners [docusate sodium], psyllium, methylcellulose, calcium polycarbophil, bisacodyl, senna)
# Treatment for IBS-C

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psyllium</td>
<td>Moderately effective; single study reported improvement with calcium polycarbophil</td>
</tr>
<tr>
<td>Wheat or corn bran</td>
<td>No more effective than placebo in relief of global IBS symptoms; Not recommended for routine use</td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>Shown to improve stool frequency, but not abdominal pain in 1 small study</td>
</tr>
<tr>
<td></td>
<td>No publications of placebo-controlled, randomized studies of laxatives in IBS-C</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Short-term course of a non-absorbable antibiotic is more effective than placebo for global improvement of IBS and for bloating. No data to support long-term safety and effectiveness</td>
</tr>
<tr>
<td>Probiotics</td>
<td>In single organism studies, lactobacilli do not appear effective for patients with IBS; bifidobacteria and some probiotic combinations demonstrate some efficacy</td>
</tr>
</tbody>
</table>

## Treatment for IBS-C

<table>
<thead>
<tr>
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<tr>
<td><strong>Antispasmodics</strong></td>
<td>Certain antispasmodics may provide short-term relief of abdominal pain/discomfort</td>
</tr>
<tr>
<td><em>(hyoscine, cimetropium, pinaverium, peppermint oil)</em></td>
<td>Evidence for long-term efficacy is not available; safety and tolerability evidence is limited</td>
</tr>
<tr>
<td><strong>Lubiprostone</strong></td>
<td>8 µg BID is more effective than placebo in relieving global IBS symptoms in women with IBS-C</td>
</tr>
<tr>
<td><strong>Tricyclic antidepressants</strong></td>
<td>More effective than placebo at relieving global IBS symptoms;</td>
</tr>
<tr>
<td><strong>Selective serotonin reuptake inhibitors</strong></td>
<td>Appear to reduce abdominal pain</td>
</tr>
<tr>
<td></td>
<td>Limited data on safety and tolerability</td>
</tr>
<tr>
<td></td>
<td>Tricyclic antidepressants may worsen constipation</td>
</tr>
<tr>
<td><strong>Psychotherapy</strong></td>
<td>Cognitive therapy, dynamic psychotherapy, hypnotherapy (not relaxation therapy) are more effective</td>
</tr>
<tr>
<td></td>
<td>in relieving global symptoms of IBS</td>
</tr>
</tbody>
</table>

Lubiprostone for IBS-C
Data From 2 Phase 3 Studies


**Response Rate (%)**

- Placebo N = 385
- Lubiprostone (8 µg BID) N = 769

Combined intent to treat population
Monthly responder for $\geq 2/3$ months during treatment

$P = 0.001$

Note the different dose!
For chronic constipation
lubiprostone: 24 µg BID
Lubiprostone – Symptom Change IBS-C

Baseline Score

Mean Change from Baseline

Abdominal Discomfort/Pain

Bloating

Constipation Severity

Stool Consistency

Straining

Nonresponder

Responder

§Score: 0 (absent); 1 (mild); 2 (moderate); 3 (severe); 4 (very severe)
†Score: 0 (very loose/watery); 1 (loose); 2 (normal); 3 (hard); 4 (very hard/little balls)


* P < 0.001
When to Change/Add Therapy for an Unresponsive Patient?

• No studies have examined this question\(^1\)
• Stepped Treatment Of Older adults on Laxatives (STOOL) trial was designed to investigate the efficacy of adding a second agent when the first constipation therapy failed\(^2\)
  – It closed early with only 19 enrolled participants
• In general, the prescribing clinician may elect to combine therapy depending on the patient’s response and lingering symptoms; recommended more often for patients with severe symptoms
• Combine agents with different mechanisms of action, such as lubiprostone with senna, or an antispasmodic with a laxative for IBS-C

Post-Stroke Patient

Special Considerations

• Recent studies have reported constipation in 55% of patients at the acute stage (4 weeks)\(^1\), and in 30% ≥ 3 months\(^2\) following stroke

• Patient limitations
  – Positioning problems
  – Reduced peristalsis
  – Immobility

Treatment Strategy*

1. Appropriate assessment of bowel function, frequency, consistency
2. Tailor a specific bowel management program to facilitate/initiate defecation
3. Careful documentation with a bowel diary
4. Glycerin suppositories, laxatives, motility agents to promote defecation

