

5-step plan to treat constipation in psychiatric patients

Algorithm can individualize treatment when drugs or other factors are binding

Mr. W, age 50, presents to the psychiatry clinic with obsessive-compulsive disorder (OCD) symptoms. At his first interview, he says he spends every waking hour obsessing over whether or not he does things “right.” These thoughts force him to compulsively check and recheck everything he does, from simple body movements to complex computer tasks.

He has a history of OCD since age 8, with intermittent episodes of major depression. He reports that several years ago, he had a “miraculous” response to clomipramine for several weeks but has not responded to any other medication. Nevertheless, he continues taking clomipramine, 50 mg/d, hoping that it “might eventually do some good.” He adds that when he tried to increase the dose, he suffered from “terrible constipation” despite regular use of a methylcellulose fiber supplement.

The psychiatrist discontinues clomipramine and starts Mr. W on duloxetine, 90 mg/d. At the next visit, Mr. W complains that his constipation is much worse, so the psychiatrist decreases duloxetine to 60 mg/d, which eventually provides some relief. Because Mr. W has minimal response to duloxetine after 6 months, the psychiatrist adds olanzapine. Although this agent is anticholinergic, the patient had responded to a previous trial of this antipsychotic. Soon after, Mr. W experiences severe constipation.

Psychiatric patients face a host of potential causes of constipation, including:

- use of psychotropics and other medications
- decreased eating or physical activity as a result of depression or another psychiatric disorder

continued



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Nathaniel S. Winstead, MD, MSPH

Staff Physician, Section of Gastroenterology and Hepatology
Ochsner Clinic Foundation
Clinical Associate Professor of Medicine
Department of Internal Medicine

Daniel K. Winstead, MD

Professor and Chairman
Department of Psychiatry and Neurology

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Tulane University School of Medicine
New Orleans, LA



Constipation

Clinical Point

Patients who report straining, incomplete evacuations, or other symptoms may meet constipation criteria despite having daily bowel movements

Box 1

Diagnostic criteria for functional constipation

1. 2 or more of the following
 - a. Straining*
 - b. Lumpy or hard stools*
 - c. Sensation of incomplete evacuation*
 - d. Sensation of anorectal blockage/obstruction*
 - e. Manual maneuvers to facilitate defecation*
 - f. Fewer than 3 defecations per week

2. Loose stools are rarely present unless the patient takes a laxative

3. Patient does not meet criteria for irritable bowel syndrome

* Must be present during $\geq 25\%$ of defecations
Source: Reference 8

Table 1

Colorectal cancer screening recommendations*

Test	Frequency
Fecal occult blood testing (FOBT)	Annually
Sigmoidoscopy	Every 5 years
FOBT and sigmoidoscopy	Every 5 years
Double contrast barium enema	Every 5 years
Colonoscopy	Every 10 years

* For patients age ≥ 50 . For higher-risk patients, it is reasonable to begin screening at a younger age
Source: Reference 10

- medical comorbidities that decrease gastrointestinal (GI) motility.

Constipation carries a tremendous cost in terms of resources and quality of life.¹⁻⁷ This condition also can make patients stop taking medications. You can help patients avoid the discomfort and quality-of-life consequences by promptly diagnosing constipation and following a 5-step treatment algorithm that has shown value in our clinical practice.

What to look for

When evaluating a patient who complains of constipation, first determine what he or she means by “constipation.” Do not rely on

frequency of bowel movements as the only criterion for diagnosis. Under Rome Committee for Functional Gastrointestinal Disorders guidelines for diagnosis of chronic (or functional) constipation, patients who move their bowels daily may meet criteria for chronic constipation if they experience straining, incomplete evacuation, or other symptoms (Box 1).⁸

Many patients who complain of constipation have daily, regular bowel movements that produce hard, difficult-to-pass stool or require straining or manual maneuvers. Take a careful history including:

- stool frequency and quality
- straining
- manual maneuvers (disimpaction or manual pelvic floor support)
- sensation of blockage or incomplete evacuation.

In women, take a history of childbirth and obstetric or gynecologic surgery. Also determine the timing of symptom onset related to any new prescription or over-the-counter medications or supplements.

