



IBS

(IRRITABLE BOWEL SYNDROME)

Physiology / MOD



Prevalence



Burden



Diagnosis



Treatment



Clinical Trial Summaries



Pipeline Table



CIC

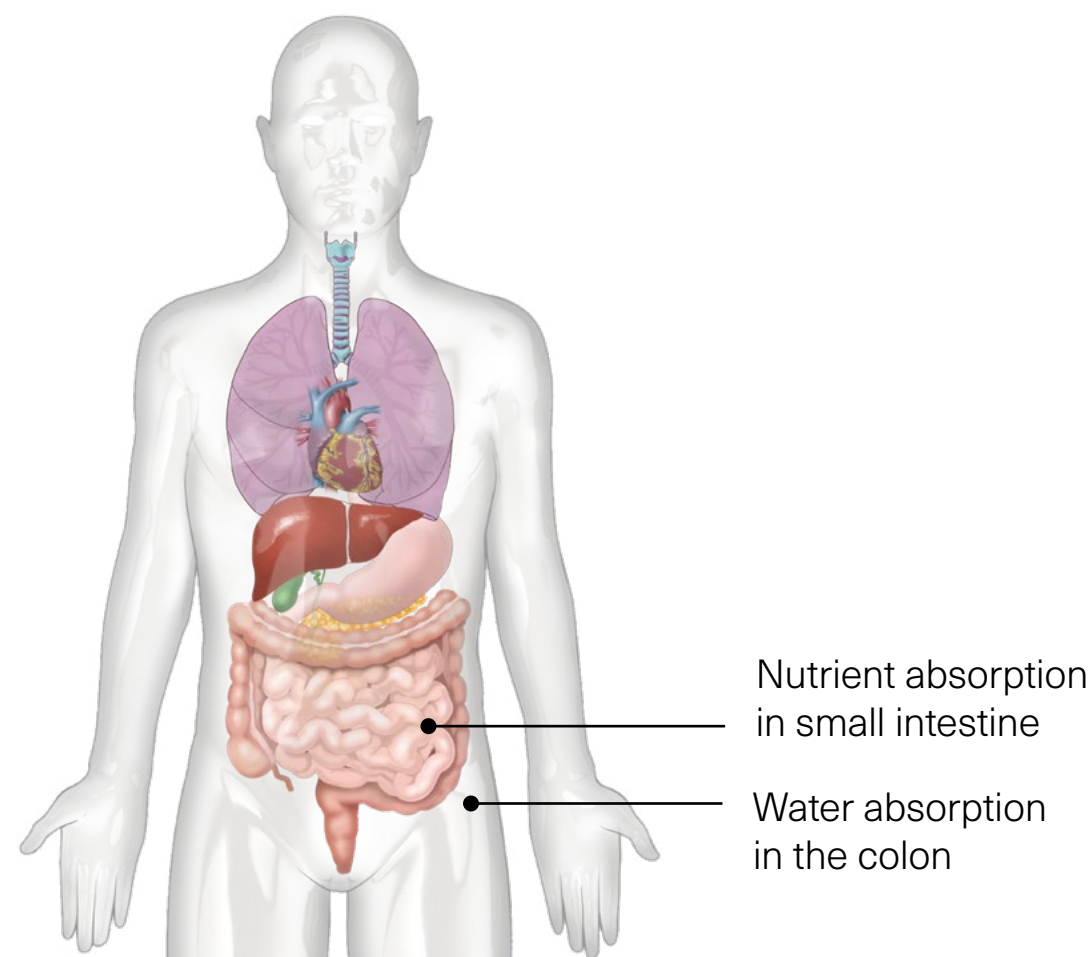
Although CIC Has No Identifiable Cause, Several Factors May Contribute to CIC Development

Pathophysiology¹⁻³

VISCERAL SENSORY
ABNORMALITIES

SLOW MUSCLE
CONTRACTIONS

INCREASED WATER
ABSORPTION



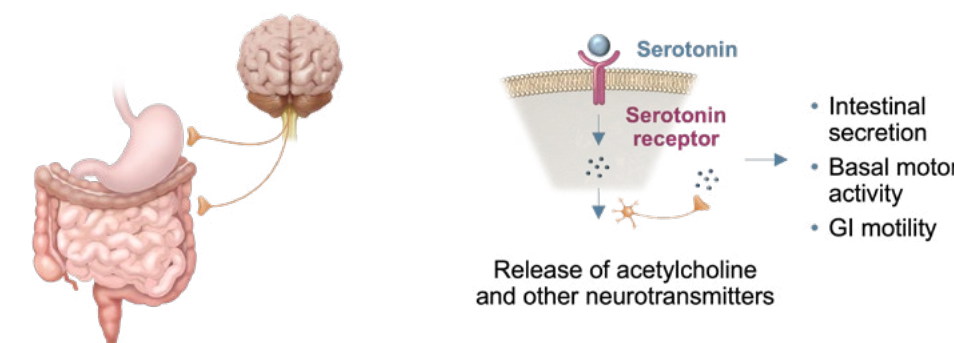
Additional Risk Factors⁴

- Medications
- Old age
- Fiber deficiency in diet
- Little to no exercise
- Mental health condition
- Female gender
- Dehydration

IBS

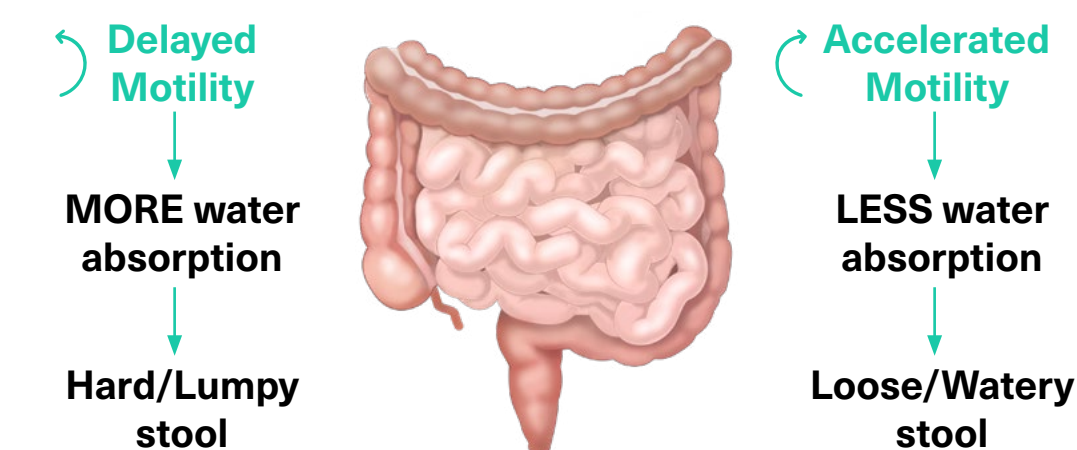
The Precise Cause of IBS Is Unknown, but a Combination of Factors May Contribute to IBS Development

Brain-gut Interaction^{1,2}

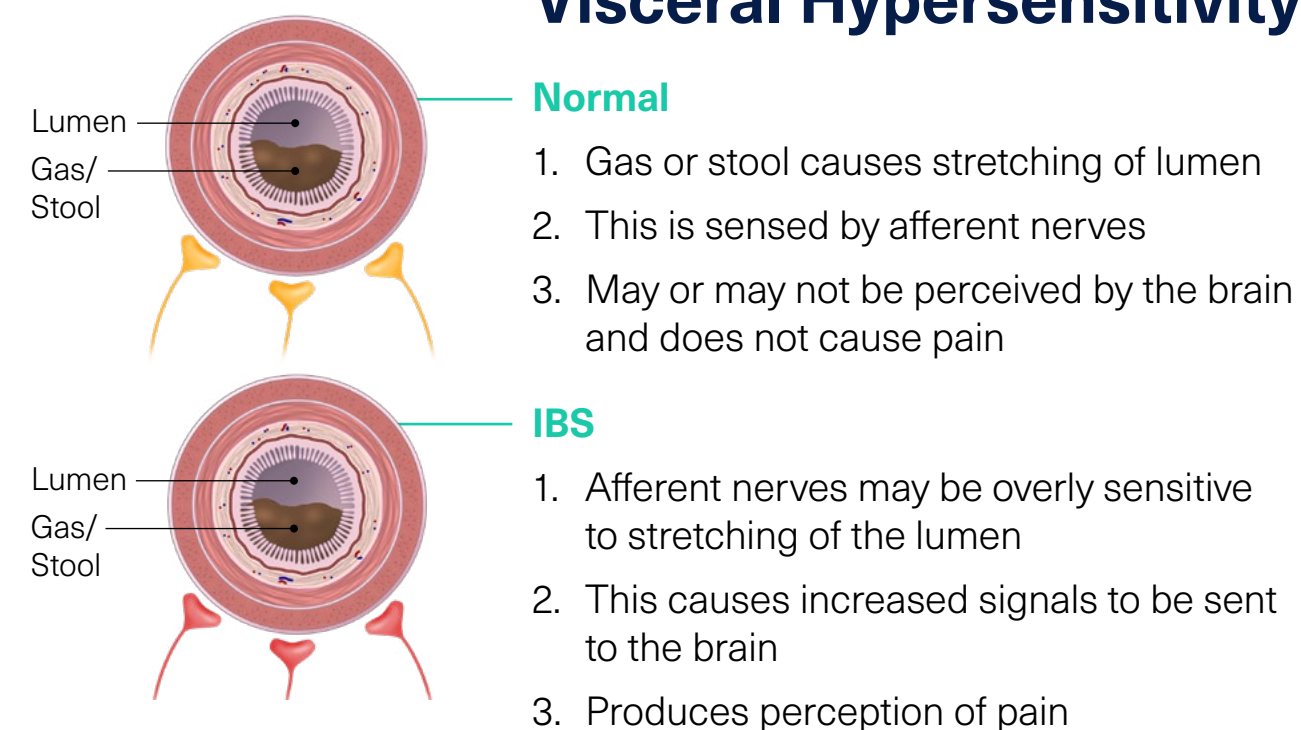


Food, hunger, emotions, and stress impact the bidirectional communication between the GI tract and the nervous system. The neurotransmitter serotonin is a key mediator, and alteration of serotonergic signaling has been implicated in IBS.

