World Gastroenterology Organisation Global Guidelines

A Global Cascade Approach to Diagnosis and Management of Chronic Constipation

2025

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Abbreviations

Abbreviations	Full Form
AGA	American Gastroenterological Association
CBT	Cognitive Behavioral Therapy
CI	Confidence Interval
CSBM	Complete Spontaneous Bowel Movement
GC-C	Guanylate Cyclase-C
IBS	Irritable Bowel Syndrome
IBS-C	Irritable Bowel Syndrome, Constipation-predominant
MR	Magnetic Resonance
NNH	Number Needed to Harm
NNT	Number Needed to Treat
NTC	Normal Transit Constipation
PAC-QOL	Patient Assessment Constipation – Quality of Life questionnaire
PAC-SYM	Patient Assessment Constipation – Symptoms questionnaire
PEG	Polyethylene Glycol
PTNS	Percutaneous Tibial Nerve Stimulation
SNS	Sacral Nerve Stimulation
STARR	Stapled Trans-Anal Rectal Resection
STC	Slow Transit Constipation
TTNS	Transcutaneous Tibial Nerve Stimulation
WGO	World Gastroenterology Organisation

1 Introduction

Chronic constipation is a prevalent gastrointestinal disorder characterized by infrequent bowel movements, which is typically defined as fewer than three per week, and is often accompanied by symptoms such as straining, hard stools, and a sensation of incomplete evacuation ([1], [2]). Globally, the prevalence of chronic constipation varies, affecting approximately 9-20% of the global population ([3], [4]). This disorder disproportionately impacts women and older adults, leading to significant health-related quality of life impairments and increased healthcare utilization ([5] [6] [7] [8]). Chronic constipation is classified into primary types—normal transit constipation, slow transit constipation, and defecatory disorders—and secondary causes related to medications, metabolic disorders, or structural abnormalities.

The pathophysiology involves colonic sensorimotor disturbances and pelvic floor dysfunction. Management follows a stepwise approach, beginning with lifestyle modifications such as increased fiber and fluid intake, regular exercise, and progressing to pharmacological options, including osmotic and stimulant laxatives, intestinal secretagogues, and prokinetic agents for refractory cases ([9]). Diagnostic evaluation may involve anorectal manometry and colonic transit studies to identify underlying mechanisms.

Given the substantial burden of chronic constipation on individuals and healthcare systems, there is a critical need for standardized, evidence-based guidelines. This document provides comprehensive recommendations to support healthcare professionals in effectively diagnosing and managing chronic constipation across diverse clinical settings worldwide.

This World Gastroenterology Organisation (WGO) guideline focuses on adult patients and does not specifically discuss children or special groups of patients (such as those with spinal cord injury).

1.1   Cascades—a resource-sensitive approach

The WGO "cascades" recognize the global variations in disease epidemiology, sociocultural factors, and healthcare systems. These differences often make it impractical to implement a single universal gold-standard approach. Instead, the WGO Guidelines provide a tiered framework that offers context-specific and resource-sensitive recommendations, ensuring adaptability to diverse healthcare settings.

This Global WGO Guideline introduces a series of cascades designed to guide the diagnosis and management of chronic constipation, making them applicable across different regions and healthcare infrastructures. Developed for healthcare professionals, including primary care physicians and gastroenterologists, this guideline aims to support clinical decision-making for chronic constipation in a manner that is both globally relevant and locally applicable, ultimately enhancing patient care worldwide.

> **Cascade:** a hierarchical set of diagnostic, therapeutic, and management options for dealing with risk and disease, ranked according to available resources.

2   Definition and pathogenesis

The term "constipation" varies in meaning and perception across patients, cultures, and regions, likely influenced by dietary habits, lifestyle, and societal norms. While physicians typically define constipation as infrequent bowel movements (usually <3 bowel movements per week), patients often describe a broader range of symptoms, including hard stools, incomplete evacuation, abdominal discomfort, bloating, straining, anorectal blockage, and the need for manual maneuvers.

Cultural and regional differences are known to significantly impact how constipation is experienced and reported by patients ([10]). Studies have shown that bowel movement patterns and symptom perception can vary across populations, with differences observed between countries such as India and the United States ([11]) whereby chronic constipation patients in India have more frequent (median of 5 vs. 3 bowel movements/week) and softer bowel movements (48% vs 65.5% proportion of patients with Bristol stool types 1 and 2) compared to those in the United States. In some regions, softer stools and more frequent defecation are reported despite similar diagnostic criteria. In palliative care, definitions often prioritize patient-reported symptoms over stool frequency ([12]).

Standardized criteria, such as those established by the Rome Foundation (Rome IV), define functional constipation based on key symptoms, including straining, hard stools, a feeling of anorectal obstruction, and reduced bowel movement frequency ([13]). Similarly, the American Gastroenterological Association (AGA) emphasizes both stool frequency and associated symptoms in its definition. Differences in the medical definition and variations in the reported symptoms make it difficult to provide reliable epidemiologic data. Even with the use of standardized clinical definitions, variations in constipation prevalence suggest that genetic, environmental, and dietary factors play a role in symptom manifestation. These differences underscore the importance of a culturally sensitive approach to diagnosis and management, ensuring that treatment strategies are tailored to the specific needs of diverse populations worldwide.

2.1   Pathogenesis and risk factors

Chronic constipation is a multifactorial disorder with complex pathogenesis and pathophysiology. The pathogenesis of chronic constipation involves alterations in colonic motility, neuroenteric function, rectal and anal coordination, gut microbiota, and central nervous system regulation. Overall, it can be broadly categorized into primary (idiopathic) and secondary forms. Primary chronic constipation includes normal transit constipation (NTC), slow transit constipation (STC), and defecatory disorders (**Table 1**). Defecatory or Evacuation disorder may be associated with a paradoxical anal contraction or involuntary anal spasm, which may be an acquired behavioral disorder of defecation in two-thirds of patients.

