

*Optimizing
Disease Management*



DMIBS-C

and Chronic
Idiopathic
Constipation

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Disclosures

All faculty, course directors, planning committee, content reviewers and others involved in content development are required to disclose any financial relationships with commercial interests. Any potential conflicts were resolved during the content review, prior to the beginning of the activity

The following individual has a relevant financial relationship with a commercial interest:

Faculty	Commercial Interest Name	What Was Received	For What Role	For what Clinical Area/Disease State
Nimish Vakil, MD, FACP, FACG, AGAF, FASGE	Ironwood Pharmaceuticals	Consulting Fee	Attending advisory board	IBS-C

There will be references to the unlabeled and currently unapproved use of sodium picosulfate (limited availability in the US)

Educational Objectives

Identify symptoms specific to CIC to distinguish it from IBS-C.

Diagnose CIC or IBS-C based on patients' presenting symptoms.

Describe the Rome IV criteria for CIC and IBS-C, and demonstrate how disease severity affects patient QOL.

Discuss the clinical guidelines for non-pharmacologic and pharmacologic options to treat patients with CIC and IBS-C.

Identifying the Patient

IBS-C vs CIC

- Pain related to bowel movements is the main differentiating feature
 - IBS-C: pain and constipation are both dominant symptoms
 - CIC: pain is not a predominant symptom and is not frequent or severe
- There is some overlap and crossover between the two conditions

Definitions – Rome IV

- IBS is a functional bowel disorder in which recurrent abdominal pain is associated with defecation or a change in bowel habits
- **Criteria for a diagnosis:**
 - Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with 2 or more of the following criteria:
 1. Related to defecation
 2. Associated with a change in frequency of stool

Definitions – IBS-C

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its 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

More than 25% of bowel movements are Bristol types 1 & 2 and less than 25% are types 6 & 7

OR

Patient reports that abnormal bowel movements are usually constipation

Must meet the IBS pain criteria

Chronic Idiopathic Constipation

- CIC, also known as functional constipation (FC), is a functional bowel disorder in which symptoms of difficult, infrequent, or incomplete defecation predominate.
- Patients with CIC should not meet IBS criteria, although abdominal pain and/or bloating may be present but are not predominant symptoms.
- Symptom onset should occur at least 6 months before diagnosis, and symptoms should be present during the last 3 months.

Diagnostic Criteria for CIC

- **C2. Diagnostic Criteria for CIC**
 1. Must include 2 or more of the following:
 - a. Straining during more than one-fourth (25%) of defecations
 - b. Lumpy or hard stools (BSFS 1-2) more than one-fourth (25%) of defecations
 - c. Sensation of incomplete evacuation more than one-fourth (25%) of defecations
 - d. Sensation of anorectal obstruction/blockage more than one-fourth (25%) of defecations
 - e. Manual maneuvers to facilitate more than one fourth (25%) of defecations (eg, digital evacuation, support of the pelvic floor)
 - f. Fewer than 3 spontaneous bowel movements per week

Pathophysiology of IBS

- **Environmental Contributors to IBS Symptoms**
 - Early life stressors (abuse, psychosocial stressors)
 - Food intolerance
 - Antibiotics
 - Enteric infection
- **Host Factors Contributing to IBS Symptoms**
 - Altered pain perception
 - Altered brain-gut interaction
 - Dysbiosis
 - Increased intestinal permeability
 - Increased gut mucosal immune activation
 - Visceral hypersensitivity



Prevalence and Burden

- 35 million adults suffer from CIC
- 13 million people suffer with IBS-C
- These conditions are among the most common gastrointestinal (GI) complaints and worrisome reasons for frequent clinician visits.
- Over a 10-year period, the mean all-cause medical costs of a patient with CIC has been estimated at >\$40,000.¹
- IBS affects about 11% of the population globally, but only 30% of people who experience the symptoms of IBS consult physicians.²
- Approximately a third of IBS patients have the constipation-dominant subtype (IBS-C).³
- The damaging effect of IBS on health-related QOL has been found equivalent to the effects of such chronic diseases as asthma and migraine.⁴

1. Herrick LM, Spaulding WM, Saito YA, et al. Longitudinal direct medical costs associated with irritable bowel syndrome-constipation and chronic idiopathic constipation in a population-based sample over a 10-year period. *Gastroenterology*. 2013;144:S-383. Abstract Su1040.

2. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clin Epidemiol*. 2014;6:71-80.

3. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta analysis. *Clin Gastroenterol Hepatol*. 2012;10:712-721.

4. Cremonini F, Lembo A. IBS with constipation, functional constipation, painful and non-painful constipation: Pluribus... Plures? *Am J Gastroenterol*. 2014;109:885-886.