Altered Motility of the GI Tract²⁻⁴



Visceral Hypersensitivity^{2,5,6}



Local inflammation, alterations in gut flora, and psychological factors may also contribute to IBS.



The Mechanism
of Abdominal
Pain in IBS

1. Velio P, Bassotti G. *J Clin Gastroenterol.* 1996;22:190-196. 2. Tortora GJ, Derrickson B. *Principles of Anatomy and Physiology*, 13th ed. Hoboken, NJ: John Wiley and Sons, Inc.; 2012. 3. Lacy BE. *Am J Manag Care.* 2019; 25(4 Suppl):S55-S62. 4. National Digestive Diseases Information Clearinghouse. Accessed April 18, 2022. <https://www.niddk.nih.gov/health-information/digestive-diseases/constipation>

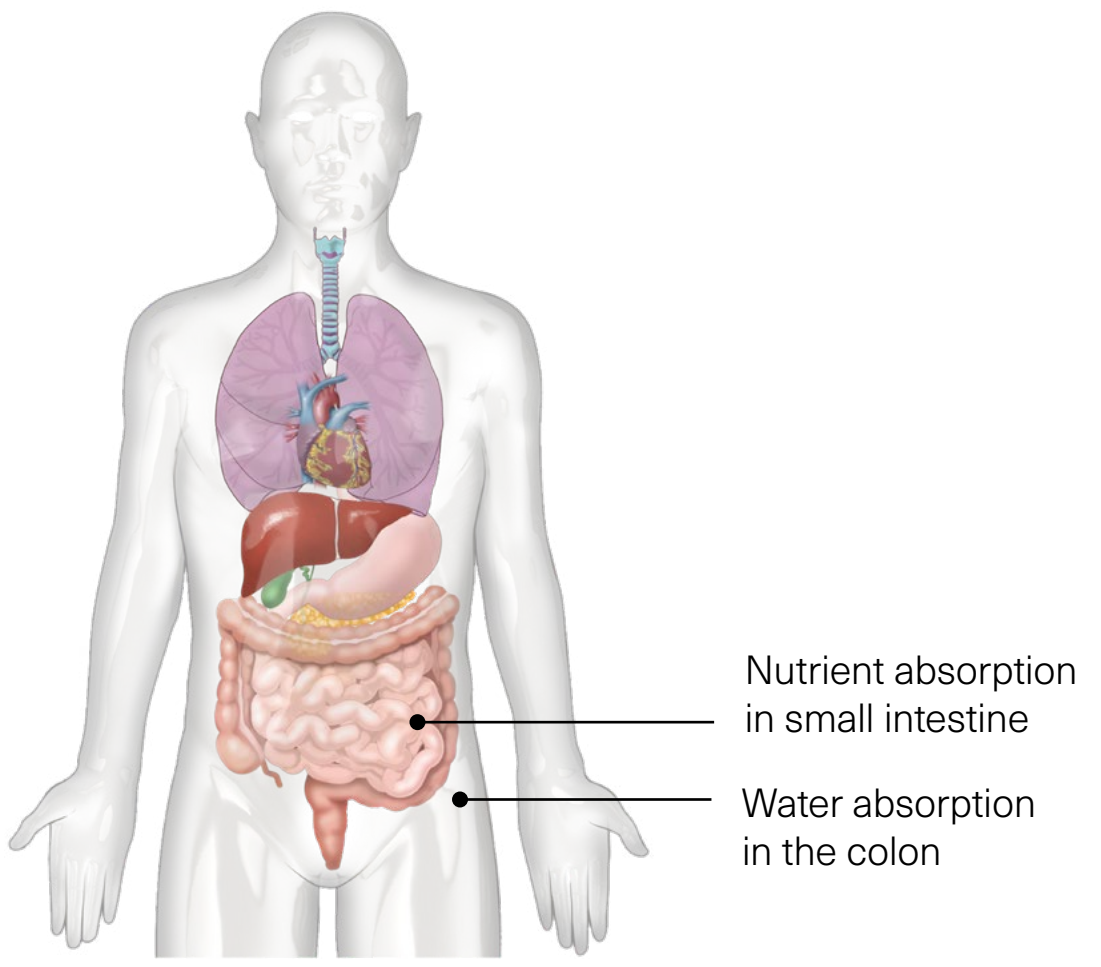
1. Fichna J and Storr MA. *Front Pharmacol.* 2012; 3(127):1-12. 2. Wald A, Talley NJ, Grover S. <http://www.uptodate.com/contents/pathophysiology-of-irritable-bowel-syndrome> 3. Feldman M, Friedman LS, and Brandt LJ. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management*. 9th ed. Philadelphia, PA: Saunders Elsevier; 2010. 4. Chey WD and Cash BD. *Curr Gastroenterol Rep.* 2006;8:273-81. 5. Delvaux M. *Gut.* 2002;51(Suppl. 1):i67-i71. 6. Karantanos T, Markoutsaki T, Gazouli M et al. *Gut Pathog.* 2010;2:3

CIC

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- SLOW MUSCLE CONTRACTIONS
- INCREASED WATER ABSORPTION



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IBS

The Precise Cause of IBS Is Unknown, but a Combination of Factors May Contribute to IBS Development

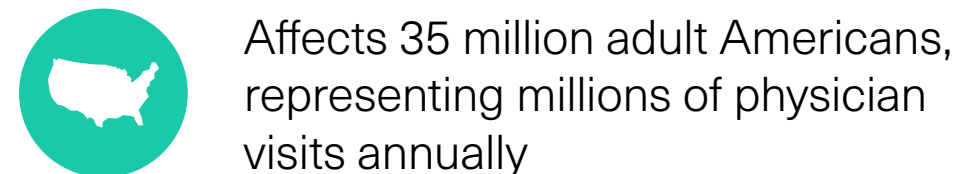
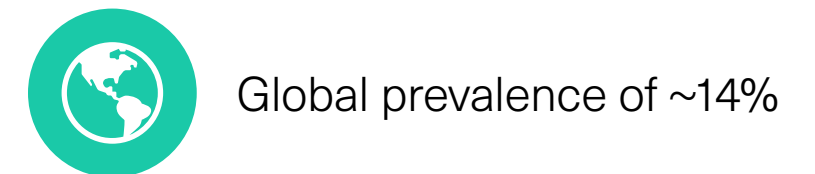
The Mechanism of Abdominal Pain in IBS

Prevalence

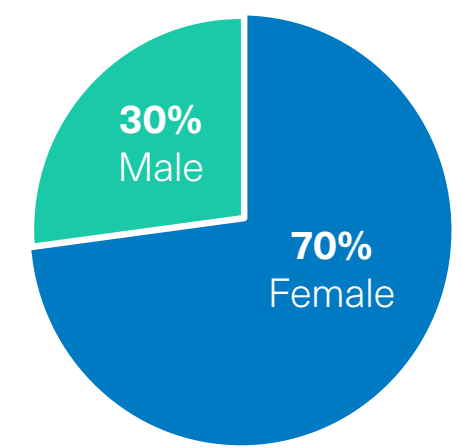
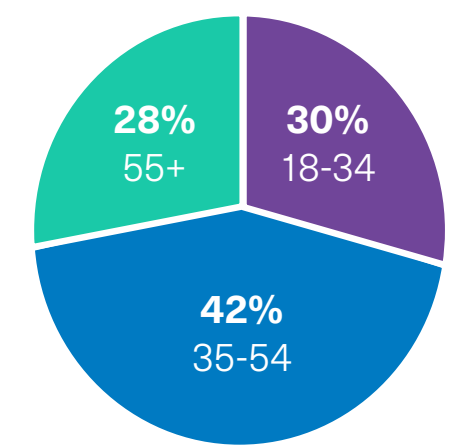
CIC

