**INTRODUCTION**

Chronic constipation, widely prevalent and commonly seen in clinical practice, can have a significant impact on patients’ quality of life. It also has a major impact on the U.S. economy in terms of both health care costs and lost productivity.

Commonly accepted treatments vary in terms of their efficacy and safety—and both physicians and their patients have expressed a strong desire for improved therapeutic options. This article provides a brief overview of chronic constipation, including its definition, potential impact, and treatment. The objective is to give managed care decision makers and prescribing physicians the means to make informed choices about this all-too-prevalent condition.

**WHAT IS CHRONIC CONSTIPATION?**

Although chronic constipation is a common digestive complaint in North America, the definition of constipation varies widely. Physicians tend to think of constipation as strictly a matter of frequency, namely, defecation every three to four days or less. Patients, however, usually define constipation more by its symptoms, such as straining and hard stools, rather than by the actual frequency of defecation.

In order to devise a uniform standard, the Rome Committee defined functional constipation as a unique category separate from chronic constipation. The consensus-based Rome III criteria of functional constipation are shown in Table 1. These criteria have been revised from the Rome II criteria. The main difference between Rome II and Rome III criteria lies in the less restrictive time frame for symptoms. Whereas Rome II criteria require symptoms to be present for at least 12 weeks (not necessarily consecutive) in the previous 12 months, Rome III criteria require symptoms to originate from six months prior to diagnosis, and to be currently active (i.e., the patient meets the criteria) for three months.

**A SYMPTOM-ORIENTED DISORDER**

There is a widespread misconception that the most common symptom of chronic constipation is infrequent bowel movements (i.e., fewer than three bowel movements a week). In fact, one study of patients who met the Rome II criteria for chronic constipation found that most reported more than three bowel movements per week. Much more commonly reported was straining during a bowel movement, hard or lumpy stools, a feeling of incomplete evacuation, sensations that the stool could not be passed, and abdominal fullness or bloating (Figure 1).

**SUBTYPES OF PRIMARY CHRONIC CONSTIPATION**

Primary chronic constipation has been divided into three pathophysiological subtypes: (1) slow-transit constipation, (2) dyssynergic defecation, and (3) normal-transit constipation. There is a significant overlap among different types of constipation, and symptoms alone cannot differentiate the various types.

**Slow-transit constipation**, also known as colonic inertia, is the diagnosis when the measured colonic transit time is pro-

---

**Table 1: Rome III Criteria**

<table>
<thead>
<tr>
<th>1. The Rome III guidelines define patients with chronic constipation as having two or more of the following symptoms for the last three months, with symptom onset at least six months prior to diagnosis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• straining in at least 25% of defecations</td>
</tr>
<tr>
<td>• lumpy or hard stools in at least 25% of defecations</td>
</tr>
<tr>
<td>• sensation of incomplete evacuation in at least 25% of defecations</td>
</tr>
<tr>
<td>• sensation of anorectal obstruction or blockage for at least 25% of defecations</td>
</tr>
<tr>
<td>• manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation or support of the pelvic floor)</td>
</tr>
<tr>
<td>• Fewer than three defecations per week</td>
</tr>
</tbody>
</table>

2. Loose stools are rarely present without the use of laxatives.

3. There are insufficient criteria for irritable bowel syndrome.

---

Disclosure: Dr. Tuteja has disclosed that he has received honoraria from, and has served on the Advisory Boards of, Takeda Pharmaceuticals and Novartis Pharmaceuticals. He has also received research grant support from Novartis. This article was supported in part by a grant to the authors from Takeda.
Chronic Constipation

longed. This type of constipation most commonly occurs in young women who present with infrequent defecation and bloating.6,7