Table 1   Pathophysiology of functional constipation

Pathophysiologic subtype	Mechanisms
1) **Isolated Slow-Transit Constipation (STC)**	Reduced colonic propulsive activity or increased uncoordinated motor activity in the distal colon -> prolonged stool transit - Reduced high-amplitude propagating contractions (HAPCs) - Reduced interstitial cells of Cajal (ICCs) density - Reduced acetylcholine-mediated colonic contractions
2) **Normal-Transit Constipation (NTC)**	Normal colonic transit despite abnormal colonic sensation, such as increased sensitivity to abdominal pain and bloating - Associated with visceral hypersensitivity - Altered seronergic pathways (5-HT3 and 5-HT4 receptors) impairing colonic sensation and motility
3) **Pelvic Floor Dysfunction or Defecatory Disorders (sometimes referred to as functional outlet obstruction or anorectal dyssynergia)** ○ **Normal Transit** ○ **Slow transit**	Inadequate rectal propulsive forces and/or increased outlet resistance - Up to 50% also have delayed colonic transit - Increased rectal compliance - Decreased rectal sensation - Abnormal coordination of pelvic floor muscles (external anal sphincter and/or puborectalis muscle)

Studies have identified protective and risk factors associated with chronic constipation, which are summarized in **Table 2**.

Table 2   Protective and Risk (Modifiable and non-modifiable) Factors of Chronic Constipation

Protective Factors	Risk Factors	
	Modifiable	**Non-Modifiable**
Regular Physical Activity	Sedentary Lifestyle	Female sex
High Dietary Fiber Intake	Poor sleep quality and mental health	Older age
Adequate Fluid Intake or Hydration	Medications: opioids, benzodiazepines, antidepressants, antispasmodics, anticonvulsants	Lower income and educational levels
Regular Defecation Habits	Medical comorbidities: Diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease, ischemic heart disease	
Probiotics and Prebiotics		

2.2   Associated conditions and medications

Table 3   Possible causes and constipation-associated conditions

Mechanical obstruction
- Colorectal tumor
- Diverticulosis / Diverticulitis
- Strictures (inflammatory, malignant, or infective)
- External compression from tumor/other
- Large rectocele
- Megacolon
- Postsurgical abnormalities (eg, adhesions)
- Anal fissure
- Haemorrhoids
- Fecal impaction

Neurological disorders/neuropathy
- Autonomic neuropathy
- Cerebrovascular disease
- Cognitive impairment/dementia
- Depression

- Multiple sclerosis
- Parkinson disease
- Spinal cord tumours / injury
- Spina Bifida

Endocrine/metabolic conditions

- Chronic kidney disease
- Dehydration
- Diabetes mellitus
- Heavy metal poisoning
- Hypercalcemia
- Hypermagnesemia
- Hyperparathyroidism
- Hypokalemia
- Hypomagnesemia
- Hypothyroidism
- Multiple endocrine neoplasia II
- Porphyria
- Uremia

Gastrointestinal disorders and local painful conditions

- Irritable bowel syndrome
- Abscess
- Anal fissure
- Fistula
- Hemorrhoids
- Levator ani syndrome
- Megacolon
- Proctalgia fugax
- Rectal prolapse
- Rectocele
- Solitary rectal ulcer syndrome
- Volvulus

Myopathy

- Amyloidosis
- Dermatomyositis
- Scleroderma
- Systemic sclerosis

Dietary

- High-protein or high-fat diet
- Fluid depletion
- Low fiber diet
- Anorexia
- Excessive intake of caffeine and alcohol

Miscellaneous

- Cardiac disease
- Degenerative joint disease
- Immobility

Others

- Pregnancy
- Pelvic floor dysfunction

Table 4   Medications associated with constipation

Prescription drugs

- Tricyclic antidepressants: Amitriptyline, Imipramine
- Antiepileptics: Carbamazepine, Phenytoin
- Antihistamines: Diphenhydramine, Doxylamine
- Antiparkinson drugs: Benztropine, Trihexyphenidyl
- Antipsychotics: Clozapine, Thioridazine
- Antispasmodics: Hyoscyamine, Mebeverine
- Calcium-channel blockers: Verapamil, Diltiazem
- Beta blockers: Atenolol, Propranolol
- Diuretics: Thiazide, Loop diuretics
- Monoamine oxidase inhibitors: Phenelzine, Selegiline
- Opiates: Morphine, Oxycodone
- Sympathomimetics: Isoprenaline, Phenylephrine
- Antacids: Calcium and Aluminum-containing
- Iron and Calcium supplements
- Oral contraceptives
- Nonsteroidal anti-inflammatory drugs: Ibuprofen, Aspirin
- Overactive bladder drugs: Oxybutynin
- Antidiarrheal agents: Loperamide

3   Diagnosis

3.1   Epidemiology and Impact

Chronic constipation is highly prevalent among adults in the community ([14]) with an estimated global prevalence of 14%. In older adults, the prevalence is higher, reaching up to 32% in Africa, and is lowest in Asia at 13% ([15]). According to a more recent epidemiological study by the Rome Foundation, applying the Rome IV criteria, there is a significant variability in the prevalence of chronic constipation between geographical areas ([16]) with an estimated global prevalence of 11.7% (95%CI 11.4-12.0%) ([5]). The prevalence is twice as often in women as in males ([3]). Additionally, functional constipation was observed to be less common among obese participants in Europe ([17]). This was in contrast with general evidence that chronic constipation is correlated with higher body mass index ([18]). In hospitalized patients, chronic constipation is present in more than half of the patients ([19]).