CIC Is Among the Most Frequently Occurring Functional GI Disorders¹⁻⁴

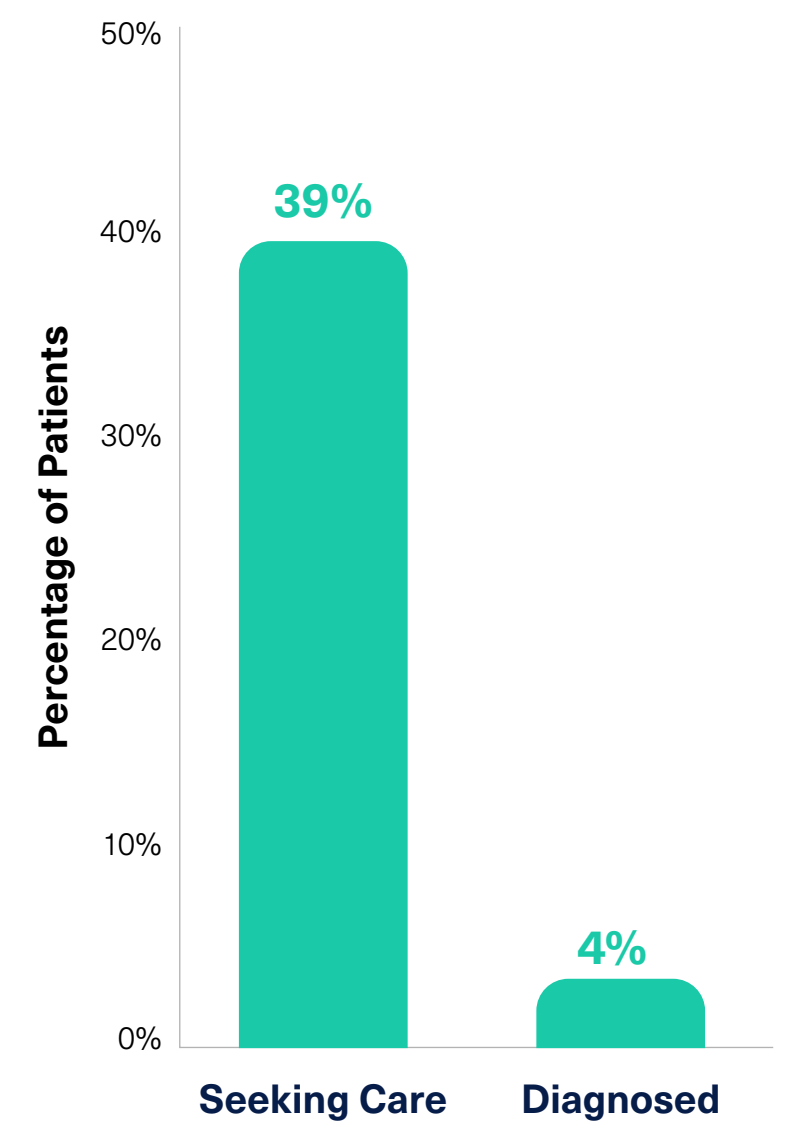
Incidence and Prevalence



Patient Demographics



CIC Patient Overview



IBS

IBS Is a Common GI Complaint in the US and Worldwide¹⁻⁹

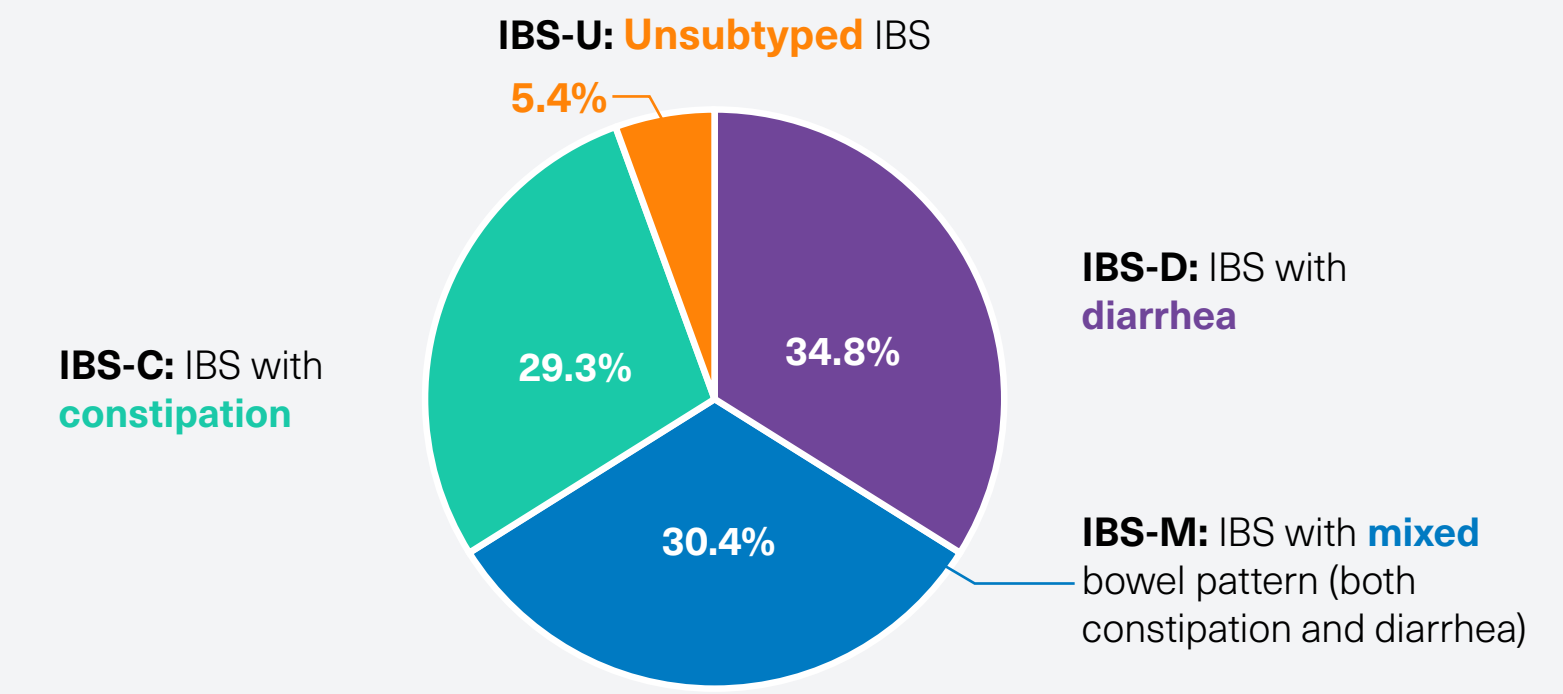
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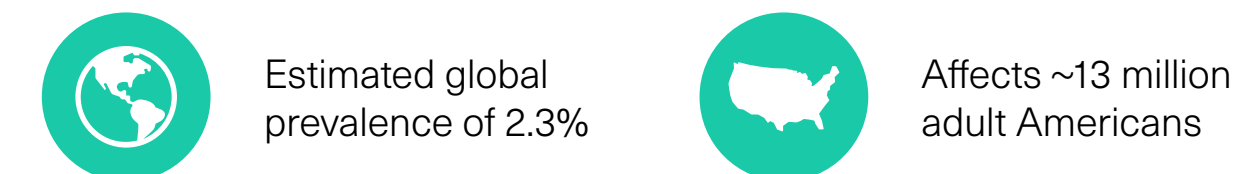
IBS Definition *i*

IBS Key Characteristics *i*

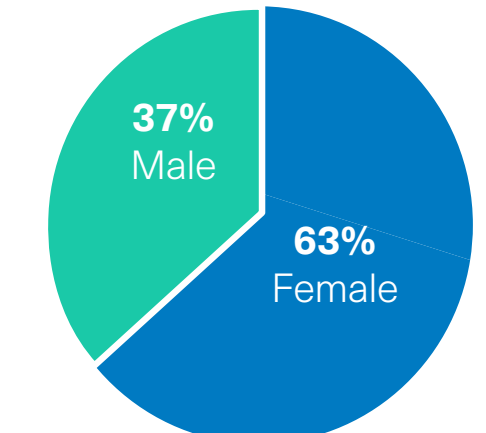
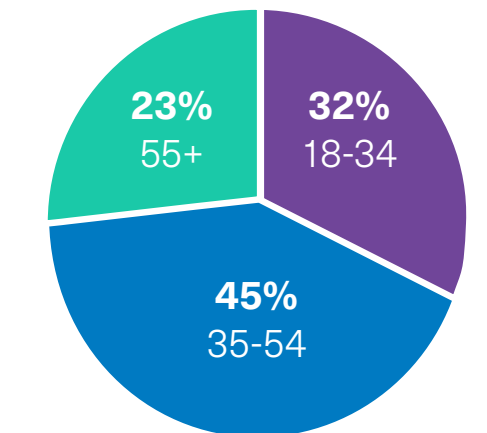
IBS Subtypes



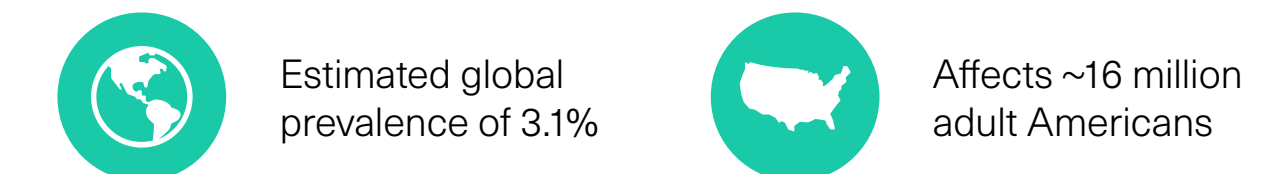
IBS-C Incidence and Prevalence



IBS-C Patient Demographics



IBS-D Incidence and Prevalence



IBS-D Patient Demographics

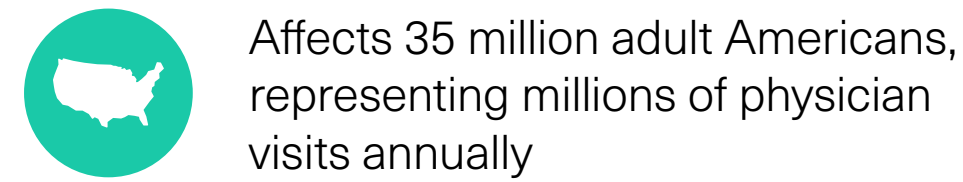
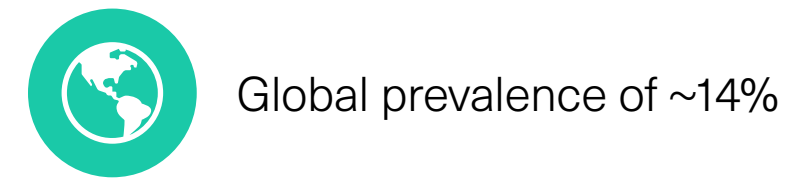
In contrast to IBS-C, IBS-D is **more common in men than in women**

Prevalence

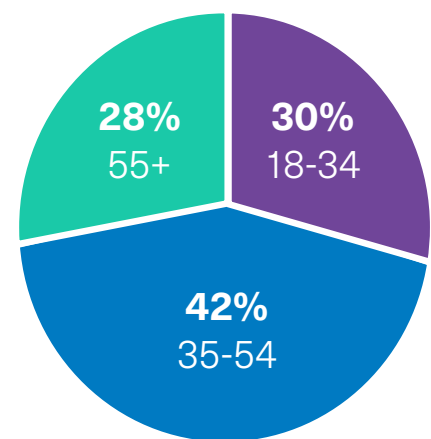
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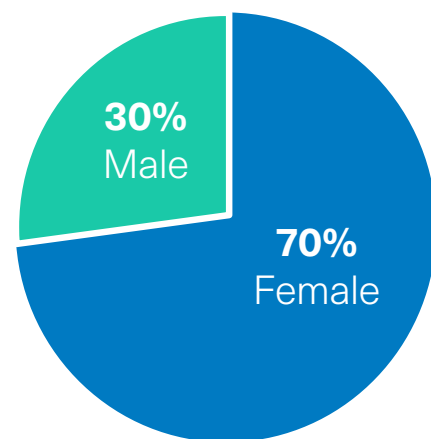
Incidence and Prevalence