*Treatment strategy based on clinical experience

Patient With Dementia

Contributing Factors

- Immobility
- Dehydration
- Inadequate food intake
- Depression
- Cognitive deficits
- Cannot find the bathroom
- Inability to undress
- Cannot ask for help
- Cannot sense the urge to defecate
- Use of psychotropic drugs

Treatment Strategy*

1. Appropriate assessment of bowel function
2. Establish a bowel routine, regular toileting program
3. Suppositories, stool softeners, bulking agents
4. Careful documentation (bowel diary, effectiveness of treatments, etc.)
5. Involve family or health care team (in a nursing facility)
6. Address nutritional/fluid needs

*Treatment strategy based on clinical experience
Patients Treated With Opiates

Special Considerations
- Opioids inhibit GI propulsive motility and secretion
- GI effects of opioids are mediated primarily by µ-opioid receptors within the bowel
- Constipation is a common and troubling side effect
- Patients do not develop tolerance to the effects of opiates on the bowel

Treatment Strategy*
1. Laxative therapy should be initiated proactively with start of opiate use
2. Magnesium hydroxide, senna, lactulose, bisacodyl, stool softener
3. A combination of a stimulant and stool softener is often required
4. Laxative doses may need to be increased along with increased doses of opioids
5. Titrate doses of laxatives according to response prior to changing to an alternative laxative
6. When laxative therapy is inadequate, consider methylnaltrexone

*Treatment strategy based on clinical experience
A Role for Peripheral μ-opioid Receptor Antagonists?

• Methylnaltrexone
  – Novel, quaternary μ-opioid receptor antagonist
  – Does not antagonize the central (analgesic) effects of opioids or precipitate withdrawal
  – FDA approved for treatment of opioid-induced constipation in patients with advanced illness, receiving palliative care, when laxative therapy has been inadequate
  – Subcutaneous injection; one dose (0.15 mg/kg) every other day as needed, no more than 1 dose in a 24 hr period
  – Abdominal pain and flatulence most common adverse events

Neurologic Disorders: Parkinson’s Disease

Special Considerations
• Constipation occurs in at least 2/3 of patients
• Multifactorial:
  – Slow colonic function
  – Defecatory dysfunction
  – Enteric and central nervous system
  – Antiparkinsonian medications
    ➢ Anticholinergic agents
    ➢ Dopaminergic agents
• Underlying illness is chronic and uncorrectable

Treatment Strategy*
1. Adjust medications if possible
2. Initiate pharmacologic therapy
   – May need to use medications from several classes
   – Osmotic laxatives, CI channel activators, stimulant laxatives

*Treatment strategy based on clinical experience
Chronic Constipation Secondary to Diabetes

Special Considerations
• Constipation occurs in 20% of patients with diabetes
• Related to duration of diabetes > 10 years
• Diabetic autonomic neuropathy
• Gastrocolic reflex may be absent, delayed, blunted
• Constipation may be severe and can lead to megacolon

Treatment Strategy*
1. Optimize diabetes care
2. Stepwise pharmacologic therapy
   – Exclude slow transit
   – Bulking agents, osmotic laxatives, Cl channel activators, stimulant laxatives

*Treatment strategy based on clinical experience

Complications of Chronic Constipation

- Fecal impaction\textsuperscript{1,2}
  - Identified in up to 40\% of elderly adults hospitalized in United Kingdom
- Intestinal volvulus/obstruction\textsuperscript{2}
- Urinary and fecal incontinence\textsuperscript{2}
- Stercoral ulceration/ischemia\textsuperscript{2}
- Bowel perforation\textsuperscript{2}
- Possible increased risk of colorectal cancer (controversial)\textsuperscript{3,4}

Fecal Impaction

Recognition/Identification

• Maintain high level of vigilance for institutionalized patients or patients in the hospital
  – Absence of bowel movement, absence of bowel sounds
  – Fecal soiling, fecal incontinence of liquid stool
• Assessment
  – Digital rectal exam
  – Abdominal x-ray

Treatment Strategy*

1. Prevention!!
2. Treat from below
   • Enema, suppository
   • Manual disimpaction with prior pain medication
3. Treat from above
   • Osmotic laxatives
4. Institution of preventative measures
   • Diet, laxatives, bowel regimen