Dyssynergic defecation is also known as pelvic floor dys- syner gia, obstructed defecation, outlet obstruction, or anismus.7,8 It is caused by a lack of coordination between the abdominal and pelvic floor muscles during defecation, which leads to an inability to defecate.8,9 This condition often results in a feeling of anal blockage, severe straining, and the need to remove impacted stool.10 However, symptoms alone cannot be used to diagnose dyssynergic defecation. Both symptoms and physiological tests are required to make a diagnosis.8

Patients with normal-transit (functional) constipation have normal colonic transit times6 and normal pelvic-floor function. This is the most prevalent of all chronic constipation subtypes.6,11 Abdominal pain and bloating can be present.3 Patients with constipation–predominant irritable bowel syndrome (IBS-C) experience a normal transit time, and it can be difficult to differentiate functional constipation from IBS-C.10

Although there is a significant overlap in symptoms between the three subtypes, identifying the predominant cause of chronic constipation is highly useful, because treatment strategies vary.7

EPIDEMIOLOGY

Prevalence

The exact number of people who experience chronic constipation is not known. The prevalence varies according to the demographic features and the definition used. Studies of prevalence have estimated the rate to be as high as 27%, but 15% is the more commonly accepted number.1

Demographic patterns from several studies suggest that chronic constipation is more prevalent in certain populations such as women and people older than 65 years of age.6,12 For every man who experiences chronic constipation, it is thought that two to three women have the same disorder.12,13 The rate of chronic constipation for patients over 65 years of age has been reported to be as high as 40%, signaling that this group of patients is particularly at risk.13

Quality of Life

Patients with chronic constipation report lower levels of general well-being.14 Constipation has been associated with depression.14,15 Subjects with self-reported constipation also have significantly lower quality-of-life scores in all domains of the Short-Form Health Survey (SF-36) (Figure 2).16

Economic Impact

In 2001, there were more than 5.7 million outpatient visits made for the diagnosis and management of constipation, with an estimated cost of $29 million (in 1985 dollars) for ambulatory physician visits.17,18 In one study, a diagnostic evaluation for chronic constipation alone cost, on average, an estimated $2,752 per patient.19 The annual cost of care related to constipation for nursing-home patients, including expenses for labor and supplies, has been estimated at $2,253.20 Although serious complications are still somewhat rare, when they do occur, they can easily translate into substantial costs in the hospital setting. For example, in 2003, volvulus related to constipation cost Medicare just over $48,000 per patient. During that same time period, constipation-related hemorrhoids, intestinal impaction, and ulcers cost Medicare in the range of $9,000 to $21,000 per patient (Table 2).21

Indirect costs can also take a significant toll. In one study, patients with functional constipation missed 21.9 days of work or school in the previous year (an adjusted mean number), compared with 4.9 days for patients without a func-

continued on page 99
Chronic Constipation

A survey of slightly more than 550 patients who met the Rome II criteria found that 12% of the employed patients reported missing days from work or school during the previous month, and 60% reported impairment at work (a 21% reduction in productivity). An estimated 13.7 million days of restricted activity and 3.4 million days of disability associated with time spent in bed are reported annually as a result of constipation.

**MEDICAL COMPLICATIONS OF CHRONIC CONSTIPATION**

If left untreated, chronic constipation can have serious consequences. It has been suggested that it can lead to pudendal nerve damage, resulting in fecal incontinence and rectal prolapse. Chronic constipation has also been associated with urological abnormalities, urinary tract infections and hemorrhoids may also be associated with constipation.

An analysis of more than 100,000 Medicaid patients who made at least one physician visit for constipation was performed. These patients, when compared with controls, experienced a significantly higher risk of comorbidities such as intestinal impaction, anal fissure, hemorrhoids, and volvulus (Table 3). One limitation of this study was that because chronic constipation is so common, the control group probably included patients who had the disorder but who