Patient Demographics

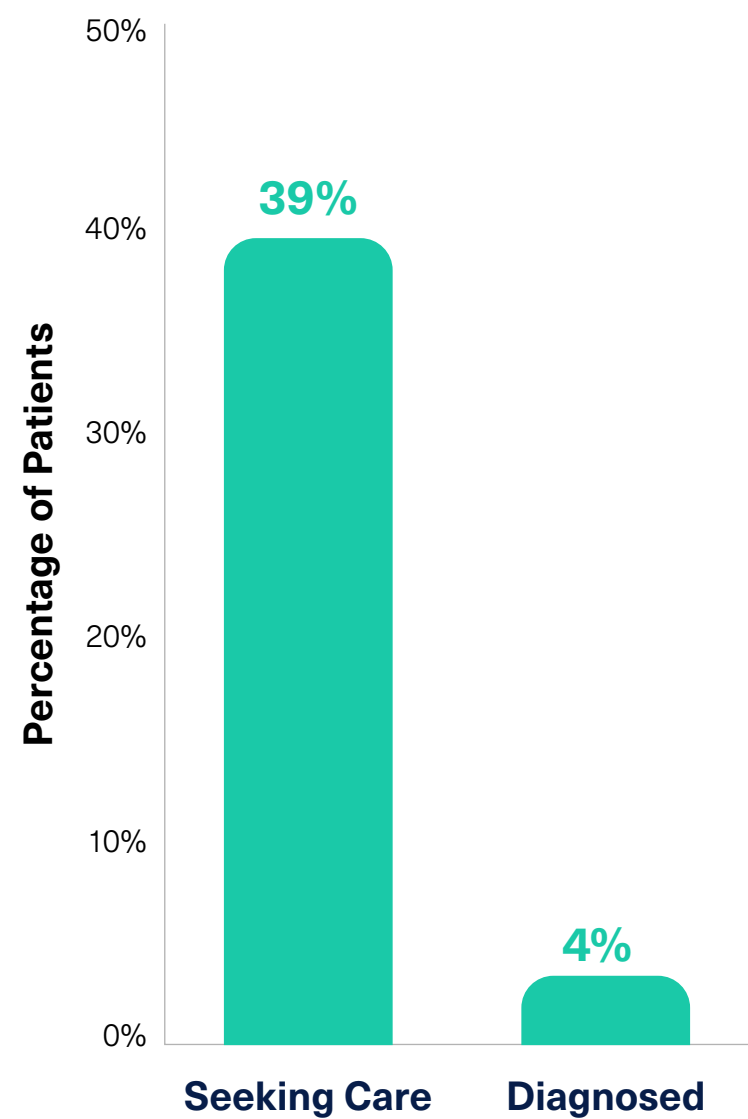


Age



Gender

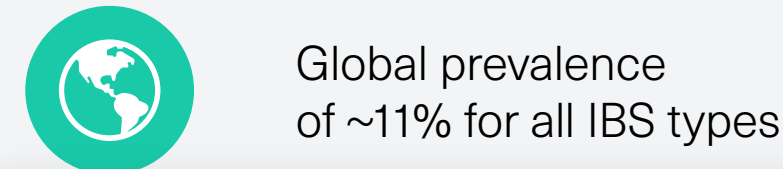
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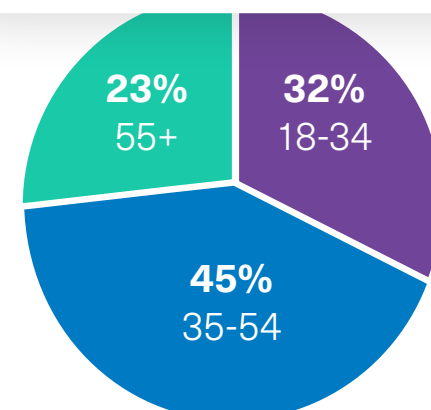
Incidence and Prevalence



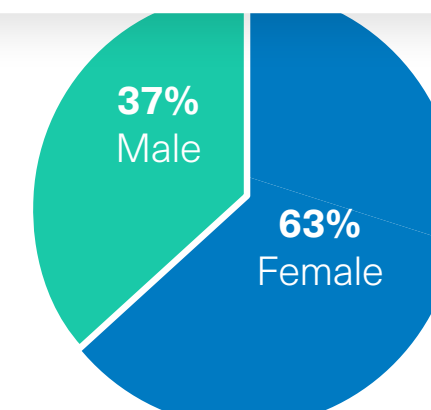
IBS Definition

- Irritable:** Abnormally sensitive to stimulus
- Bowel:** Pertaining to the intestines
- Syndrome:** A condition characterized by associated set of symptoms

1. Drossman DA. Accessed April 18, 2022. <https://ifgd.org/resources/publication-library/irritable-bowel-syndrome-ibs/> 2. National Digestive Diseases Information Clearinghouse. Accessed April 18, 2022. <https://www.niddk.nih.gov/health-information/digestive-diseases/irritable-bowel-syndrome>

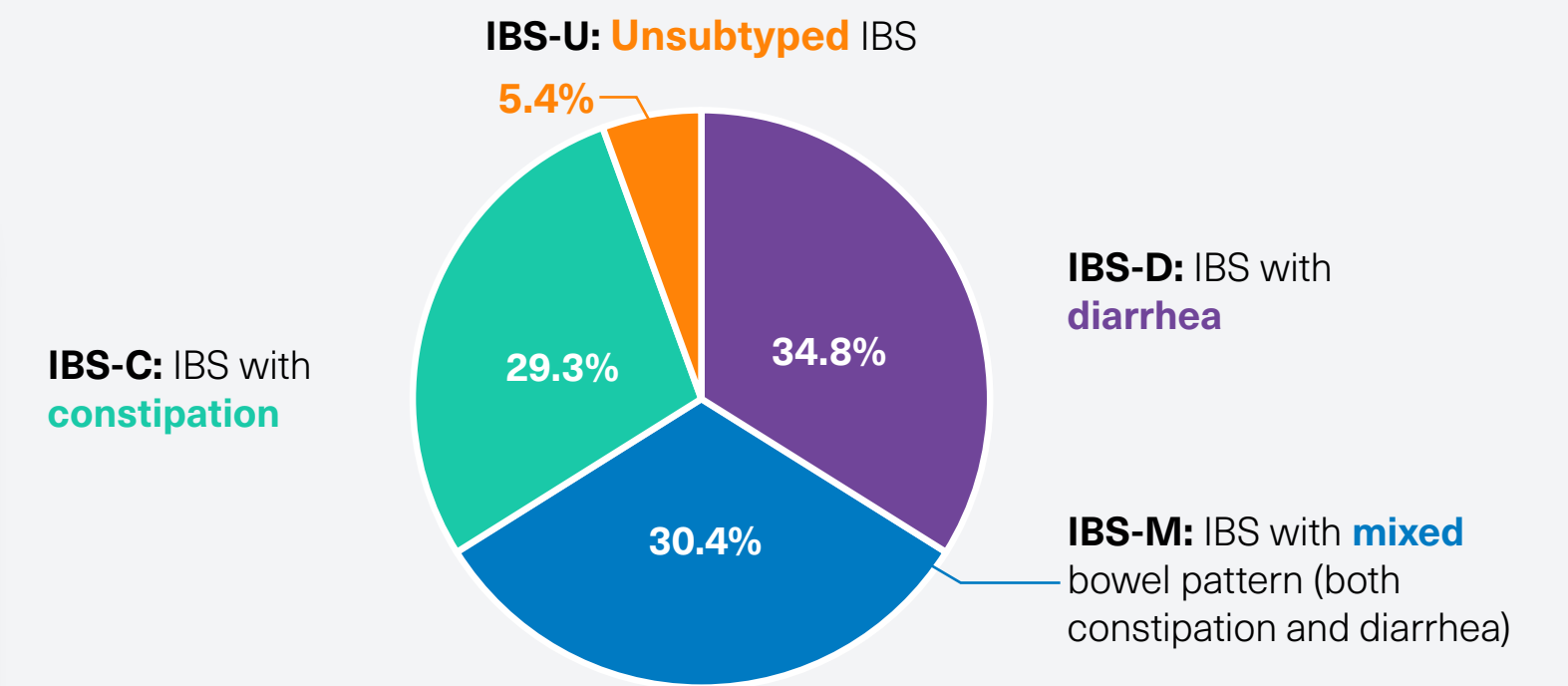


Age

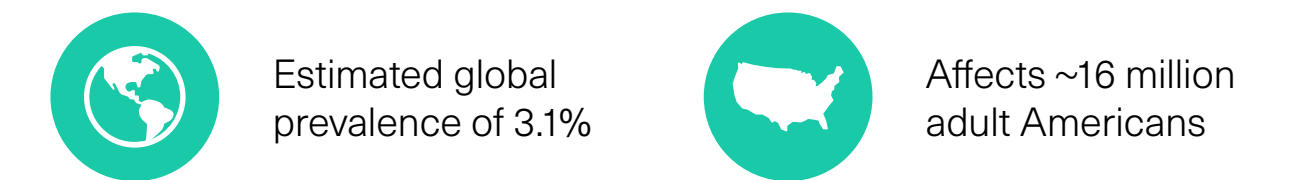


Gender

IBS Subtypes



IBS-D Incidence and Prevalence



IBS-D Patient Demographics

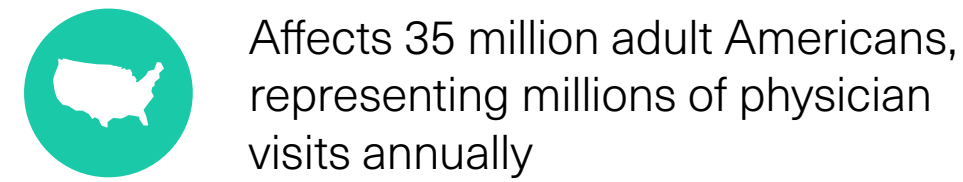
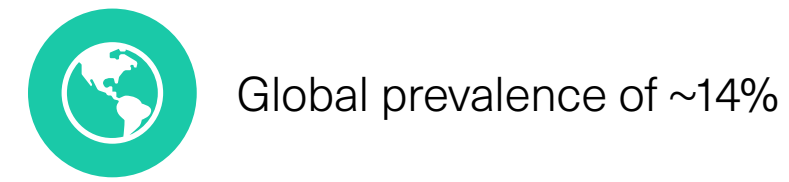
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Prevalence