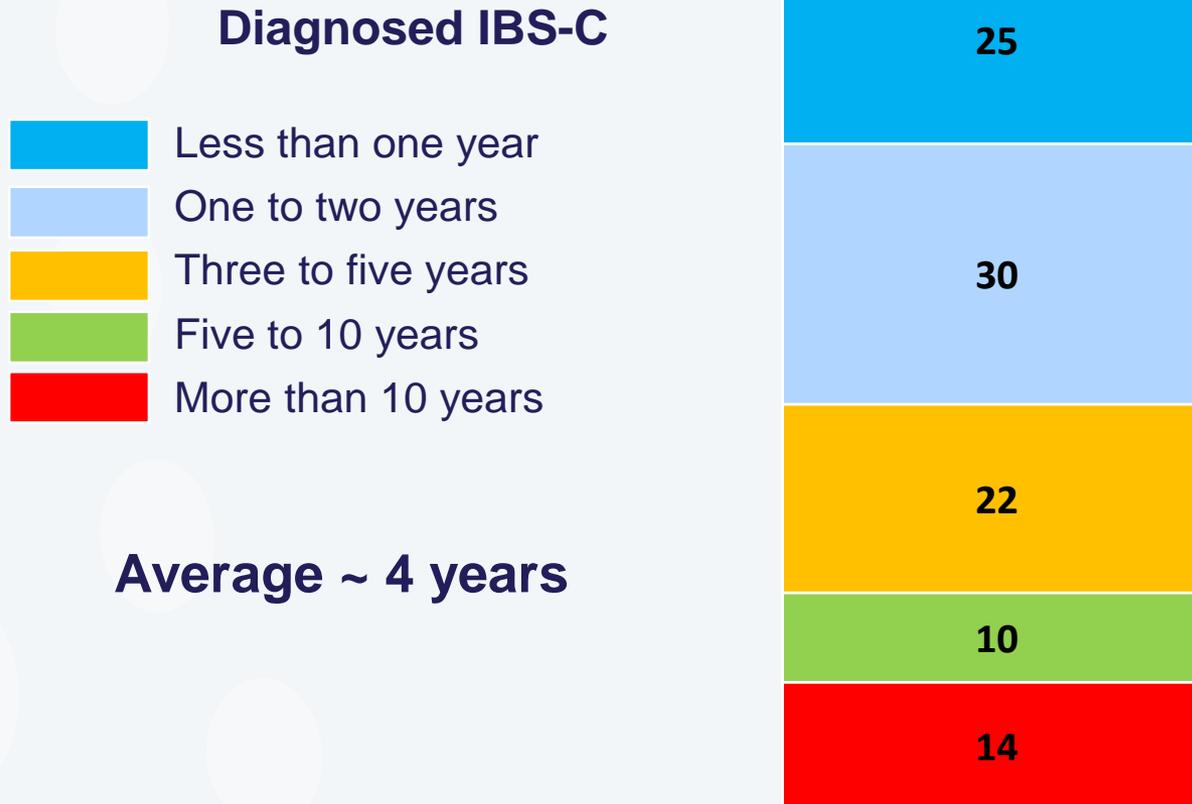
AGA Survey on IBS

- Largest survey on IBS conducted by the American Gastroenterological Association
- 3200 sufferers and 300 gastroenterologists
- Results online at:

<http://ibsinamerica.gastro.org/files>

IBS_in_America_Survey_Report_2015-12-16.pdf

How Long Did it Take to Get to a Diagnosis in Patients with Chronic Constipation?



Evaluating the Patient with Constipation

- **Physical examination**
 - Abdominal masses
 - Distended colon
 - Rectal exam: spasm, tenderness, stool
 - Dyssynergic defecation can be diagnosed by asking the patient to bear down (sensitivity 75%, specificity 87%)

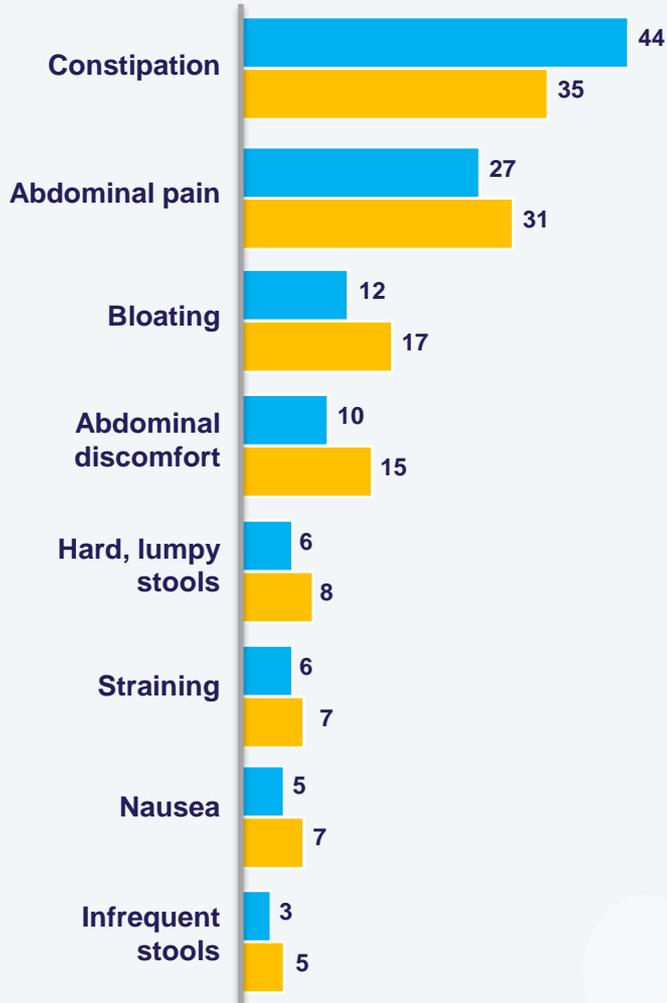
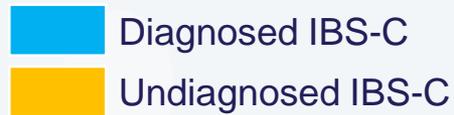
Laboratory Tests in Chronic Constipation

- CBC
- Thyroid testing is controversial
- Celiac testing more relevant for diarrhea
- A positive diagnosis can be made with a minimum of testing