‘Alarm’ symptoms. For psychiatrists, the most important part of the Rome guidelines are the “alarm” symptoms:

- age ≥ 50 years
- family history of colon cancer or polyps
- family history of inflammatory bowel disease (ulcerative colitis or Crohn’s disease)
- rectal bleeding, anemia
- weight loss >10 pounds
- new onset of chronic constipation without apparent cause in an elderly patient
- severe, persistent constipation refractory to conservative management.⁹

Refer a patient with any of these symptoms to a specialist for endoscopic or clinical evaluation. Follow United States Preventative Services Task Force recommendations for colorectal cancer screening of all patients age ≥ 50 (Table 1).¹⁰

Determining the cause

Common causes of constipation include altered visceral sensitivity, decreased GI

Don't overlook 2 easily missed constipation causes

Outlet obstruction, caused by inappropriately contracting posterior pelvic floor muscles during defecatory effort, is the cause of 5% to 10% of constipation cases.¹ Patients are not aware of this pelvic floor incoordination. Often, they will give a history of straining even for soft or liquid stool.

Consider outlet obstruction in women with history of multiple vaginal childbirths or pelvic or gynecologic surgery, particularly if they fail to respond to usual measures to treat constipation. For adequate relief,

these patients often require anorectal biofeedback, which teaches them to relax the posterior pelvic floor.^{11,12}

Habitually suppressing the gastrocolic reflex—the urge to defecate after eating—causes some patients difficulty moving their bowels. Counsel these patients to sit on the toilet for several minutes after the morning meal to relearn this behavior. Some may need several weeks of daily enema or glycerine suppository use to retrain themselves to have bowel movements after the morning meal.

motility, alterations in pelvic and anorectal musculature, and alterations in the enteric nervous system. Systemic causes are less common and include electrolyte abnormalities (hypercalcemia and hypokalemia) and endocrine disorders (hypothyroidism and diabetes mellitus).

Some patients' constipation is caused by involuntarily contracting the pelvic floor muscles or suppressing the urge to defecate (**Box 2**).^{1,11,12} Suspect this in patients who strain repeatedly to pass soft or liquid stool.

Medication side effects are probably the most common constipation cause psychiatrists will encounter. Many psychotropics have anticholinergic effects that decrease GI motility and cause constipation. The most commonly implicated drugs are:

- older tricyclic antidepressants (such as amitriptyline)
- antipsychotics.

Among antipsychotics, clozapine, thioridazine, olanzapine, and chlorpromazine probably have the greatest anticholinergic effects.¹³ Many selective serotonin reuptake inhibitors also can cause constipation.

Older psychiatric patients with constipation may be taking medications for medical conditions—particularly alpha, beta, and calcium channel blockers—that may have synergistic effects on slowing bowel motility. For these patients you may not have the luxury of making multiple medication changes. The correct management

strategy may be to add docusate sodium, a stool softener available over-the-counter as Colace.

Other psychiatric-related causes. Patients with depression may experience decreased stool output because of a lack of food intake or physical activity. These causes may be effectively addressed by treating the depression.

Give special consideration to patients with eating disorders and those who routinely use laxatives. A patient who is not eating will not produce the same amount of stool as one who eats regularly.

Constipated patients may require escalating doses of laxatives to obtain symptom relief; this does not constitute laxative abuse but rather tachyphylaxis. Chronic laxative use has not been shown to permanently decrease colonic motility,¹⁴ but patients who use laxatives chronically may have altered expectations of what is normal.

CASE CONTINUED

Recurring symptoms

After discontinuing Mr. W's olanzapine and duloxetine, the psychiatrist prescribes polyethylene glycol solution (MiraLax) and instructs Mr. W to increase his daily fluid and fiber intake. Although the solution works well, Mr. W complains of the cost. He then resumes methylcellulose and starts taking magnesium hydroxide chewable tablets (Milk of Magnesia) every 2 to 4 days as needed for constipation.