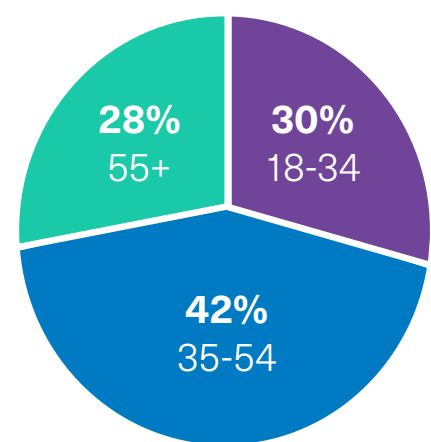
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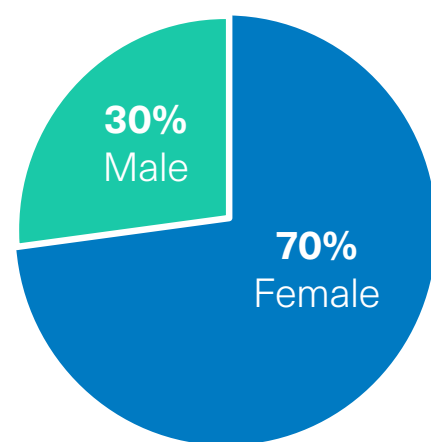
Incidence and Prevalence



Patient Demographics

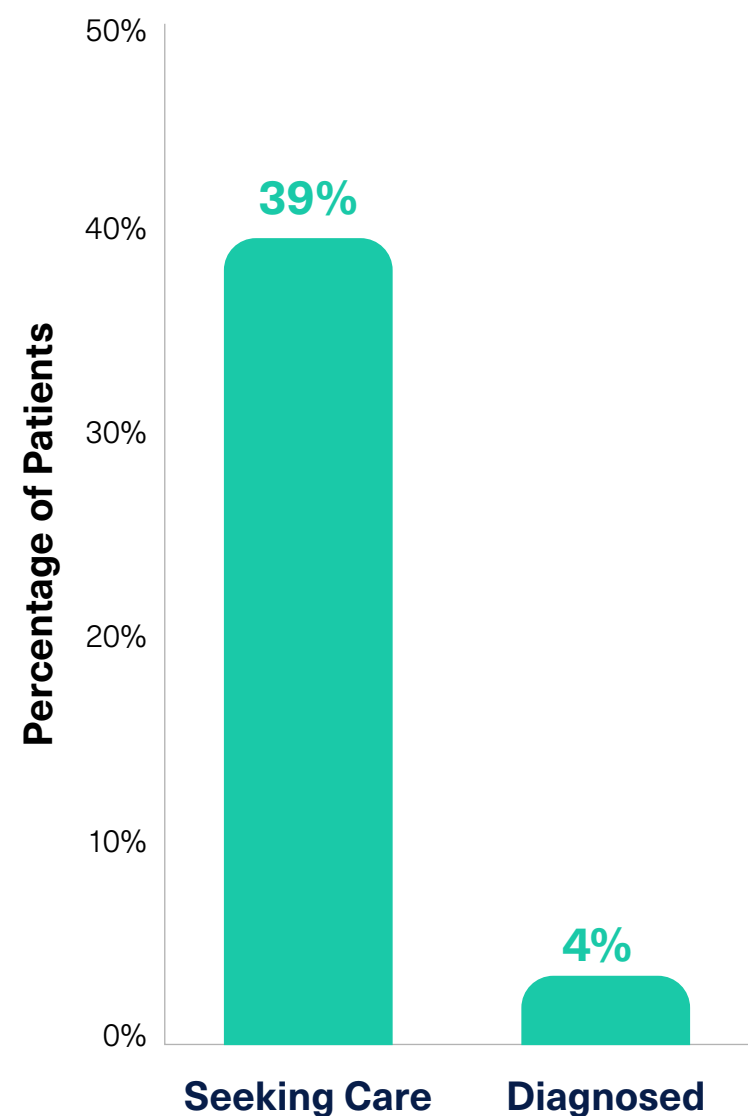


Age



Gender

CIC Patient Overview



IBS

IBS Is a Common GI Complaint in the US and Worldwide¹⁻⁹

Incidence and Prevalence



IBS Key Characteristics

Pain Is a Hallmark of IBS

IBS Considerations

- Involves the small and large intestines
- Does not cause permanent harm to the intestines or lead to other serious GI diseases
- May resemble other GI disorders

Common IBS Symptoms

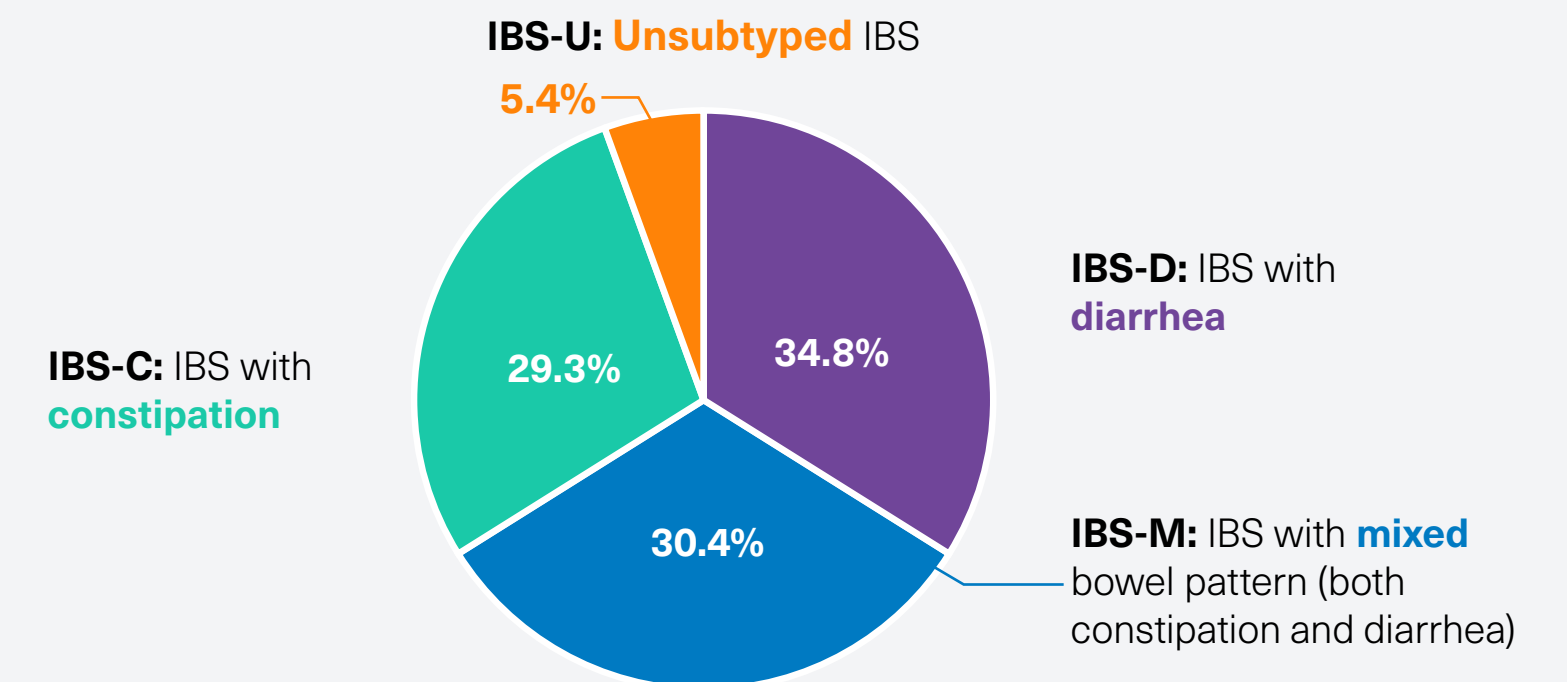
- Abdominal pain
- Bloating
- Flatulence
- Discomfort

1. Drossman DA. Accessed April 18, 2022. <https://iffgd.org/resources/publication-library/irritable-bowel-syndrome-ibs/> 2. National Digestive Diseases Information Clearinghouse. Accessed April 18, 2022. <https://www.niddk.nih.gov/health-information/digestive-diseases/irritable-bowel-syndrome>

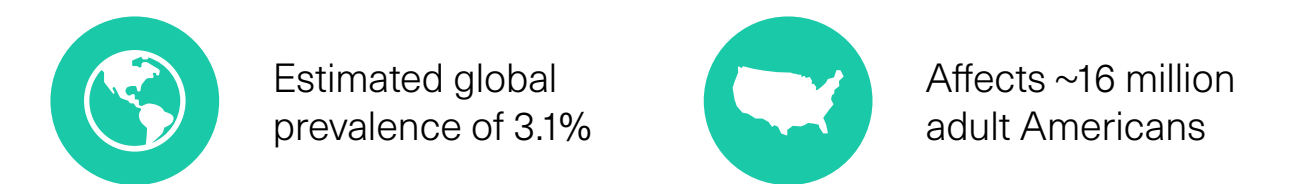


1. Canavan C, West J and Card T. *Clin Epidemiol.* 2014; 6:71-80. 2. Grundmann O, Yoon SL. *J Gastroenterol Hepatol.* 2010;25:691-699. 3. Hungin APS, Chang L et al. *Aliment Pharmacol Ther.* 2005;21:1365-1375. 4. Longstreth GF, Thompson WG, Chey WD, et al. *Gastroenterology.* 2006;130:1480-1491. 5. Palsson O, Whitehead W, et al. *Gastroenterology.* 2020;158:1262-1273. 6. Oka P, et al. *Lancet Gastroenterol Hepatol.* 2020; 5(10):908-917. 7. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc. 8. Howden LM, and Meyer JA. Age and Sex Composition: 2010. Washington, DC: U.S. Census Bureau; May 2011. 9. Lovell RM, Ford AC. *Am J Gastroenterol.* 2012;107(7):991.