Having the Constipation Conversation

Most Bothersome Symptom Reported by IBS-C Patients



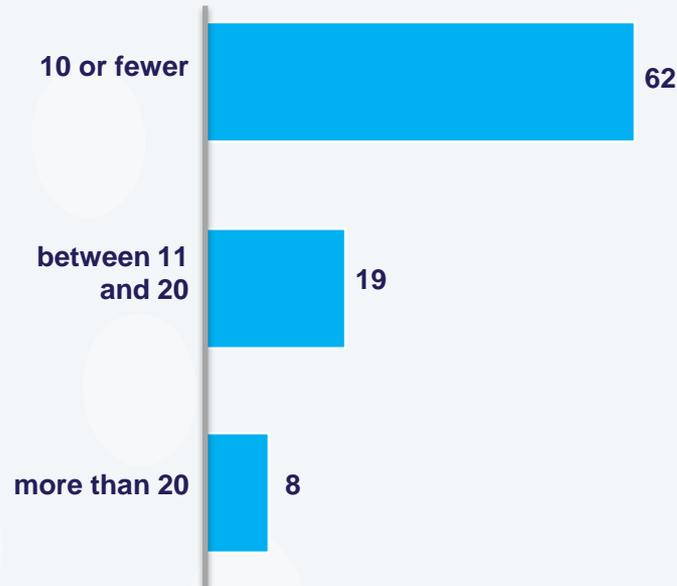
Effect of IBS on Daily Life

Effect of IBS on Daily Life Choices



Impact on Productivity

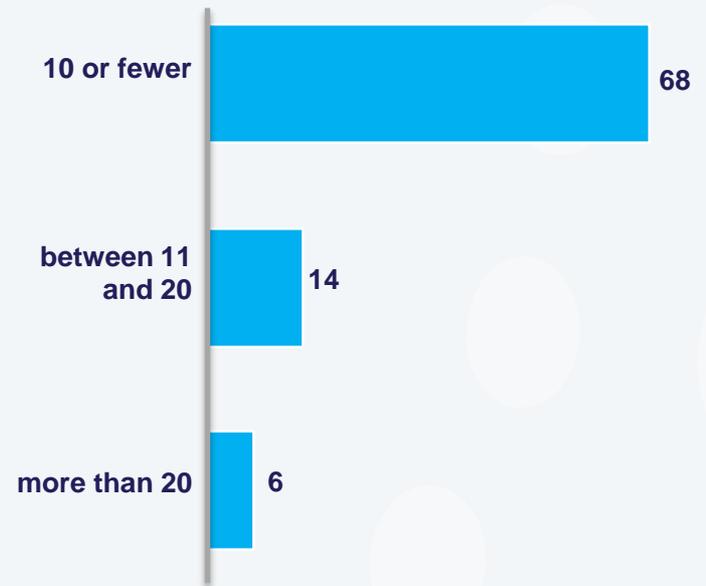
How many days do these symptoms interfere with your productivity?



Average ~ 9 days

Base: Total respondents, N=3254

How many days do these symptoms interfere with your ability to participate in a personal activity?