Chronic constipation is frequently self-diagnosed by the patients. Many patients do not have education on the physiology of the gut and consider difficult evacuation as natural ([20]). Only 20% of people with chronic constipation seek medical care ([4]) partly due to stigma and embarrassment, especially among the elderly ([21]). This means that many constipated patients remain underdiagnosed, as many avoid discussing their symptoms with a doctor ([22]). The report also found that between 2017 and 2018, nearly 200 people were hospitalized daily due to chronic constipation, totaling over 160,000 bed days per year. Treatment costs exceeded £160 million, including more than £70 million for unplanned admissions and over £90 million for laxative use ([23]). Therefore, effective diagnostic evaluation by gastrointestinal specialists should prioritize identifying patients most likely to benefit from targeted diagnostic assessment and specialized treatment according to available health-care resources.

3.2   Diagnostic criteria for functional constipation

To diagnose constipation, physicians may ask about the frequency of the stools, the form of the stools, and if difficulties in defecation exist. Some patients focus on their symptoms related to bowel movements and hence overdiagnose constipation. Diagnostic criteria for chronic constipation by the Rome Foundation Working Committees are shown in Table 5 ([24]).

Table 5   Rome IV criteria for functional constipation

- Must include **two or more** of the following:
    - Straining during more than ¼ (25%) of defecations
    - Lumpy or hard stools (Bristol Stool Form Scale 1-2) more than ¼ (25%) of defecations
    - Sensation of incomplete evacuation in more than ¼ (25%) of defecations
    - Sensation of anorectal obstruction/blockage in more than ¼ (25%) of defecations
    - Manual maneuvers to facilitate more than ¼ (25%) of defecations (e.g., digital evacuation, support of the pelvic floor)
    - Fewer than three spontaneous bowel movements per week
    - Loose stools are rarely present without the use of laxatives

> o   Insufficient criteria for irritable bowel syndrome
>
> *Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

3.3   Patient evaluation

Constipation is generally considered a symptom-based disorder, which is advocated together with a limited number of tests to rule out other diagnoses. The medical history and physical examination of patients with constipation should focus on identifying possible causative conditions and alarm symptoms.

- Stool consistency, as assessed using the Bristol Stool Form Scale (Fig. **1**), is a better indicator of colon transit than stool frequency.

Type 1	Separate hard lumps like nuts (difficult to pass)
Type 2	Sausage-shaped but lumpy
Type 3	Like a sausage, but with cracks on the surface
Type 4	Like a sausage or snake, smooth and soft
Type 5	Soft blobs with clear-cut edges (passed easily)
Type 6	Fluffy pieces with ragged edges, a mushy stool
Type 7	Watery, no solid pieces (entirely liquid)

Figure 1   The Bristol Stool Form Scale: a measure to assist patients in reporting on stool consistency (Reproduced with permission from Lewis SJ and Heaton KW, et al, Scandinavian Journal of Gastroenterology 1997;32:920–4)[25]. ©1997 Informa Healthcare

- Detailed symptom description; symptom diary and several validated questionnaires are available (Patient assessment of constipation – symptoms questionnaire [PAC-SYM], Patient assessment of constipation – quality of life questionnaire [PAC-QOL], Cleveland Clinic Constipation Scoring System, among others). Symptoms assessed included those mentioned in Table 5, but may also include bloating, pain, malaise, unsatisfactory defecation, among others.
- History of and current usage of laxatives; frequency and dosage
- Current medical conditions, past medical and surgical history, any neurological (e.g., Parkinson's disease) or psychiatric disorders
- Lifestyle, dietary habits (fiber intake), physical activity, and fluid consumption
- Medication review, including prescription and over-the-counter drugs
- Use of narcotics; the underlying reasons for overuse should be checked
- Use of suppositories or enemas

- Physical examination:
  — Abdominal exam to exclude gastrointestinal masses
  — Detailed and focused anorectal examination to identify:
    - Fissures
    - Hemorrhoids
    - Fecal impaction
    - Strictures, rectal prolapse, rectocele
    - Impaired anal squeeze and push effort
    - Paradoxical or nonrelaxing puborectalis contraction
    - Rectal mass
- Blood tests (if indicated): complete blood count, comprehensive metabolic profile, serum calcium and glucose levels, and thyroid function tests

3.4   Alarm symptoms

The presence of alarm symptoms and warning signs must be carefully evaluated based on the clinical history (Table 6), and to identify common causes that can lead to secondary constipation.

Table 6   Alarm symptoms

- Changes in stool form or habit
- Unintentional weight loss
- Iron-deficiency anemia
- Obstructive symptoms
- Abdominal swelling or mass
- Recent onset or night-time symptoms
- Rectal bleeding
- Rectal prolapse
- Unintentional weight loss

3.5   Indications for advanced diagnostic tests

Advanced diagnostic studies of colonic, rectal, and anal function (Table 7) are recommended in patients in whom organic causes of constipation have been excluded; who have failed first-line conservative therapies, such as optimization of stool consistency, bowel habit training, and lifestyle advice; and who are refractory to standard pharmacological treatments.

Table 7 Physiological tests for chronic constipation (reproduced with permission from Rao SS, Gastrointest Endosc Clin N Am 2009;19:117–39)[26]

Test	Strength	Weakness	Comment
Colonic transit study with radiopaque markers	Inexpensive and widely available	Methodological variability; questionable validity	Useful for classifying patients according to pathophysiological subtypes (slow, normal, or rapid colonic transit)
Balloon expulsion test	Simple, inexpensive, bedside assessment of the ability to expel a simulated stool; identifies evacuation disorder	Lack of standardization	Normal balloon expulsion test does not exclude dyssynergia; should be interpreted alongside results of other anorectal tests
Anorectal manometry	Identifies evacuation disorder, rectal hyposensitivity, rectal hypersensitivity, impaired rectal compliance, and Hirschsprung disease	Lack of standardization	Useful for establishing diagnoses of Hirschsprung disease, evacuation disorder, and rectal sensory disorder