---

**Table 2**  **Hospital Cost Per Patient in 2003: Complications and Comorbidities of Constipation**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>ICD-9</th>
<th>Medicare (Mean Charge)</th>
<th>Commercial (Mean Days)</th>
<th>Length of Stay (Mean Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal impaction</td>
<td>560.30</td>
<td>$11,307</td>
<td>$7,844</td>
<td>3.7</td>
</tr>
<tr>
<td>Anal fissures</td>
<td>565.0</td>
<td>$13,949</td>
<td>$11,923</td>
<td>3.0</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>455.6</td>
<td>$9,757</td>
<td>$9,049</td>
<td>2.3</td>
</tr>
<tr>
<td>Volvulus</td>
<td>560.2</td>
<td>$48,812</td>
<td>$35,034</td>
<td>9.8</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>560.9</td>
<td>$17,141</td>
<td>$13,598</td>
<td>4.8</td>
</tr>
<tr>
<td>Ulcers (stercoral/rectal)</td>
<td>569.41</td>
<td>$21,495</td>
<td>$20,547</td>
<td>5.7</td>
</tr>
</tbody>
</table>

had not been assigned an International Classification of Diseases (ICD-9) code or who had not sought care for the condition. This would have reduced the magnitude of the relative risks.

TREATMENT OPTIONS

Chronic constipation is an undertreated disorder. Only 26% of patients meeting the Rome II diagnostic criteria for this condition are thought to seek medical attention.29

Many patients mistakenly believe that constipation is a temporary and personal problem rather than a medical problem. In addition, the social stigma and embarrassment surrounding discussions of bodily functions may deter some people from seeking medical help. Attempts to self-treat with over-the-counter products resulted in slightly more than $700 million in sales of laxatives in 2004.30

For those who do eventually seek medical care for this disorder, there are currently three treatment options: lifestyle and dietary changes, pharmacological treatments, and biofeedback.

Lifestyle and Dietary Alterations

Lifestyle adjustments are typically suggested as a first line of treatment; these usually entail an increase in fluid intake, fiber consumption, and exercise. There is a shortage of adequately controlled trials evaluating the efficacy of these lifestyle changes.31 Habit training to achieve a regular bowel movement schedule has been studied primarily in children.32

Increasing fluid intake does not appear to affect stool volume output, probably because most of the ingested water is absorbed in the small intestine before it can enter the colon.33 Similarly, regular exercise (as perceived by the average person) has no established link to constipation relief.34,35

Dietary fiber, believed to alleviate constipation by improving gastrointestinal transit and producing larger, softer stools, can be increased with the addition of high-fiber foods (such as vegetables and whole grains) to the diet or by taking commercially available supplements. Unfortunately, increasing fiber has a tendency to cause undesirable side effects, such as bloating and increased flatulence, that make long-term patient compliance less likely.36

Pharmacological Agents

Bulking Agents

Bulking agents are concentrated forms of fiber and are composed of naturally occurring psyllium or synthetic polysaccharides or cellulose derivatives. They add water and additional solid material to stool, which may improve chronic constipation in a manner similar to that of fiber naturally contained in the diet. Fluid intake should be increased. The side effects are similar to those associated with dietary fiber (i.e., bloating and flatulence).36

Osmotic Laxatives

Osmotic laxatives are hypertonic agents that draw water into the colon. They include saline laxatives such as magnesium hydroxide (milk of magnesia) and sodium phosphate (phosphate soda). Both oral and rectal forms of sodium phosphate (such as a Fleet enema) are available. However, a small amount of magnesium and phosphate is actively absorbed in the small intestine, and hypermagnesemia and hyperphosphatemia can occur, especially in patients with renal failure.

Other osmotic laxatives include lactulose, sugar alcohols (sorbitol or mannitol), and polyethylene glycol (PEG).

Lactulose is a synthetic disaccharide that is broken down by bacteria in the colon to yield organic acids and carbon dioxide to lower the pH and soften the stool. The main disadvantages of lactulose are abdominal distention, flatulence, and its overly sweet taste.36

Sorbitol and mannitol, like lactulose, are poorly absorbed in the small intestine and produce abdominal distention and flatulence.