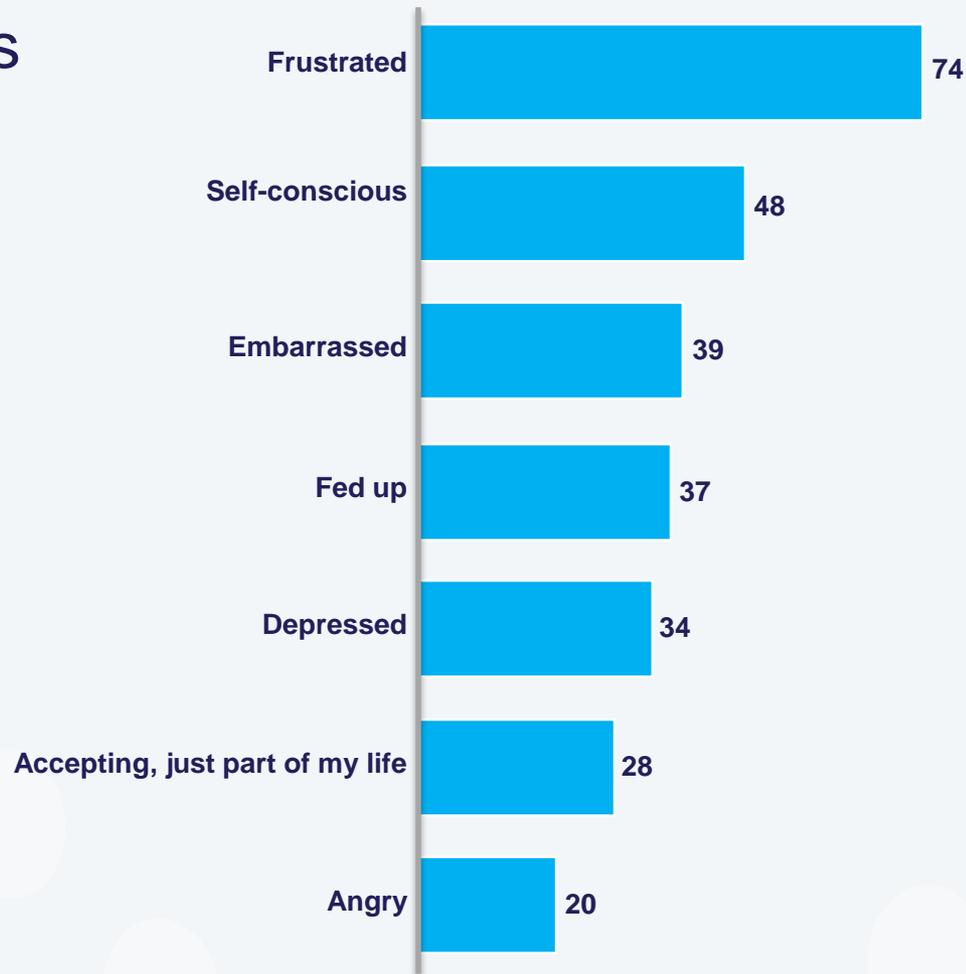
Average ~ 8 days

Base: Total respondents, N=3254

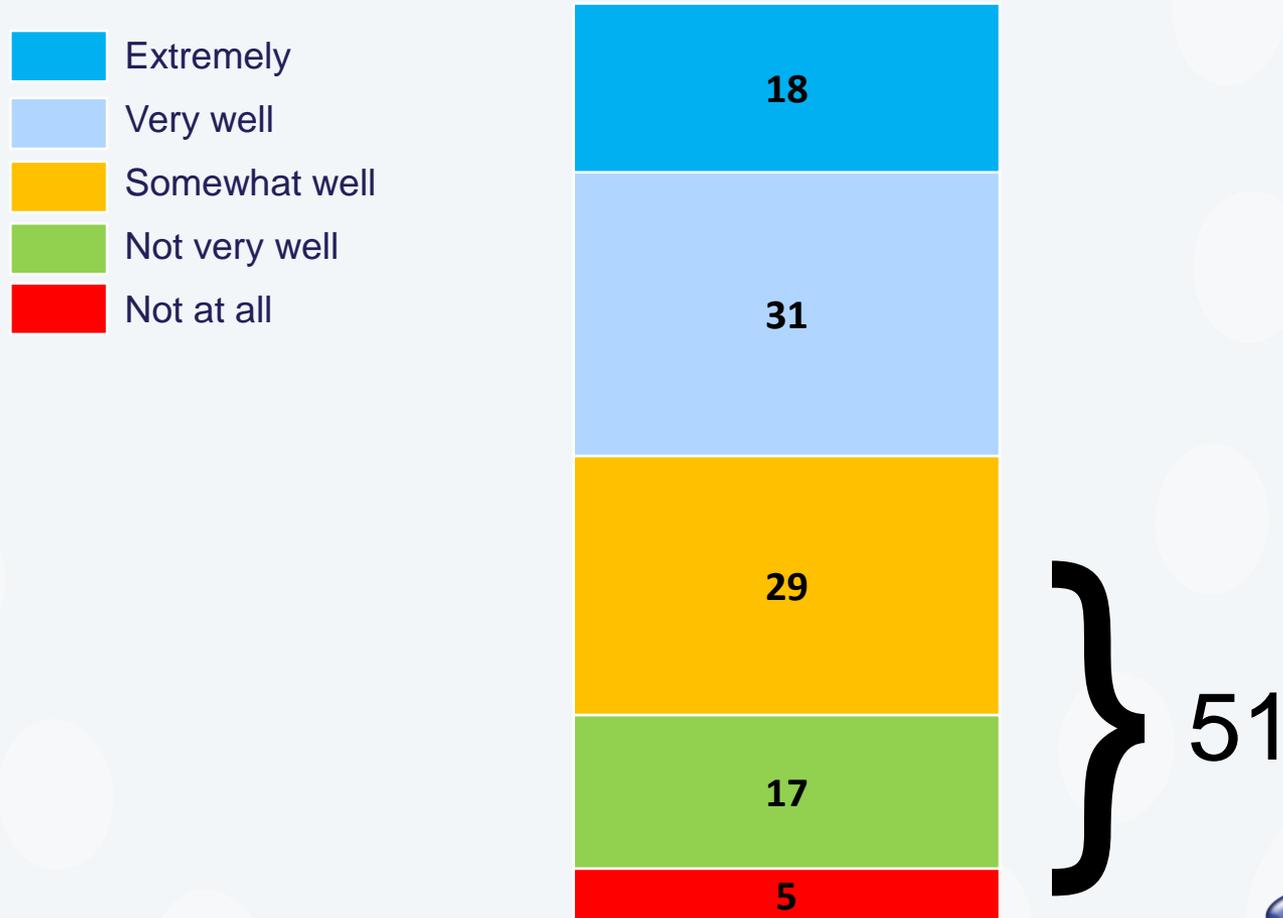


Emotions About IBS

Emotions

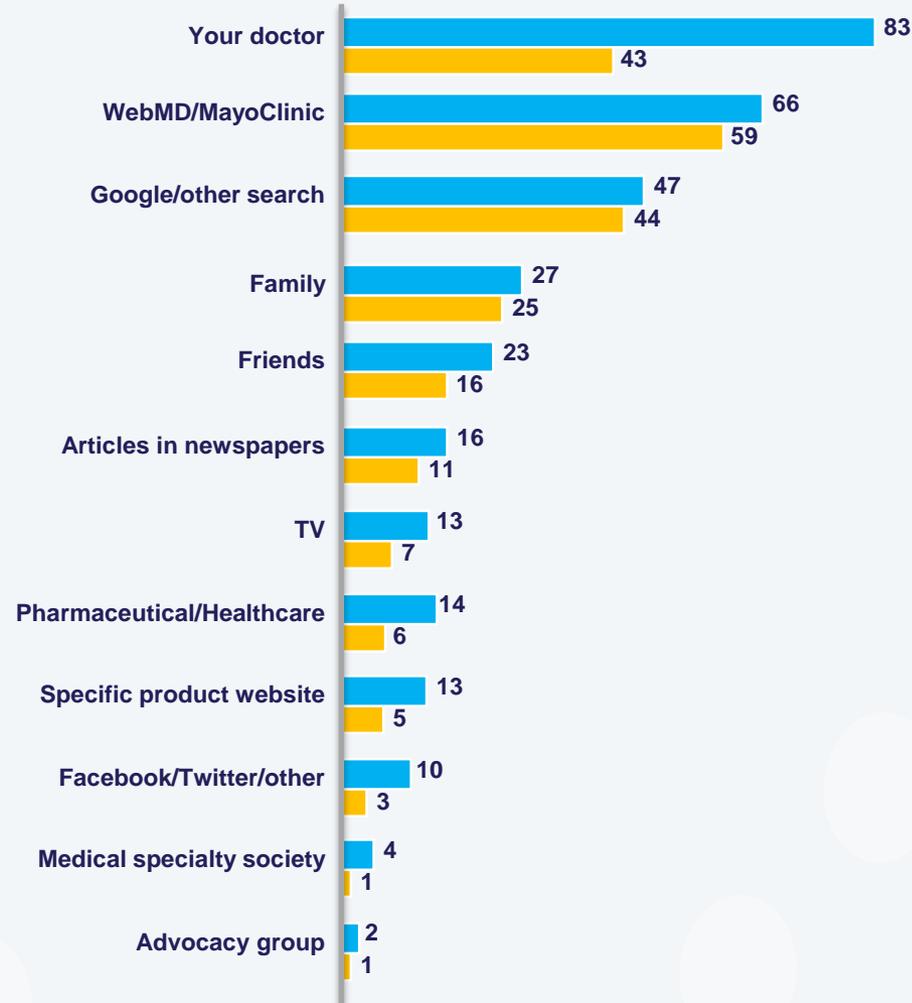
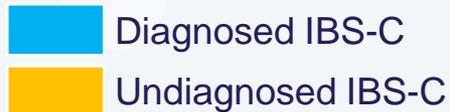


How Well Does Your Health Care Provider Understand the Burden of your Symptoms?