3.6   Transit measurement

The 5-day marker retention study is a simple method for measuring colonic transit. Markers are ingested on one occasion, and remaining markers are quantified on a plain abdominal radiograph after 120 hours. Transit is considered delayed if more than 20% of the markers remain in the colon. Distal accumulation of markers may indicate an evacuation disorder, and in typical cases of slow-transit constipation, almost all markers remain, and markers are seen in both the right and left colon. The protocol may have to be modified according to the gut transit time of the local population. For example, in India, a protocol consisting of 20 marker ingestions at three different times (0, 12, and 24 hours), followed by abdominal radiographs at 36 and 60 hours has been recommended [27]. Several companies produce markers, but in low-resource settings, markers can also be made from a patient-safe radiopaque tube by cutting it into small pieces (2–3 mm long). A suitable number of markers (20–24 pieces) can be placed in gelatin capsules to facilitate ingestion.

3.7   Clinical evaluation

Classification of the patient's constipation should be possible based on the clinical history and appropriate examination and testing (Table 8). We must understand that constipation is a clinical syndrome presenting different symptoms that manifest differently in each person. These symptoms can be influenced by geographic location, diet, physical activity, and other factors.

Table 8   Constipation categories based on clinical evaluation

Constipation type	Typical findings
Normal-transit constipation, constipation-predominant IBS	• Patient history, no pathology at physical inspection/examination • Pain and bloating • Sensation of incomplete evacuation
Isolated slow-transit constipation	• Slow colonic transit • Normal pelvic floor function

Defecatory disorders:
 	
  - Normal transit
 	
  - Slow transit
	• Prolonged/excessive straining
	• Difficult defecation even with soft stools
	• Patient applies perineal/vaginal pressure to defecate
	• Manual maneuvers to aid defecation
	• High basal sphincter pressure (anorectal manometry)

Secondary constipation	• Known drug side effects, contributing medication (opioids) • Proven mechanical obstruction • Metabolic disorders—abnormal blood tests

3.8   Recommended cascade options for investigating severe and treatment-refractory constipation

LEVEL 3
Extensive resources

a) MR proctography
b) Anorectal manometry
c) Sphincter EMG

LEVEL 2
Medium resources

e) Defecography

LEVEL 1
Limited resources

a) Medical history and general physical examination
b) Anorectal examination, 1-week bowel habit diary card
c) Transit study using radiopaque markers
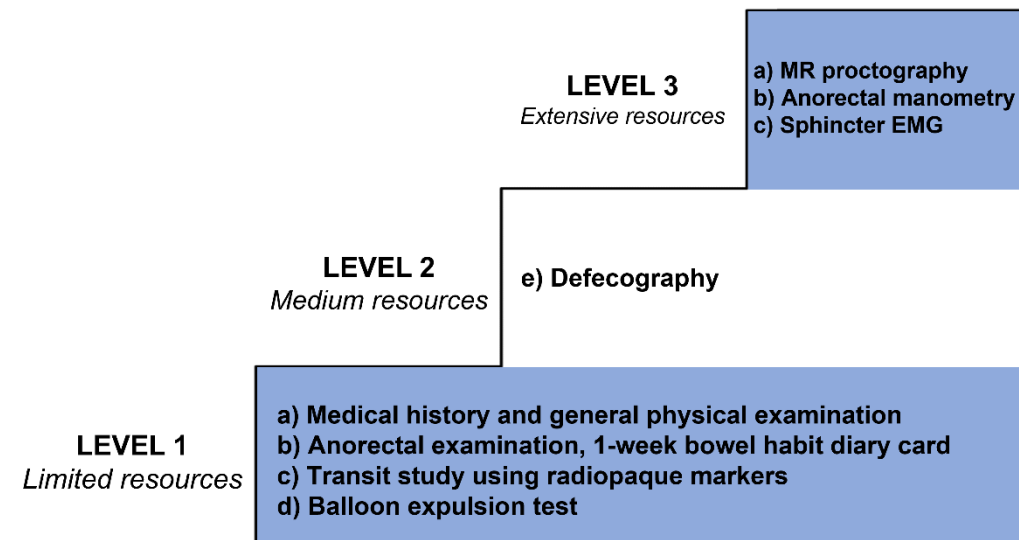d) Balloon expulsion test

Figure 2   Recommended cascade approach to investigation of severe or treatment-refractory chronic constipation

4   Treatment

4.1   General scheme for approach and management of constipation

1. Patient history + physical examination

↓

2. Classify the patient's type of constipation—see Table 8 regarding constipation categories

↓

3. Medical approach in uncomplicated normal-transit constipation without alarm symptoms	- Soluble fiber, milk of magnesia - Add lactulose/PEG - Add bisacodyl/sodium picosulfate - Adjust medication as needed

↓

4. In initial treatment-failure constipation, need to consider secondary constipation, blood or imaging tests or IBS-C	- Standard blood test and colonic anatomic evaluation (imaging test like barium defecography) to rule out organic causes; manage the underlying constipation causing the pathology - A proportion of patients will have a normal/negative clinical evaluation and may meet the criteria for constipation-predominant IBS (IBS-C)

↓

5. If treatment fails, continue with specialized testing (this may only apply to the "extensive resources" level)	- Identify STC with a radiopaque marker study - Exclude evacuation disorder with anorectal manometry and balloon expulsion test, and treat the evacuation disorder (biofeedback therapy) - Evaluate anatomic defects with MR proctography