IBS Subtypes



IBS-D Incidence and Prevalence



IBS-D Patient Demographics

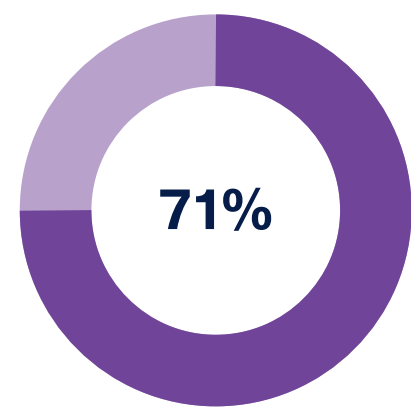
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Burden

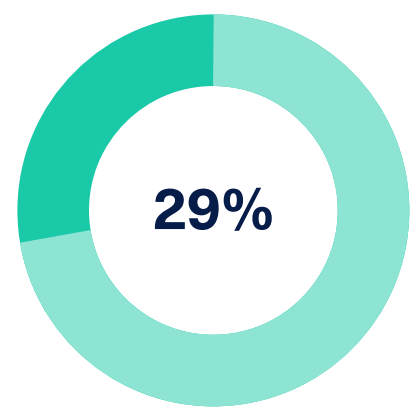
CIC

CIC Patients Experience Symptoms Beyond Constipation¹

Patient Symptom Overview *i*

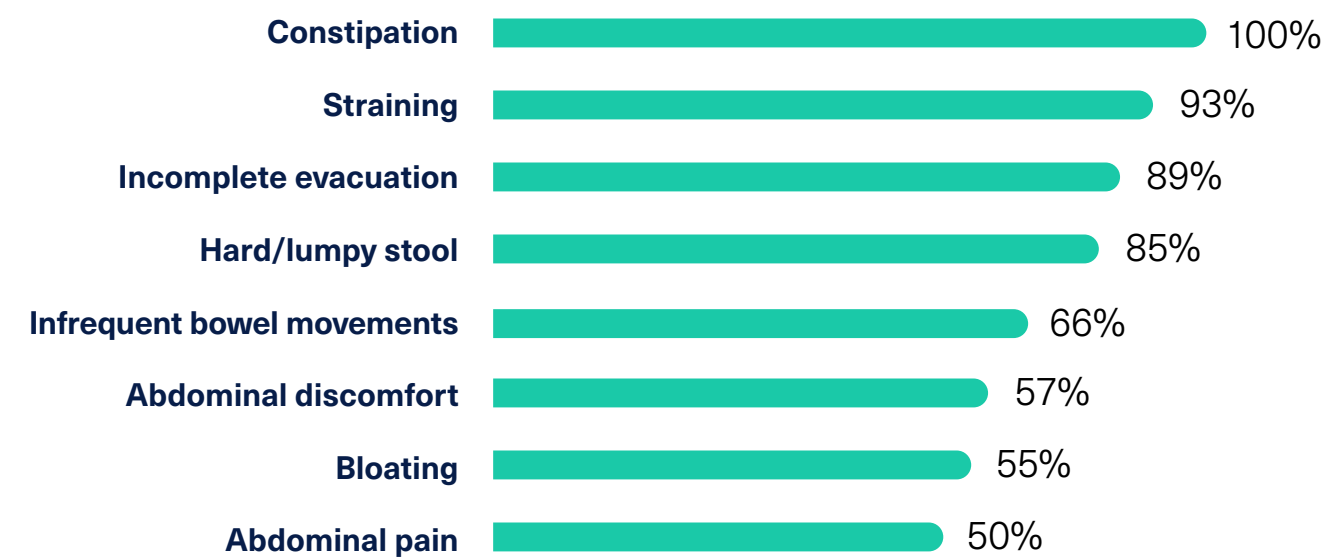


% of CIC patients with abdominal symptoms



% of CIC patients with constipation only

Most Frequent CIC Symptoms



BURDEN OF IBS

IBS Is Among the Most Common Reasons for a Physician Visit and Is Associated With Significant Costs²⁻⁷



IBS accounts for:

- 12% of primary care visits
- 20-40% of gastroenterologist visits



IBS in the United States:

- Is the 7th most common diagnosis by physicians
- Represents >\$20 billion/year in healthcare spending



Patients with IBS:

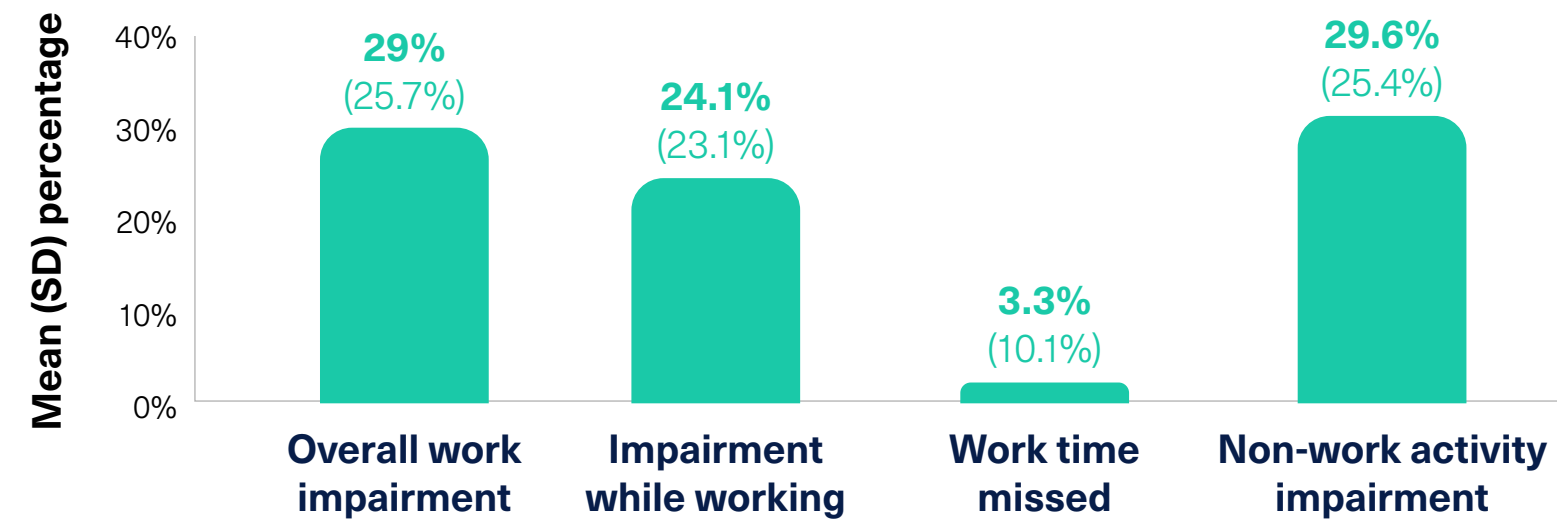
- Use more diagnostic tests and medications
- Miss work more often
- Have lower work productivity
- Are hospitalized more often



- IBS symptoms affect productivity an average of 8.0 days out of the month, and those with the condition miss ~1.5 days of work/school per month
- In exchange for 1 month of relief from IBS, more than half of IBS patients reported they would be willing to give up caffeine or alcohol, 40% would give up sex, 25% would give up cell phones, and 21.5% would give up the internet for 1 month

IBS

Impact of IBS-C and CIC on Patients' Quality of Life and Work Productivity¹



- IBS-C and CIC have a substantial impact on work productivity and daily activity interpreted as the proportion of time that work or non-work activity is affected
- Overall work impairment was due more to presenteeism (impairment while working) than absenteeism (work time missed)

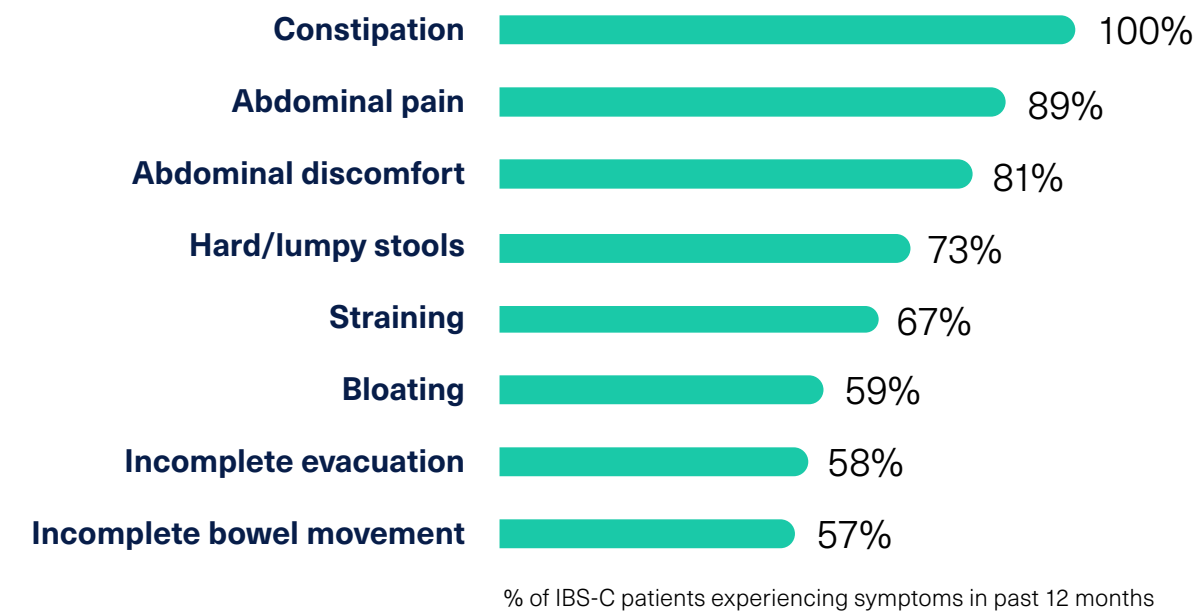
IBS

IBS Is Characterized by Abdominal Pain Associated With Altered Bowel Habits

Abdominal Pain Is a Defining Symptom of IBS-C *i*

Patients with IBS-C manifest abdominal pain as a dominant symptom.