Clinical Point

Patients who use laxatives chronically may have altered expectations of what is normal in terms of bowel movements



Constipation

Clinical Point

Advise constipated patients that they may need to try multiple OTC agents to find one that is tolerable and effective for them

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Algorithm

A stepwise approach to managing constipation

Step 1

Recommendation	Comments
Increase activity or daily walking	Not rigorously studied in constipated patients; exercise is associated with decreased orocecal transit time ¹⁵
Increase fluid intake	Not rigorously studied in constipated patients ⁸
Increase dietary fiber intake	Not rigorously studied in constipated patients ⁸

Step 2

Recommendation	Comments
Fiber supplements	Psyllium compounds may be superior to methylcellulose, polycarbophil, and bran ¹¹

Step 3

Recommendation	Comments
Over-the-counter laxative pills	Senna compounds are derived from plants

Step 4

Recommendation	Comments
Over-the-counter laxative solutions	Milk of Magnesia is very inexpensive

Step 5

Recommendation	Comments
Prescription laxatives	Lubiprostone causes fetal loss in animals; tegaserod is available only under a treatment investigational new drug protocol

The psychiatrist prescribes mirtazapine for OCD symptoms, but soon stops this regimen because Mr. W complains of worsening constipation. Next Mr. W is started on fluvoxamine, which he had tried briefly many years before. The dosage is gradually titrated to 150 mg/d. Although Mr. W's OCD improves somewhat, he complains of agitation and once again of worsening constipation.

Treatment algorithm

To minimize trial and error, we use a stepwise approach to treating constipation (*Algorithm*).^{8,11,15} Although many standard recommendations have not been evaluated in large randomized controlled trials, they are supported by decades of observed actions among clinicians and thus remain valuable.

Multiple nonprescription agents are available to treat constipation, including:

- bulking agents (fiber supplements)
- lubricating agents
- stool softening agents
- stimulant and osmotic laxatives (*Table 2, page 38*).⁸

Advise patients that they may need to try multiple agents to find one that is tolerable and effective.

Steps 1 & 2. When initial attempts at increasing physical activity, fluid, and dietary fiber fail to yield a response, fiber supplements are commonly used as a second step in managing constipation. We advocate beginning with a supplement that contains psyllium—such as Fiberall or Metamucil—because psyllium has been shown to increase stool frequency. Supplements that contain methylcellulose (Citrucel), polycarbophil (such as Equalactin and Mitrolan), or bran have either not shown efficacy or have not been studied rigorously enough to merit recommendation.¹⁰ Some patients respond to other fiber products, but start a fiber-naïve patient with a psyllium-containing supplement.

Fiber supplements may cause increased gas and bloating, so start at a low dose and gradually increase over several weeks to mitigate these side effects.

Step 3. If fiber supplements fail, try a stimulant or osmotic laxative. Senna compounds such as Ex-Lax and Senokot and bisacodyl products such as Correctol and Dulcolax are stimulant laxatives. For patients who prefer natural therapies, we point out that senna is derived from plants.

In our experience, patients usually have tried bisacodyl before seeking treatment for constipation. Although bisacodyl may

be effective for some patients, others may need something stronger. Many gastroenterologists prefer prescribing osmotic or prescription laxatives.

Step 4. Osmotic laxatives generally are liquids, including magnesium hydroxide, polyethylene glycol solution, and the prescription agent lactulose. Magnesium hydroxide is inexpensive and can be taken chronically.

Step 5: Prescription medications

Tegaserod is a partial 5-HT₄ agonist and stimulator of GI motility and secretion. It also decreases visceral sensitivity.¹⁶ Tegaserod's manufacturer voluntarily withdrew the drug from the market because it may increase risk of cardiovascular ischemic events, including angina, heart attack, and stroke. Tegaserod is available only under a treatment investigational new drug (IND) protocol that includes obtaining approval from a local institutional review board. We recommend that psychiatrists should not prescribe tegaserod but refer patients to experienced gastroenterologists or other GI specialists.

Lubiprostone is a selective chloride channel activator that works only in the gut and results in net fluid excretion and increased stool frequency. The molecule is a prostaglandin derivative and is poorly absorbed.¹⁷

Because lubiprostone has been shown to cause fetal loss in animals (at the equivalent of 2 and 6 times the recommended human dose), women of reproductive age should use contraception while taking lubiprostone and carefully consider the risks and benefits of lubiprostone use during pregnancy.