↓

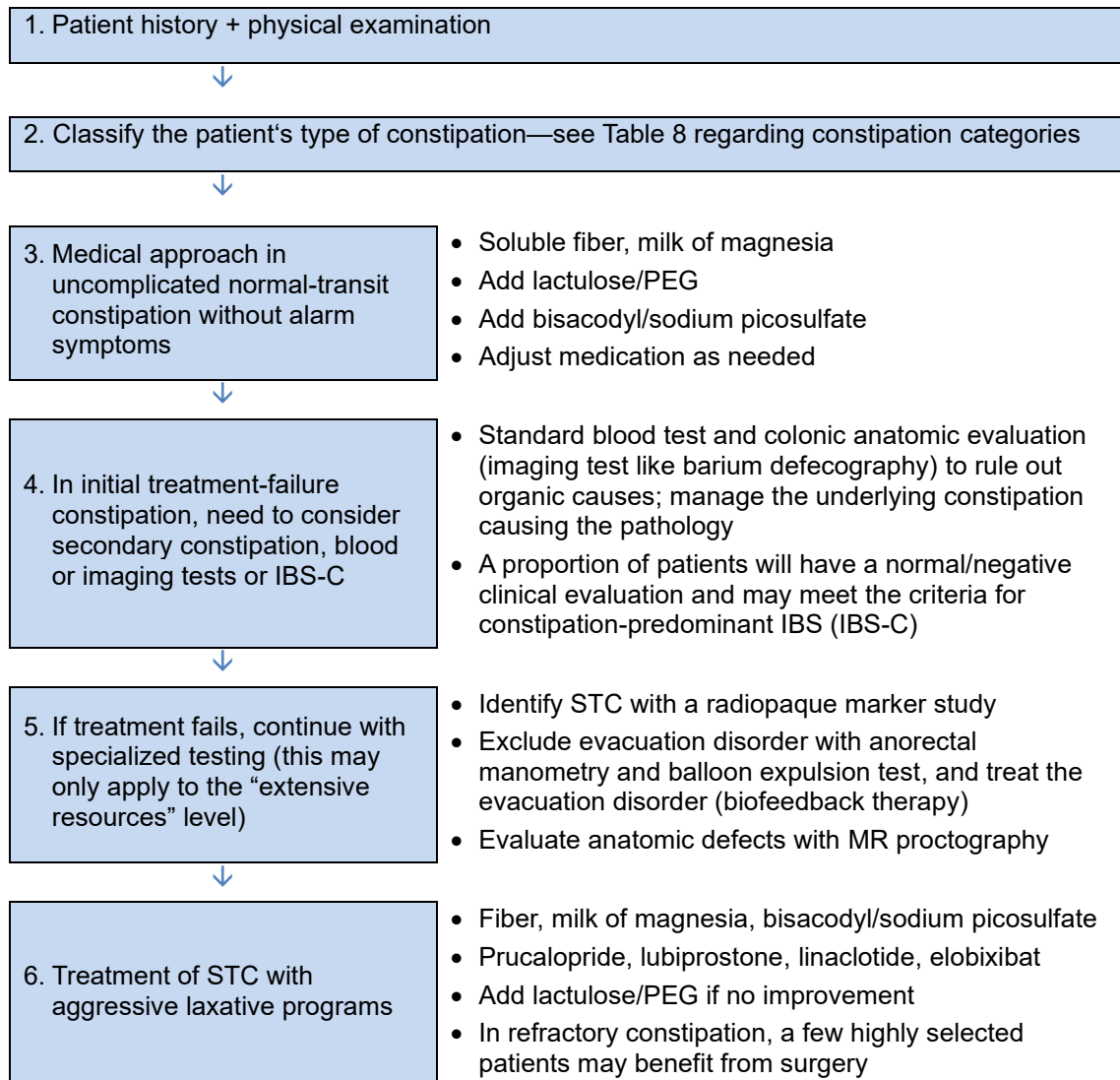| 6. Treatment of STC with aggressive laxative programs	- Fiber, milk of magnesia, bisacodyl/sodium picosulfate - Prucalopride, lubiprostone, linaclotide, elobixibat - Add lactulose/PEG if no improvement - In refractory constipation, a few highly selected patients may benefit from surgery

Figure 3   General approach and management of constipation. IBS, irritable bowel syndrome; MR: Magnetic Resonance; PEG, polyethylene glycol; STC, slow-transit constipation.

4.2   Diet and Supplementary Fiber

Fiber in diet and or supplementation is considered as the first-line treatment for patients with chronic constipation, as suggested by most guidelines, including those from the British, American, and European professional societies. Dietary fibers are carbohydrates (both natural and synthetic) that resist digestion in the small intestine of humans. There are three main types of fibers: soluble, insoluble, and fermentable. Detailed descriptions of these types of fiber can be found in the WGO Practice Guideline publication, 'Diet and the Gut' (https://www.worldgastroenterology.org/guidelines/diet-and-the-gut).

Whole-grain products, fruits, vegetables, nuts, and seeds are good sources of dietary fiber. Fiber supplementation using psyllium has shown benefits in the management of chronic constipation [28]. Improvements in bowel movement frequency and consistency may be observed by gradually increasing dietary fiber to a target dose of 20–30 g of total dietary and/or supplementary fiber per day. Fiber should be introduced gradually into the diet over weeks rather than days, to allow the body to adjust. Of note, evidence for the efficacy of fiber is notably lacking for individual constipation subtypes: metabolic, neurological, diet-related, myogenic, drug-related, and pelvic floor dysfunction.

In patients with obstructive diseases of the intestine, a high-fiber diet should be avoided. Fiber supplements should also be avoided in patients with defecatory disorders [29]. Increasing fiber in the diet too quickly can also lead to symptoms such as gas, bloating, and abdominal cramping, so gradually increasing intake of fiber should be advised.

4.3   Pharmacological therapy – An evidence-based summary

Sections 4.5 and 4.6 provide the stepwise cascade approach, and the evidence-based summary of each pharmacological treatment is mentioned in this section, as provided in Table 9.