People with Undiagnosed Constipation Are Talking to Many People, but Not Their Doctor

IBS-C



4 in 10 Constipated Patients Wait 3 Years or Longer Before Seeking a Diagnosis

Duration of Symptoms Before Diagnosis

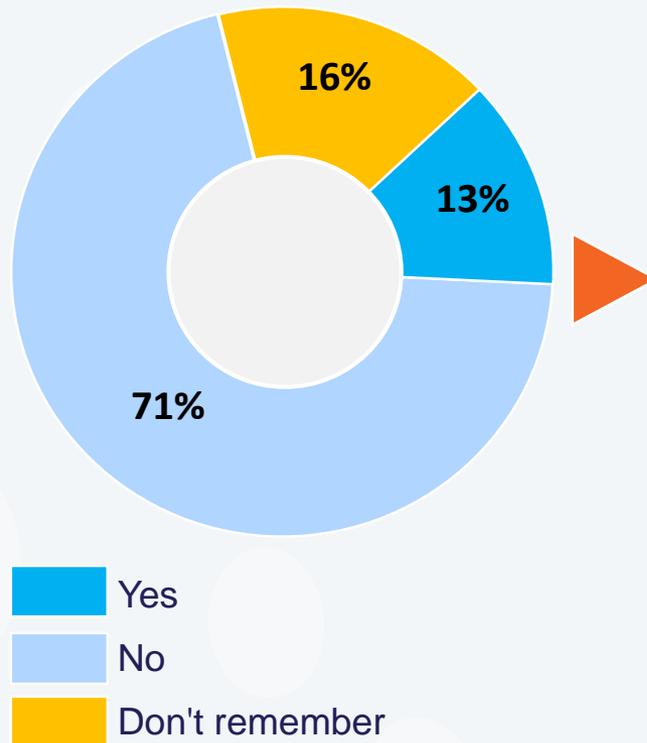


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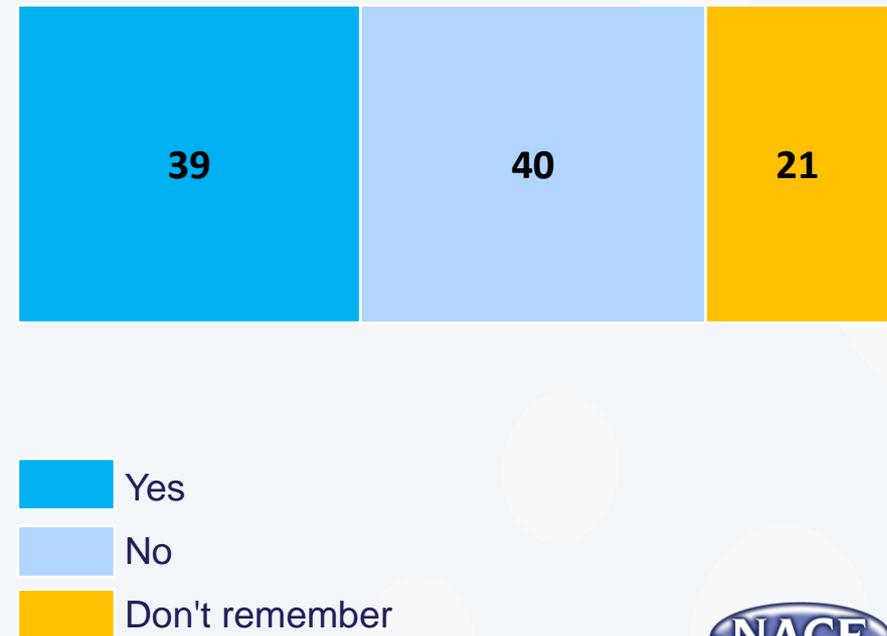
Patients Without Diagnosis Are Often Not Asked About GI Symptoms

Has a health care professional ever asked you about gastrointestinal symptoms or regularity during an annual check-up or exam?



Did you tell your health care professional about your gastrointestinal symptoms?

% of health care professional asked about gastrointestinal symptoms during checkup, (N=75)



Modeling the Conversation About IBS-C and CIC

- **Speak up early**
 - Ask questions about bowel movement frequency and consistency
 - Remember that 2 of 3 patients find it more comfortable to talk about STDs than about bowel movements
- **Speak up completely**
 - Health care providers tend to move quickly past bowel symptoms
 - Elicit symptoms and impact on life with empathy
- **Speak up often**
 - It may take more than one visit to establish a conversation
 - Establish follow-up visits to follow the patient



Shared Decision Making

Evaluating the Patient: Factors Exacerbating IBS

■ Over-the-Counter

- Antihistamines
- Calcium
- Iron
- Magnesium
- Nonsteroidal anti-inflammatory drugs
- Wheat bran

■ Prescription

- Antibiotics
- Antidepressants
- Antiparkinsonian drugs
- Antipsychotics
- Calcium-channel blockers
- Diuretics
- Metformin
- Opioids
- Sympathomimetics



When to Refer a Constipated Patient?

- Concerning features for organic disease
- Symptom onset after age 50
- Severe or progressively worsening symptoms
- Unexplained weight loss
- Family history of organic gastroenterological diseases, including colon cancer, celiac disease, or inflammatory bowel disease
- Rectal bleeding or melena
- Unexplained iron-deficiency anemia

Treatment: Fiber, Osmotic and Stimulant Laxatives

Laxative class	Medications	Mechanism of action	Adverse effects	Level of evidence	Grade of recommendation
Bulk (fiber) laxatives	Psyllium, calcium polycarbophil, methylcellulose, bran	Retaining water in stool, increasing stool bulk and improving consistency	Flatulence, bloating, abdominal distention; rarely causing mechanical obstruction of esophagus and colon	Psyllium – II; Others – III	B/C
Stool softeners or wetting agents	Docusate sodium, docusate calcium	Promoting luminal water binding by detergent-like action, increasing stool bulk	Intestinal cramping; irritation of throat (liquid formulation)	III	C
Stimulant laxatives	Senna, aloe, bisacodyl, sodium picosulfate	Increasing intestinal peristalsis by acting on myenteric nerve plexus, decreasing large intestinal water absorption	Abdominal discomfort, rarely electrolytes disturbance, melanosis coli	Sodium picosulfate – II; Others – III	B/C
Osmotic laxatives	PEG, lactulose, sorbitol, milk of magnesia, magnesium citrate	Osmotic water binding	Bloating, flatulence, abdominal cramping; in rare instances, electrolytes disturbances	PEG – I	A
				Lactulose – I	A
				Sorbitol/milk of magnesia – III	B/C
Mixed laxatives	Dried plums	Stool bulking and osmotic action	Flatulence, bloating	II	B

Prebiotics, Probiotics and Diet

- a) **Prebiotics and synbiotics in IBS: There is insufficient evidence to recommend prebiotics or synbiotics in IBS.**

Recommendation: weak. Quality of evidence: very low.