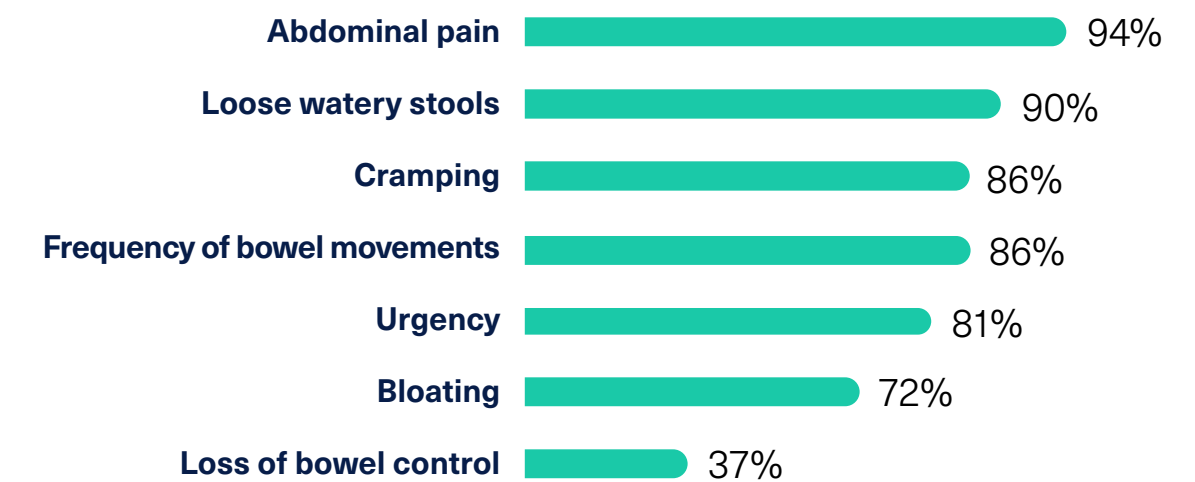
Most Frequent IBS-C Symptoms² *i*



IBS-D Is a Common GI Syndrome Characterized by Abdominal Pain Associated With Loose Bowel Movement

Diarrhea and abdominal symptoms are chronically present in IBS-D and cause significant disease burden.

Most Common Symptoms of IBS-D² *i*



1. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc. 2. International Foundation for Functional Gastrointestinal Disorders. <https://aboutibs.org/what-is-ibs/facts-about-ibs/> 3. International Foundation for Functional Gastrointestinal Disorders. <https://aboutibs.org/what-is-ibs/facts-about-ibs/statistics/> 4. Lacy BE, Rosemore J, Robertson D, et al. *Scand J Gastroenterol.* 2006;8:892-902. 5. American Gastroenterological Association. <https://www.multivu.com/players/English/7634451-aga-ibs-in-america-survey/> 6. Oka P, Parr H, Barberio, et al. *Lancet Gastroenterol Hepatol.* 2020;5(10):908-917. 7. Ballou S, McMahon C, Lee HN, et al. *Clin Gastroenterol Hepatol.* 2019; 17(12):2471-2478.

1. Taylor, DCA, Abel JL, Martin C, et al. *J Med Econ.* 2020; 23(10):1072-1083. 2. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc.

CIC=chronic idiopathic constipation. GI=gastrointestinal. IBS-C=irritable bowel syndrome with constipation. IBS=irritable bowel syndrome. IBS-D=irritable bowel syndrome with diarrhea.

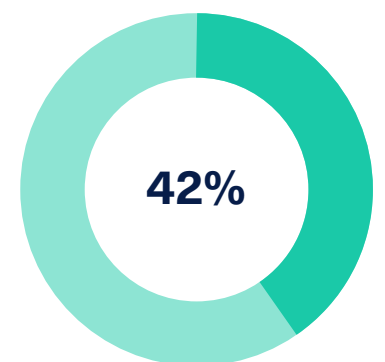
Burden

CIC

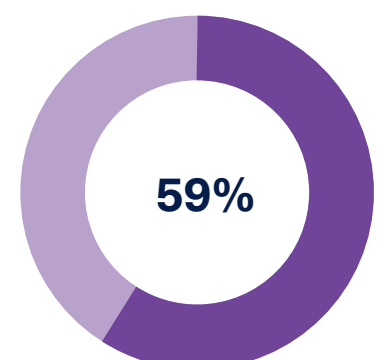
CIC Is Associated With Substantial Symptom and Disease Burden

CIC is among the most common reasons for primary care visits, and patients may experience a long road from recognition of symptoms to diagnosis.¹⁻³

Symptoms	Rated as Very Bothersome
Constipation	62%
Straining	58%
Incomplete evacuation	45%
Hard/lumpy stools	41%
Infrequent bowel movements	35%
Abdominal bloating	30%
Abdominal discomfort	30%
Abdominal pain	27%



of patients with CIC express **frustration** with their illness²



of current CIC prescription users are **dissatisfied** with their current treatment²

CIC symptoms affect patients' quality of life, with the majority of patients rating their symptoms as **extremely or very bothersome**.

1. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc. 2. Harris LA, Horn J, Kissous-Hunt M, et al. *Adv Ther*. 2017;34:2661-2673. 3. National Digestive Diseases Information Clearinghouse. <https://www.niddk.nih.gov/health-information/digestive-diseases/constipation/symptoms-causes>

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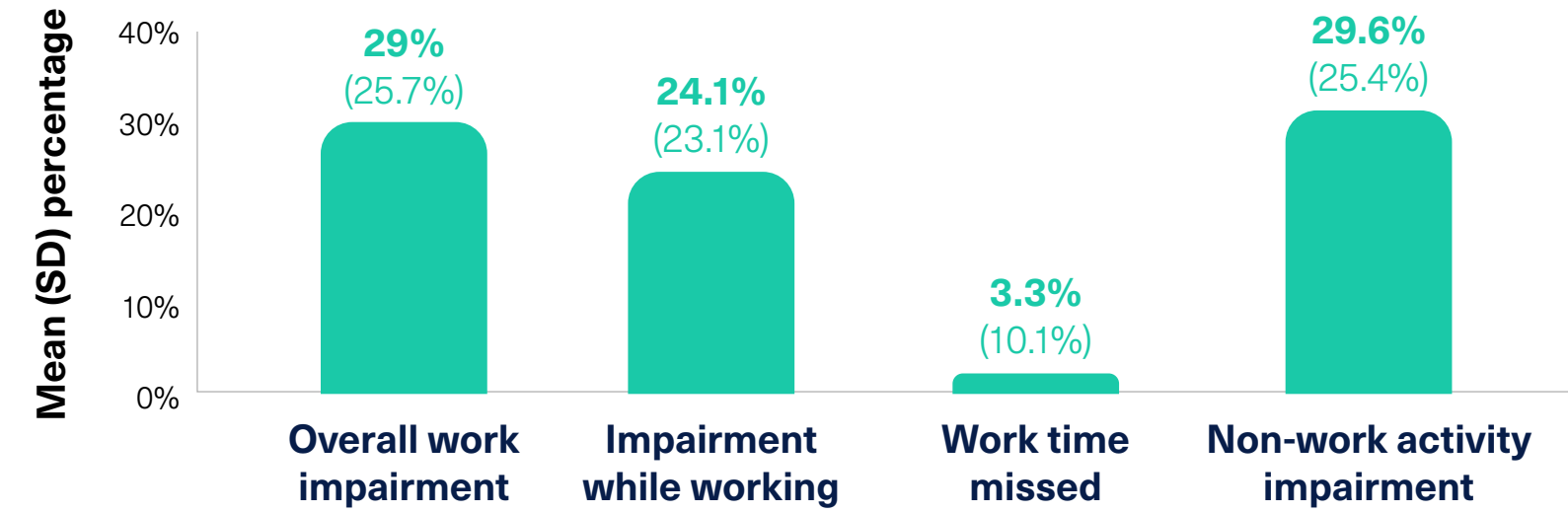


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IBS

Impact of IBS-C and CIC on Patients' Quality of Life and Work Productivity¹



- IBS-C and CIC have a substantial impact on work productivity and daily activity interpreted as the proportion of time that work or non-work activity is affected
- Overall work impairment was due more to presenteeism (impairment while working) than absenteeism (work time missed)