Table 9. Evidence-based summary of medications used for chronic constipation ([9, 30 31 32 33 34])

Medications	Dosage	Primary outcome	Efficacy NNT (95%CI)	Adverse effects NNH (95%CI)
Soluble fiber Psyllium	***Recommended initial dose** 14g/1000 kcal/day. Total daily fiber intake (dietary and supplement) 20-30 g/day **Maximum dose** Usually, there is no benefit to increasing total fiber intake over 25-30 g/day	Global symptoms Straining Pain on defecation Increase in mean number of stools/wk	2.6 3.7 6.4 3.8 stools/wk after fiber vs. 2.9 stools at baseline	5.6 Abdominal pain
Laxatives		≥3 stools/week, ≥ 3 CSBMs/week, or no need for rescue laxative use	3(2-4)	3 (2–6) Diarrhea
Osmotic laxatives		≥3 stools/week, ≥3 CSBMs/week, or a need for regular laxative use	3(2-4)	
Polyethylene glycol	**Recommended initial dose** 17 g daily **Maximum dose** No clear maximum dose			Common side effects include bloating, abdominal discomfort, and cramping
Magnesium oxide	**Recommended initial dose** 400–500 mg daily **Maximum dose** No precise maximum dose. Prior studies used 1000–1500 mg daily			
Lactulose	**Recommended initial dose** 15 g daily **Maximum dose**			

	No precise maximum dose. May cause hypernatremia and hypokalemia if patients experience significant diarrhea			
Stimulant laxatives		≥ 3 CSBMs/week	3 (2–3.5)	
Bisadocyl and Picosulphate	**Recommended initial dose** 5 mg daily **Maximum dose** 10 mg daily			
Senna	**Recommended initial dose** 8.6–17.2 mg daily **Maximum dose** No precise maximum dose. Often recommended maximum is 4 tablets twice per day			Side effects are most commonly cramping and abdominal discomfort
Intestinal secretagogues				
Linaclotide	**Recommended initial dose** 72–145 µg daily **Maximum dose** 290 µg daily	Increase in CSBMs to >1/week and ≥3 CSBMs/week for at least 75% of weeks in a 12-week trial	72 µg 12 (6–29) 145 µg 10 (6–19)	
Lubiprostone	**Recommended initial dose** 24 µg BID **Maximum dose** 24 µg BID	≥ 3–4 CSBMs/week	24 µg 4 (3–7)	4 (3–7) Total AEs
Plecanatide	**Recommended initial dose** 3 mg daily **Maximum dose** 3 mg daily	Increase in CSBMs to >1/week and ≥3 CSBM/week for at least 75% of weeks and a response in 3 of the last 4 weeks of trial	3 mg 11 (8–19) 6 mg 12 (8–23)	27 (11–89) 27 (13–72) Diarrhea
5HT agonists				
Prucalopride	**Recommended initial dose** 1–2 mg daily **Maximum dose** 2 mg daily	≥3 CSBMs/week	6 (5–9)	10 (6–29) Total AEs
Bile acid absorption inhibitor				
Elobixibat	**Recommended initial dose** 10 mg daily **Maximum dose** 15 mg daily	≥3 CSBMs/week and an increase of at least one CSBMs	3	Diarrhea 10 mg 12 (8–27), 15 mg 11(6–44) Nausea 15 mg 96 (-26 to 17), 10 mg 53 (-69 to 19) Abdominal pain 10 mg 6 (4-9), 15 mg 5 (4-8)

*The Academy of Nutrition and Dietetics recommendation

Abbreviations used : NNT-number needed to treat; NNH-number needed to harm; CI-confidence interval, CSBMs-complete spontaneous bowel movements.

4.4   Surgical approaches

It is important to note that surgical treatment should only be offered after performing physiological tests. Furthermore, this should only be done if the cause of chronic constipation lies within the colon and/or rectum (slow-transit constipation, evacuation disorder) [35]. Surgery may be an effective treatment for patients suffering from an evacuation disorder due to structural causes, as proven by imaging following failed conservative treatment. Such causes may include intussusception, rectocele, rectal prolapse, or descending perineum syndrome [36, 37]. Some patients may benefit from total colectomy with ileorectal anastomosis. The indication for colectomy must be established in a specialized and experienced tertiary center [38]. Disappointing results may be seen, with fecal incontinence due to surgery and recurrent constipation, especially in patients with evacuation disorder. Some patients may also benefit from a (reversible) colostomy to treat constipation.

4.5   Recommended cascade options for treatment of chronic constipation

Local resources and access often dictate the approach to management of chronic constipation; hence, the cascade options are provided here. Organic and functional constipation needs a different approach. The following cascade is intended for patients with chronic constipation without alarm symptoms and with little or no suspicion of a defecatory disorder. The main symptoms would be hard stools and/or infrequent bowel movements.
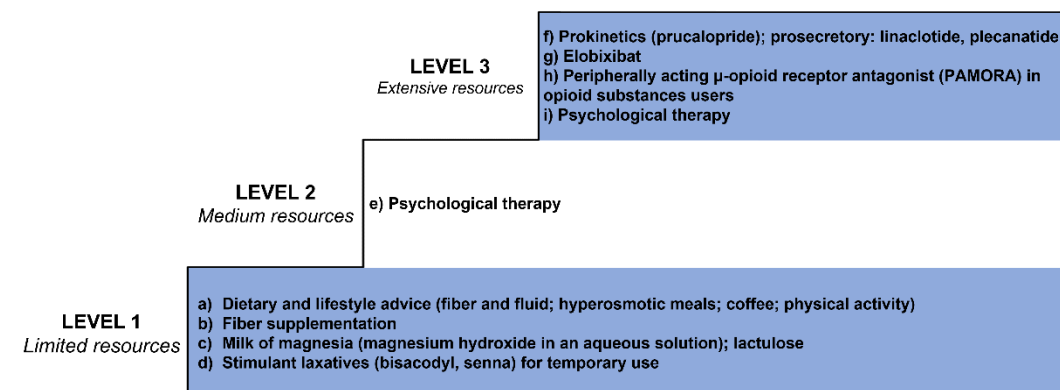
LEVEL 3
Extensive resources

f) Prokinetics (prucalopride); prosecretory: linaclotide, plecanatide
g) Elobixibat
h) Peripherally acting μ-opioid receptor antagonist (PAMORA) in opioid substances users
i) Psychological therapy