- b) **Probiotics in IBS: Taken as a whole, probiotics improve global symptoms, bloating, and flatulence in IBS.**

Recommendations regarding individual species, preparations, or strains cannot be made at this time because of insufficient and conflicting data.

Recommendation: weak. Quality of evidence: low.

- c) **FODMAPs diet plan: Used to treat IBS.**

Focuses on eliminating foods that contain sugars and fibers that can cause gas, abdominal pain and other symptoms. Eliminates foods that contain fermentable oligo-, di-, mono-saccharides and polyols.



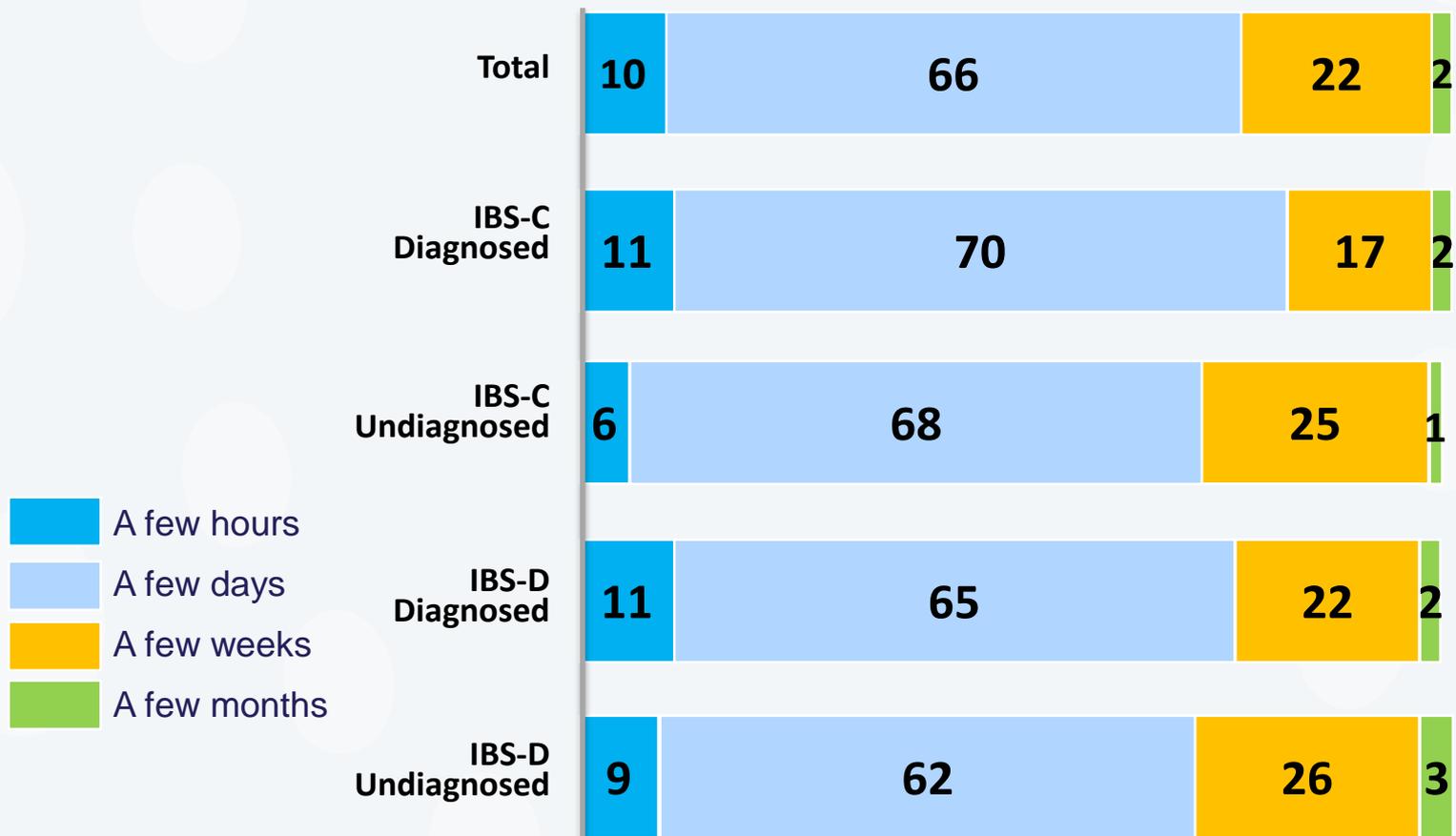
Treatment: Prescription drugs

Drugs	Mechanism of action	Indication	Usual dose	Dose adjustment	Adverse effects	Special populations
Chloride channel activators						
Lubiprostone	Selective activation of intestinal epithelial chloride channel 2, increasing chloride secretion	Chronic idiopathic constipation; IBS-C	CIC: 24 mcg taken twice daily orally IBS-C: 8 mcg taken twice daily orally	Not studied in hepatic and renal disease	Nausea, diarrhea, headache	Pregnancy class C; avoid during breast feeding
Guanylate cyclase C activators						
Linaclootide	Activation of guanylate cyclase C receptor on enterocytes, increasing cGMP, activating CFTR, increasing luminal chloride and/or bicarbonate secretion; ameliorating visceral hypersensitivity	Chronic idiopathic constipation; IBS-C	CIC: 145 mcg orally once daily IBS-C: 290 mcg orally once daily	Not studied in hepatic and renal disease	Diarrhea	Class C; not studied in breast feeding