Polyethylene glycol is an inert polymer that is not absorbed by the gut; it is excreted unchanged in the feces. It opposes the absorption of water, which results in loose stools. The PEG solution is formulated alone or with electrolyte solutions. It is commonly used for bowel cleaning before colonoscopy (e.g., CoLyte, Schwarz; GoLytely, Braintree Labs). Smaller-dose packets are available and are used in the treatment of constipation (e.g., MiraLax, Braintree Labs).

A sufficient amount of water must be used with MiraLax to avoid dehydration. It is recommended that 250 ml of water
be ingested with 17 g of MiraLax, although it might be difficult for some patients to consume this much water. This osmotic laxative is indicated for short-term, intermittent use only (up to two weeks). Nausea, abdominal bloating, cramping, and flatulence may occur with PEG formulations. Prolonged, frequent, or excessive use of PEG solutions may lead to electrolyte imbalance.

Glycerine is an osmotic agent that is absorbed well in the small intestine and is therefore used as a suppository. It draws water into the rectum to produce a bowel movement.

Stimulant Laxatives

Stimulant laxatives not only stimulate intestinal motility but also affect mucosal transport. Examples include docusate sodium (Colace), diphenylmethanes (bisacodyl), anthraquinones (Cascara sagrada and senna), and castor oil. The docusates were designed to lower surface tension and soften the stool. They also stimulate intestinal fluid and water secretion. In a placebo-controlled study, docusate had no effect on stool weight, stool frequency, stool water, or mean transit time.

Bisacodyl is available in both tablet form and as suppositories. The laxative effect of the anthraquinones is secondary to net water secretion and the stimulation of colon motility. The side effects of stimulant laxatives include abdominal cramping and melanosis coli with anthraquinones.

A randomized double-blind, placebo-controlled, crossover study in patients with chronic idiopathic constipation demonstrated that colchicine increased the number of bowel movements and accelerated colon transit time compared with placebo. Abdominal pain was more common in the treatment group.

Similarly, misoprostol stimulates intestinal transit time and has been shown to be effective in the treatment of chronic constipation. However, side effects can be a limiting factor in the use of these agents for long-term therapy.

---

Chronic Constipation

![Graph of Physician satisfaction](image)

Physician satisfaction

![Graph of Patient satisfaction](image)

Patient satisfaction

**FIGURE 3** Level of satisfaction with laxative treatment options. (Data from Schiller LR, Dennis E, Toth G. Am J Gastroenterol 2004; 99[Suppl]: S234, S234–S235.)

---

**Table 4** A Closer Look at Two Treatment Options

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Lubiprostone (Amitiza)</th>
<th>Tegaserod (Zelnorm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>Local, chloride-channel (CIC-2) activator</td>
<td>Systemic 5-HT4 agonist</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Nausea, diarrhea, headache</td>
<td>Diarrhea, headache, abdominal pain</td>
</tr>
<tr>
<td>Pregnancy rating</td>
<td>C</td>
<td>B</td>
</tr>
<tr>
<td>Indications</td>
<td>Chronic idiopathic constipation in adult men and women, no age limit</td>
<td>• IBS-C in women for 12 weeks</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Chronic idiopathic constipation in men and women ≤65 years of age</td>
</tr>
<tr>
<td>WAC/price</td>
<td>$2.43</td>
<td>$2.70</td>
</tr>
</tbody>
</table>

---

* Pregnancy rating: A = controlled studies showing no risk; B = no evidence of risk; C = risk cannot be ruled out; D = positive evidence of risk; X = contraindicated in pregnancy.

IBS-C = irritable bowel syndrome; 5-HT4 = 5-hydroxytryptamine-4; WAC = wholesale acquisition cost.

Data from various product materials, Med Lett Drugs Ther, Formulary, and IMS Health data.
Enemas and Suppositories
Enema contents may include tap water or osmotic laxatives. Glycerin and bisacodyl can be administered as a suppository, and these measures are often effective. However, their regular use can result in trauma from insertion and can damage the rectal epithelium.