*Treatment strategy based on clinical experience
Emerging Therapies

**Prucalopride**
- Selective 5-HT₄ agonist
- Does not interact with 5-HT₃ or 5-HT₁B receptors
- Increases colonic motility and transit
- Phase 3 studies have demonstrated efficacy of 2 or 4 mg prucalopride in patients with severe chronic constipation
- Adverse events included headache, abdominal pain, nausea, diarrhea

**Linaclotide**
- Guanylate cyclase agonist
- Induces intestinal fluid secretion
- Pilot study showed improved spontaneous bowel movement frequency and improved symptoms in patients with chronic constipation
- Also being studied in patients with IBS-C

# Myths and Misconceptions About Chronic Constipation

<table>
<thead>
<tr>
<th>Misconception</th>
<th>Reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases arise from autointoxication by retained stools</td>
<td>• No evidence to support this theory</td>
</tr>
<tr>
<td>Fluctuations in hormones contribute to constipation</td>
<td>• Fluctuations in sex hormones during the menstrual cycle have minimal impact on constipation, but are associated with changes in other GI symptoms</td>
</tr>
<tr>
<td></td>
<td>• Changes in hormones during pregnancy may play a role in slowing gut transit</td>
</tr>
<tr>
<td>A diet poor in fiber causes constipation</td>
<td>• A low fiber diet may be a contributory factor in a subgroup of patients with constipation</td>
</tr>
<tr>
<td></td>
<td>• Some patients may be helped by an increase in dietary fiber, others with more severe constipation may get worse symptoms with increased dietary fiber intake</td>
</tr>
<tr>
<td>Increasing fluid intake is a successful treatment for constipation</td>
<td>• No evidence that constipation can be treated successfully by increasing fluid intake unless there is evidence of dehydration</td>
</tr>
</tbody>
</table>

## More Misconceptions About Chronic Constipation

<table>
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</table>
| Stimulant laxatives damage the enteric nervous system and increase the risk of cancer | • Unlikely that stimulant laxatives at recommended doses are harmful to the colon  
  • No data support the idea that stimulant laxatives are an independent risk factor for colorectal cancer |
| Laxatives cause electrolyte disturbances          | • Laxatives can cause electrolyte disturbances, but appropriate drug and dose selection can minimize such effects                       |
| Laxatives induce tolerance                        | • Tolerance is uncommon in most laxative users, however tolerance to stimulant laxatives can occur in patients with severe constipation and slow colonic transit |
| Laxatives are addictive                           | • No potential for addiction to laxatives, but laxatives may be misused                                                               |

Patient and Caregiver Education

- Provide reassurance
- Engage patients/caregivers in a discussion of constipation
- Discuss medicines that can contribute to chronic constipation
- Discuss criteria for diagnosis, share a diagnostic algorithm
- Utilize patient questionnaire/symptom log
- Discuss treatment options, including
  - Common side effects
  - How long a treatment might take to work
  - Is it appropriate to request an alternative treatment?
- Answer questions!
- Emphasize the goals of treatment
  - Improve symptoms
  - Restore normal bowel function
  - Improve quality of life
Summary

• Chronic constipation is a common condition in the elderly

• Quality of life in elderly patients is negatively affected by the symptoms of chronic constipation and IBS-C

• Identify risk factors and secondary causes for constipation
• Be vigilant for red flags or alarm symptoms; directed tested may be necessary

• Main objective of treatment for chronic constipation is to improve patients’ symptoms, restore normal bowel function (≥ 3 bowel movements per week), improve quality of life
Summary (cont)

• Evidence-based therapeutic options for chronic constipation include psyllium, lactulose, polyethylene glycol, and lubiprostone

• Psyllium, polyethylene glycol, antibiotics, probiotics, antispasmodics, antidepressants, lubiprostone and psychotherapy are treatments for IBS-C with varying degrees of efficacy

• Long-term safety and efficacy data needed for therapeutic options for both chronic constipation and IBS-C, particularly in older (> 65) adults

• Careful recognition, assessment, treatment, and monitoring can lead to more effective patient-specific interventions that can reduce the burden of chronic constipation or IBS-C