CASE CONTINUED

Finding an effective strategy

The psychiatrist prescribes lubiprostone, 24 mcg bid, but Mr. W once again complains of the expense and says the drug does not work well. He quickly returns to his intermittent use of magnesium hydroxide tablets and occasionally takes bisacodyl tablets.

continued

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*Data compiled from a study comparing the young adult adaptive outcome of nearly 140 patients (ADHD and non-ADHD control) followed concurrently for at least 13 years.

Reference: 1. Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult outcome of hyperactive children: adaptive functioning in major life activities. *J Am Acad Child Adolesc Psychiatry*. 2006;45:192-202.

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Constipation

Clinical Point

Because probiotics are active cells, advise patients who try them to purchase supplements containing ‘live and active’ cultures

Table 2
Commonly used laxatives:
Mechanisms of action

Category	Agents
Bulk-forming	Methylcellulose (Citrucel), polycarbophil (Equalactin, Mitrolan, others), psyllium (Fiberall, Metamucil, others)
Lubricating	Glycerin (Sani-Supp), magnesium hydroxide and mineral oil (Magnolax), mineral oil (Fleet Mineral Oil, Zymenol, others)
Stool softener	Docusate sodium (Colace)
Osmotic	Magnesium hydroxide (Milk of Magnesia), polyethylene glycol (MiraLax), lactulose* (Cholac Syrup, Constulose, others), lubiprostone* (Amitiza)
Stimulant	Bisacodyl (Correctol, Dulcolax, others), castor oil (Alphamul, Emulsoil, others), senna/sennosides (Ex-Lax, Senokot, others), sodium bicarbonate and potassium bitartrate (Geo-Two evacuant)

* Available by prescription only

Source: Reference 8

To address Mr. W's OCD, the psychiatrist adds risperidone, 0.5 mg bid, to Mr. W's regimen. He has a modest response in OCD symptoms—30% of his day is now symptom-free—without worsening his constipation.

Probiotics and prebiotics

Emerging therapies for constipation include probiotics and prebiotics, which attempt to alter the gut flora and milieu.

The primary bacterial agents are *Lactobacillus* species and *Bifidobacterium* species. At least one probiotic *Bifidobacterium* product—Activia—is being marketed in the United States as a fortified yogurt.

Because limited clinical data are available on the effect of probiotics and prebiotics on constipation, their routine use is not indicated. However, patients who prefer not to take medication may wish to try them. Because these agents are active cells, advise patients to purchase a supplement with “live and active” cultures. Supplements that are shipped, stored, or sold at room temperature likely contain very few (if any) live cultures.

Investigational medications. Renzapride is a 5HT₄ receptor agonist and 5HT₃ receptor antagonist that has shown promise in a pilot study¹⁸ and is in phase III trials. Linaclotide is a peptide that activates chloride and bicarbonate secretion in the gut and may reduce visceral hypersensitivity. It too has shown promise in a pilot study.¹⁹

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Bottom Line

Psychotropic use, inactivity, and other factors may make psychiatric patients susceptible to constipation. A stepwise approach to treating constipation begins with recommending increased exercise, fluids, and dietary fiber. Progress through fiber supplementation to nonprescription and prescription laxatives as needed. Individual therapy for constipation often requires multiple therapeutic trials until a patient finds an acceptable strategy.

Related Resources

• Rome Foundation. Functional gastrointestinal disorders. www.romecriteria.org.

• Bleser S, Brunton S, Carmichael B, et al. Management of chronic constipation: recommendations from a consensus panel. *J Fam Pract* 2005;54(8):691-8.

Drug Brand Names

Amitriptyline • Elavil, Endep	Lubiprostone • Amitiza
Chlorpromazine • Thorazine	Mirtazapine • Remeron
Clomipramine • Anafranil	Olanzapine • Zyprexa
Clozapine • Clozaril	Risperidone • Risperdal
Duloxetine • Cymbalta	Thioridazine • Mellaril
Fluvoxamine • Luvox	Tegaserod • Zelnorm
Lactulose • Choloc Syrup,	
Constulose, others	

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*Data from a study comparing driving in 105 young adults with ADHD to 64 community control adults without the disorder.

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