Biofeedback
Biofeedback therapy is used mainly for the treatment of dyssynergic defecation. The goal of biofeedback is to restore a normal pattern of defecation via neuromuscular conditioning. Biofeedback therapy is a labor-intensive and multi-disciplinary approach that is not associated with any adverse effects, but it is offered only in a few centers. More controlled clinical trials are needed to validate its efficacy.

Limitations of Current Treatments
Both physicians and patients are aware of the limitations of the current laxative treatment options for chronic constipation (Figure 3). In a 2004 report, 91% of primary care physicians expressed a wish for better treatment options for constipation. Only 50% of patients being treated for chronic constipation were satisfied with their current laxative treatment. Taken together, these statistics demonstrate the need for more satisfactory therapeutic options.

Ideal treatments would address the lack of consistent efficacy and potential side effects associated with these agents, such as electrolyte imbalance. They would also be available to the large numbers of patients with chronic constipation, independent of age or sex.

Newer Agents
Tegaserod
Tegaserod (Zelnorm, Novartis) is a partial 5-hydroxytryptamine-4 (5-HT4) receptor agonist. It increases peristalsis and intestinal secretion, and it inhibits visceral hypersensitivity. Tegaserod is currently approved for the treatment of IBS-C in women and chronic idiopathic constipation in men and women younger than 65 years of age (Table 4 and Figure 4).

In clinical trials, the most common adverse events observed with tegaserod 6 mg for chronic idiopathic constipation were diarrhea, abdominal pain, and nausea. Reports of intestinal ischemia have also been noted. It is not known whether this effect is causally related to the drug. Recent data suggest that the drug is safe and effective for long-term use in those patients with chronic constipation and constipation-predominant IBS.

Lubiprostone
Lubiprostone (Amitiza, Sucampo) was approved in 2006 for the treatment of chronic idiopathic constipation in adult men and women. As a novel functional fatty acid with local activity, it increases intestinal fluid secretion by selectively activating gastrointestinal type-2 chloride channels. Lubiprostone accelerates small-bowel and colonic transit time and the passage of stools without altering serum electrolyte levels.

Multicenter clinical trials have demonstrated that lubipro-
stone provides an improvement in the percentage of patients experiencing spontaneous bowel movements within the first 24 hours after treatment when compared with placebo (Figure 5). In addition, treated patients experienced improvements in constipation-related symptoms, such as straining, abdominal bloating, and discomfort, when compared with patients receiving placebo. Results from these trials were consistent for all ages and both sexes (see Table 4).

The most common adverse events observed in those receiving lubiprostone were nausea, diarrhea, and headache. Nausea diminished when lubiprostone was administered with food.

The recommended dosage of lubiprostone is 24 mcg, administered twice daily in the form of gelatin capsules. Open-label clinical trials lasting up to 12 months reported that lubiprostone was safe and efficacious in decreasing constipation severity as well as abdominal discomfort and bloating. In addition, lubiprostone has been approved for use in patients over age 65. Lubiprostone appears to be a safe and viable treatment option for patients with chronic idiopathic constipation. A recent publication and clinical review found that on the basis of the available data and depending on overall cost, lubiprostone is worth considering for inclusion in formularies. Its place in the management of chronic constipation will be determined as it gains wider use and clinical experience.

**CONCLUSION**

Chronic idiopathic constipation is a symptom-based disorder affecting a significant portion of the American public every year. Women and the elderly are particularly at risk. This disorder also has a noteworthy impact on the economy as well as health and quality of life.

Many patients with constipation try to manage their symptoms with over-the-counter laxatives and lifestyle changes. However, if these steps do not work, new therapies are available that improve the well-being of patients with chronic idiopathic constipation.

**REFERENCES**


55. IMS Health data, August 2006.