Symptoms Return in a Few Days for Most Patients

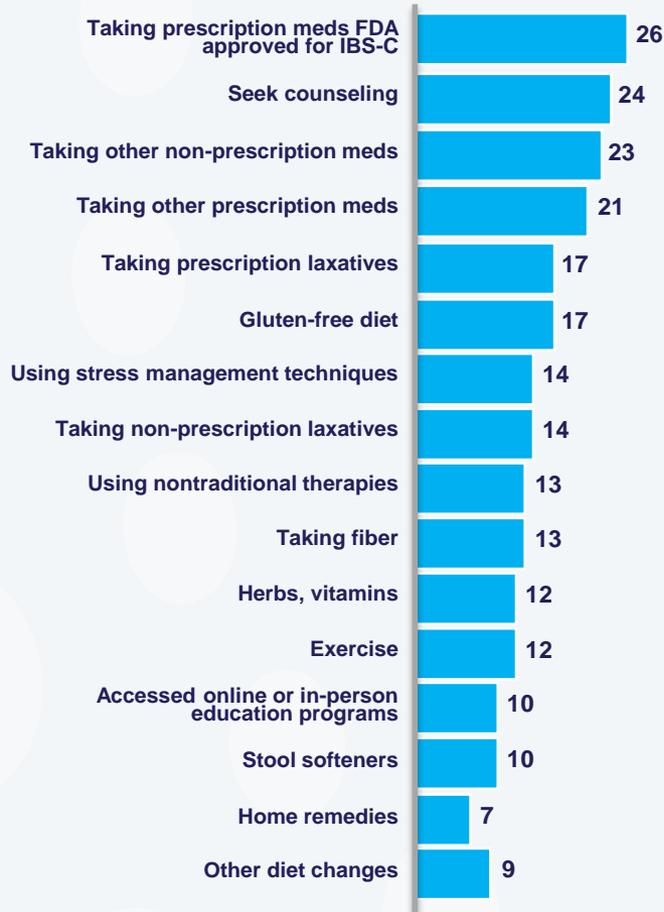
How long do you remain symptom-free before symptoms return?



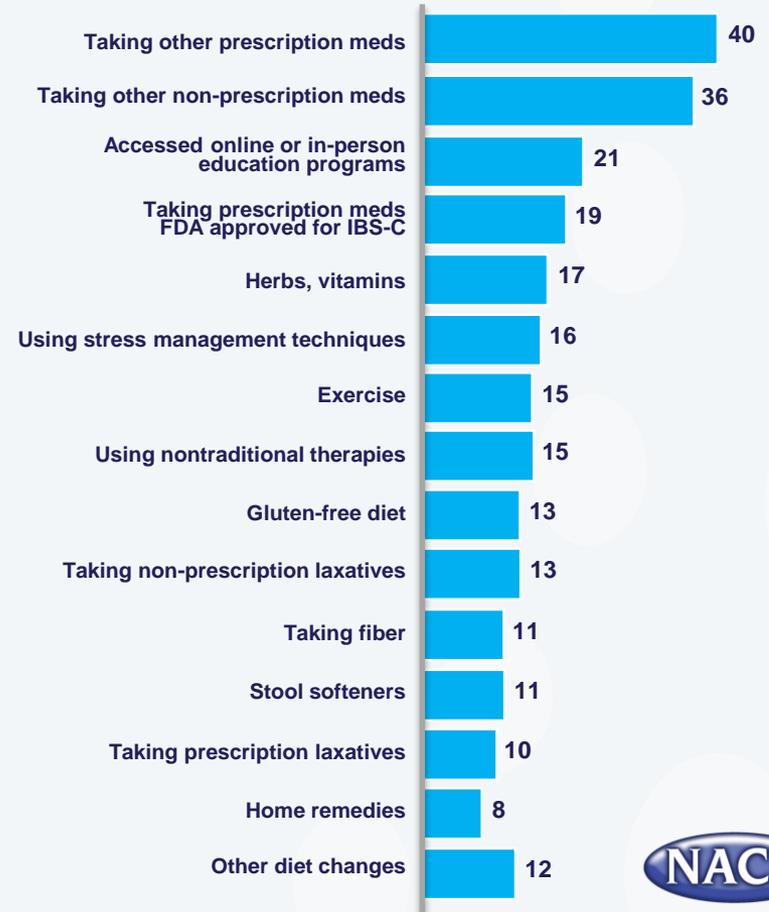
Percent of Patients Very Satisfied with Treatment