LEVEL 2
Medium resources

e) Psychological therapy

LEVEL 1
Limited resources

a) Dietary and lifestyle advice (fiber and fluid; hyperosmotic meals; coffee; physical activity)
b) Fiber supplementation
c) Milk of magnesia (magnesium hydroxide in an aqueous solution); lactulose
d) Stimulant laxatives (bisacodyl, senna) for temporary use

Figure 4   Recommended cascade approach to global treatment of chronic constipation

4.6   First-level cascade treatment approach

Symptomatic treatment of constipation is the recommended first-level cascade approach, provided that organic and secondary causes have been excluded. Please also refer to section 4.1 and 4.5.

- **Lifestyle modifications**: Besides fiber, as mentioned in section 4.2, increased fluid intake should be used to enhance colonic transit and minimize bloating. Regular exercise is strongly recommended; in particular, aerobic activities such as brisk walking, jogging, cycling, and swimming have been shown to stimulate gut motility and reduce colonic transit time. Proper toilet habits, such as responding promptly to the urge to defecate and adopting a squatting position, can also facilitate bowel movements. Finally, identifying and discontinuing medications that contribute to constipation is essential for optimal symptom control (see Table 4).

- **Osmotic laxatives** are the recommended first-line pharmacologic agents. Polyethylene glycol (PEG) and lactulose have strong clinical evidence supporting their effectiveness in treating constipation. However, lactulose is associated with a higher incidence of gastrointestinal side effects, such as bloating, flatulence, and abdominal discomfort. In some regions, magnesium oxide is also used. Please also refer to Table 9.
- **Stimulant laxatives** such as bisacodyl can be used as rescue therapy. Although effective for short-term symptom relief, their use should generally be limited to intermittent or as-needed administration to avoid potential adverse effects such as electrolyte imbalances, abdominal cramping, and the theoretical risk of colonic neuromuscular dysfunction with long-term use. Please also refer to Table 9.

4.7   Second- or third-level cascade treatment approach

When the first-level cascade approach is ineffective, then the next strategy would involve level two or level three approaches, depending on local resources or approach (also refer to section 4.1 and 4.8). Level two interventions include the following:

- **Psychological interventions**, such as cognitive behavioral therapy (CBT) and gut-directed hypnotherapy, demonstrate robust clinical efficacy for chronic constipation management. Originally established for irritable bowel syndrome (IBS), including IBS-C, these evidence-based therapies improve global symptom burden, reduce pain catastrophizing, and enhance quality of life[39,40]. These modalities are particularly beneficial for patients with comorbid anxiety, depression, or maladaptive illness behaviors and represent cost-effective components of multimodal care [41].
- **Neuromodulators** are commonly employed for visceral pain, hypersensitivity, or mood comorbidities; however, they require cautious selection. Tricyclic antidepressants (TCAs) with strong anticholinergic effects (such as amitriptyline) may exacerbate constipation and should generally be avoided [42]. Instead, clinicians should consider secondary-amine TCAs (nortriptyline, desipramine) or SNRIs in patients with predominant pain or mood symptoms, while SSRIs (e.g., citalopram) may benefit anxiety symptoms and carry lower constipation risk [43]. These agents should be prescribed within a shared decision-making framework with close monitoring of bowel habits.
- **Surgery** may be considered in carefully selected patients with medically refractory constipation, particularly those with confirmed STC, where subtotal colectomy (with ileorectal or cecorectal anastomosis) may provide symptom relief. However, adverse outcomes including postoperative incontinence, diarrhea, small bowel obstruction, or stoma requirement can occur in a minority [44,45]. Long-term data remain variable, reflecting heterogeneity in patient selection and surgical techniques. For anatomical causes such as external rectal prolapse or internal prolapse, resection rectopexy and mesh or suture rectopexy (e.g., laparoscopic ventral mesh rectopexy) demonstrate robust functional outcomes. A 2024 meta-analysis highlighted constipation improvement in 83–100% of cases with resection rectopexy, and noted lower recurrence rates with abdominal versus perineal approaches (6% vs.19.3%) with comparable complication profiles [46]. Additional studies emphasize low morbidity, favorable cosmesis, rapid recovery, and effective correction of prolapse-related constipation following laparoscopic mesh or suture rectopexy [47].

For third-level cascade interventions, which typically apply to regions with extensive resources, treatment incorporates advanced pharmacologic agents alongside cutting-edge device-based or neuromodulation therapies.

- Among **advanced pharmaceuticals (see Table 9)**, agents such as linaclotide, lubiprostone, elobixibat, and guanylate cyclase-c (GC-C) receptor agonists are well-established in current guidelines. These medications enhance intestinal secretion, reduce transit time, or modulate bile acid signaling to increase spontaneous bowel movement frequency in patients unresponsive to bulk-forming or osmotic laxatives.