Diagnosed IBS-C

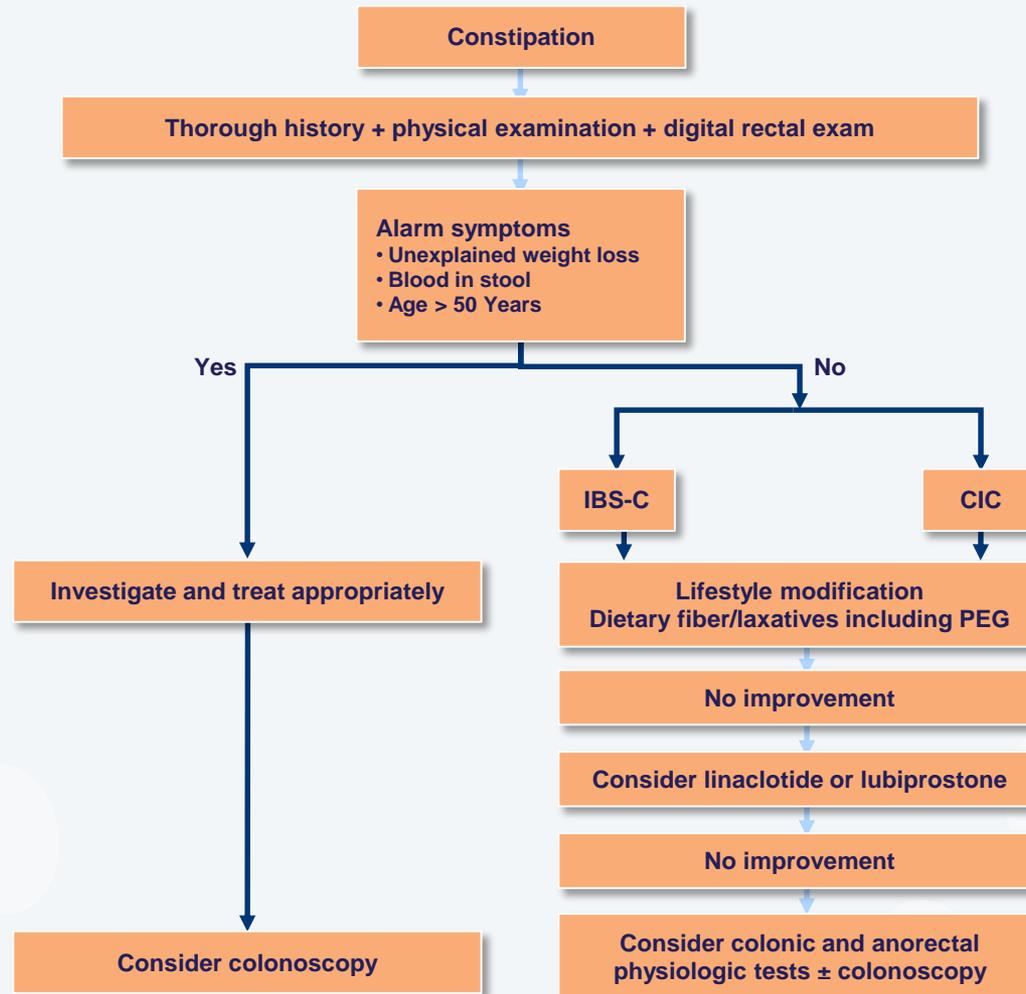
% saying "very satisfied"



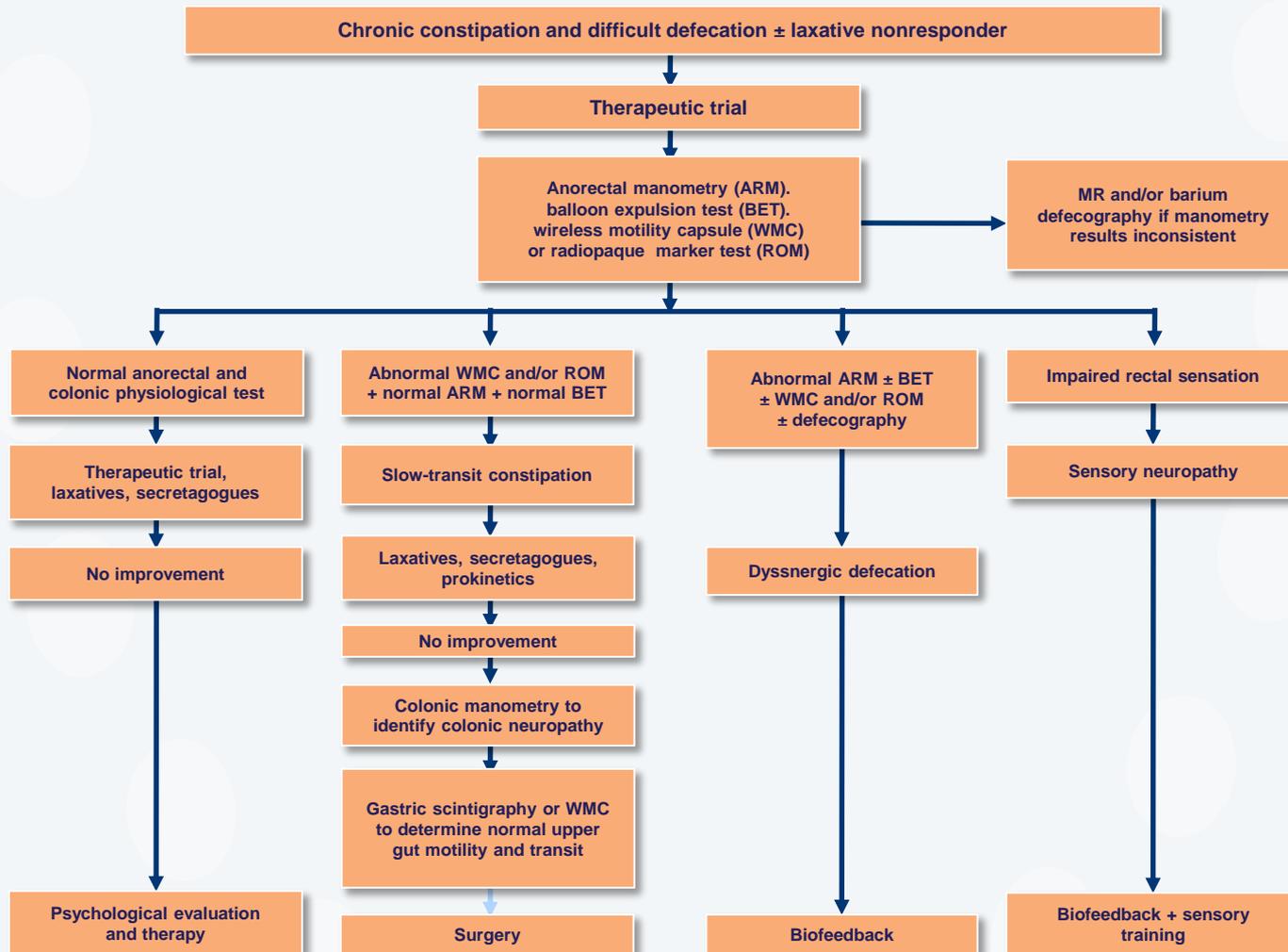
Undiagnosed IBS-C



Flow Chart for Management in Primary Care



Approach to the Patient with Refractory or Very Severe Constipation



Take Home Messages

- Chronic constipation (IBS-C and CIC) can have a major impact on patients' lives
- Be proactive in eliciting information
- Don't be afraid to make a clinical diagnosis
- If lifestyle measures and PEG don't work, move on
- Symptoms often recur and patients may need ongoing treatment and support
- Refer the patient when the symptoms are severe and fail to respond.