Regarding non-pharmacological therapies, established and emerging device-based interventions are gaining clinical acceptance:

- The **vibrating capsule** is an ingestible device delivering timed vibratory stimulation along the colon. A landmark phase 3 randomized controlled trial (n=312) demonstrated significantly higher proportions of complete spontaneous bowel movement (CSBM) responders: ≥1 CSBM/week (39% vs 22%; p=0.001) and ≥2 CSBMs/week (23% vs 11%; p=0.008) compared to placebo, with generally mild gastrointestinal adverse events [48].
- **Percutaneous (or transcutaneous) tibial nerve stimulation (PTNS/TTNS)** provides neuromodulation via the tibial nerve, targeting sacral pathways controlling colonic motility. Systematic reviews have documented symptomatic benefits; however, protocol heterogeneity and variable stimulation parameters indicate PTNS is currently best considered in specialized centers or research contexts [49].
- **Sacral nerve stimulation (SNS)**, while well-established for fecal incontinence, has not demonstrated consistent efficacy for chronic constipation. Multiple high-quality randomized controlled trials confirm lack of significant improvement in complete bowel movements, combined with procedural risks, potential reoperation requirements, and high costs, making SNS unsuitable for routine use outside research protocols [50, 51, 52].
- **Repetitive transcranial magnetic stimulation (rTMS)** remains experimental but shows promising preliminary results. Recent trials in functional constipation and disease-associated constipation (particularly Parkinson's-related) suggest improvements in bowel frequency and global symptoms [53, 54].

Furthermore, when these less-invasive and device-based treatments fail or prove unfeasible, **advanced surgical interventions** may be considered. Such procedures carry significant risks and should be reserved for highly selected patients within multidisciplinary expert centers.

Stapled Trans-Anal Rectal Resection (STARR) is a minimally invasive, transanal procedure targeting obstructed defecation secondary to internal rectal prolapse or rectocele. A systematic review emphasized that STARR is safe and effective in managing constipation due to obstructed defecation syndrome and improves patients' quality of life [55]. However, STARR carries notable complication rates up to 36% in some cohorts, including bleeding, fecal urgency, flatus incontinence, and symptom recurrence over time (recurrence rates approximately 12% at 36 months) [56, 57].

4.8   Recommended cascade options for treatment of defecatory disorder

This cascade is for patients with chronic constipation without alarm symptoms, but with a defecatory disorder.
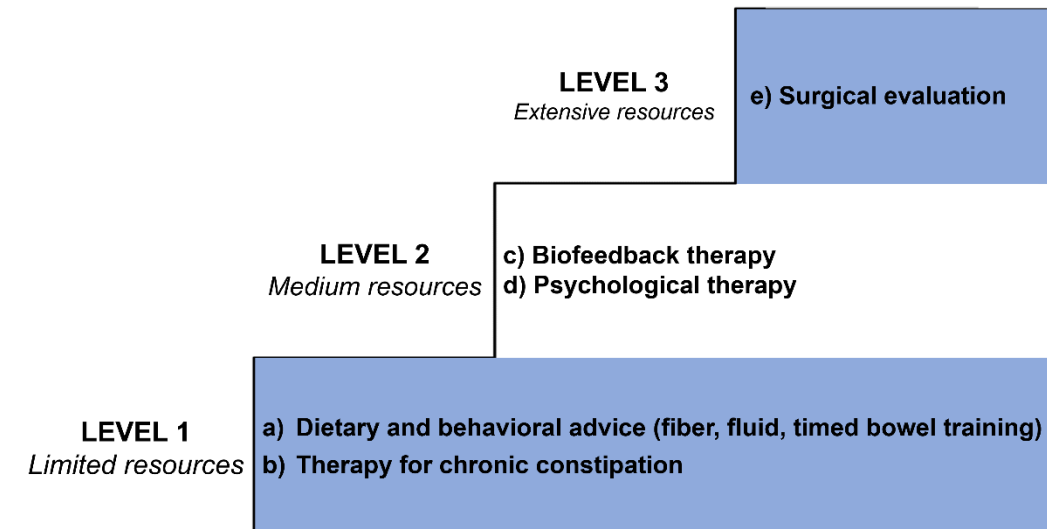

LEVEL 3
Extensive resources   **e) Surgical evaluation**

LEVEL 2
Medium resources   **c) Biofeedback therapy**
d) Psychological therapy

LEVEL 1
Limited resources   **a) Dietary and behavioral advice (fiber, fluid, timed bowel training)**
b) Therapy for chronic constipation

Figure 5   Recommended cascade approach to treatment of defecatory disorder

4.9   Defecatory Disorder

Management of defecatory disorders can be approached in a stepwise manner, beginning with interventions that require limited resources. Please also refer to cascade section 4.8.

- At **level one cascade**, the focus is on dietary and behavioral modifications, which are often the cornerstone of initial management. Patients are advised to increase dietary fiber intake, ensure adequate hydration, and adopt timed bowel training to encourage regular defecation habits. In addition, basic therapy for chronic constipation is initiated, which may include over-the-counter laxatives or stool softeners when necessary. These strategies aim to improve stool consistency and promote more effective bowel movements with minimal cost and complexity.

- If symptoms persist despite these measures, **level two cascade** interventions are considered, which require moderate resources and specialized input. **Biofeedback** therapy, particularly useful for patients with pelvic floor dyssynergia, can retrain the coordination of abdominal and pelvic floor muscles during defecation. **Neuromodulators**, such as certain antidepressants or agents that modulate visceral sensitivity, may be used to address associated pain or altered bowel sensations. **Psychological therapy** is also important, as anxiety, depression, and maladaptive coping mechanisms can exacerbate defecatory dysfunction. These targeted approaches address the multifactorial nature of defecatory disorders, particularly when behavioral modifications alone are insufficient.

- For patients with severe, refractory symptoms who do not respond to lower-tier therapies, **level three cascade** management involves extensive resource use, including surgical evaluation. Surgery is generally reserved for selected cases with structural abnormalities or severe functional impairment not amenable to conservative or minimally invasive treatments. Procedures may include correction of anatomical defects or, in rare and highly selected cases, more definitive interventions such as colectomy. Given the potential risks and long-term implications, surgical intervention is only considered after

thorough evaluation by a multidisciplinary team, ensuring that all conservative options have been exhausted and that the patient is appropriately counseled on expected outcomes and risks.

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