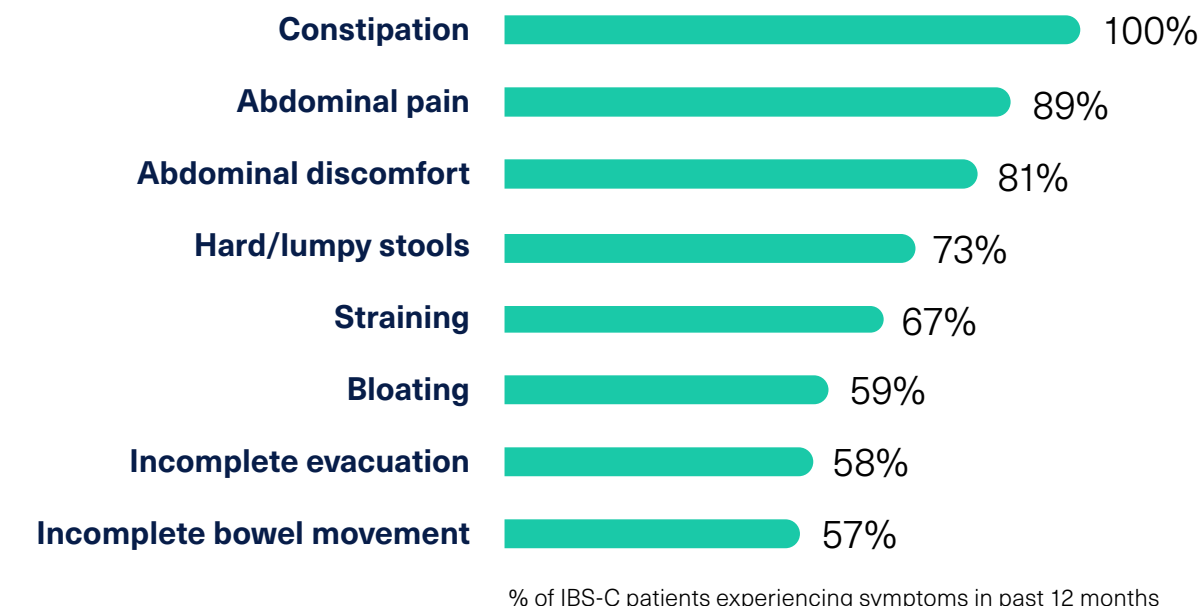
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Abdominal Pain Is a Defining Symptom of IBS-C

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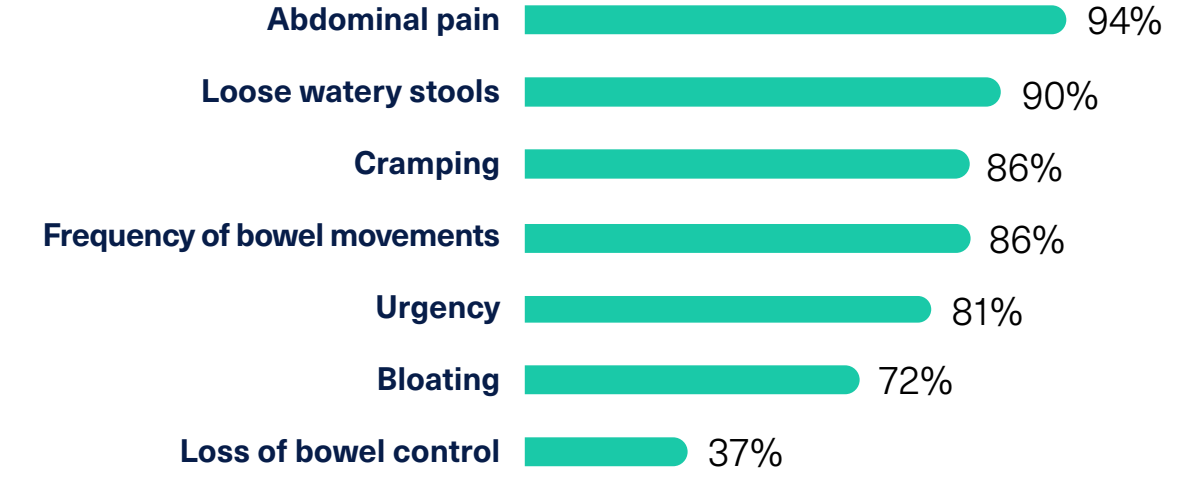
Most Frequent IBS-C Symptoms²



IBS-D Is a Common GI Syndrome Characterized by Abdominal Pain Associated With Loose Bowel Movement

Diarrhea and abdominal symptoms are chronically present in IBS-D and cause significant disease burden.

Most Common Symptoms of IBS-D²



1. Taylor, DCA, Abel JL, Martin C, et al. *J Med Econ*. 2020; 23(10):1072-1083. 2. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc.

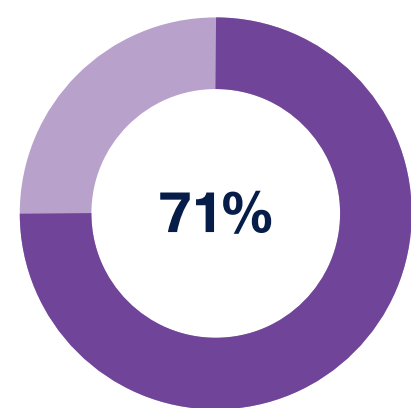


Burden

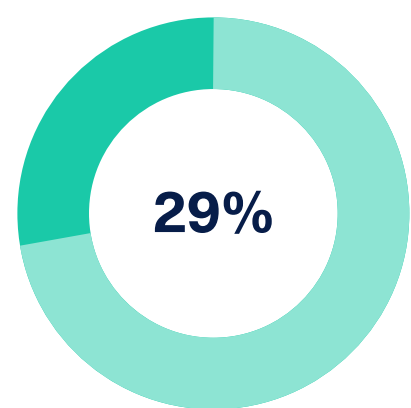
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CIC Patients Experience Symptoms Beyond Constipation¹

Patient Symptom Overview i

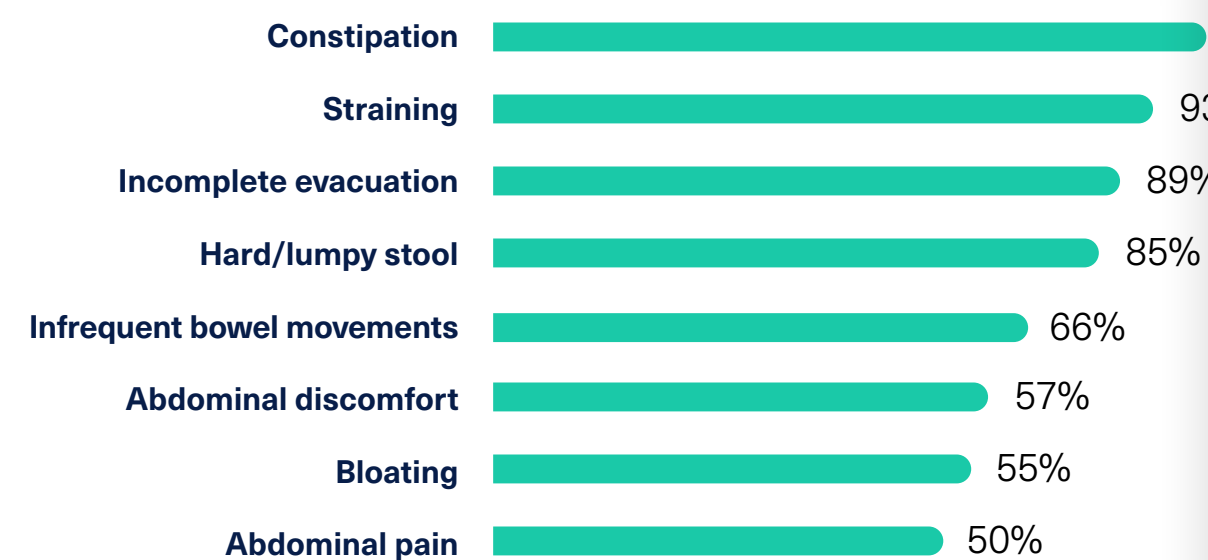


% of CIC patients with abdominal symptoms



% of CIC patients with constipation only

Most Frequent CIC Symptoms



IBS

Impact of IBS-C and CIC on Patients' Quality of Life and Work Productivity¹

40% | 29% | 29.6%

IBS-C vs CIC

Symptoms	CIC	IBS-C
Abdominal pain	Not always	✓
Bloating	Not always	✓
Constipation	✓	✓

Chronic Constipation



A key distinction between IBS-C and CIC is that IBS-C is highly associated with abdominal symptoms like pain and discomfort.

1. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc.



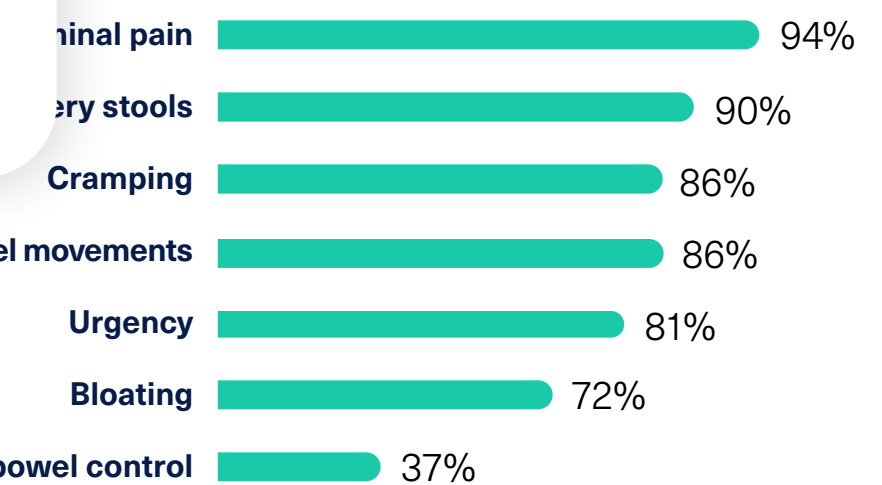
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With Altered Bowel Habits

Common GI Syndrome Characterized by Pain Associated With Loose Stools

Minimal symptoms are chronically present and cause significant disease burden.

Common Symptoms of IBS-D² i



% of diagnosed IBS-D patients experiencing symptoms in the past 12 months

BURDEN OF IBS

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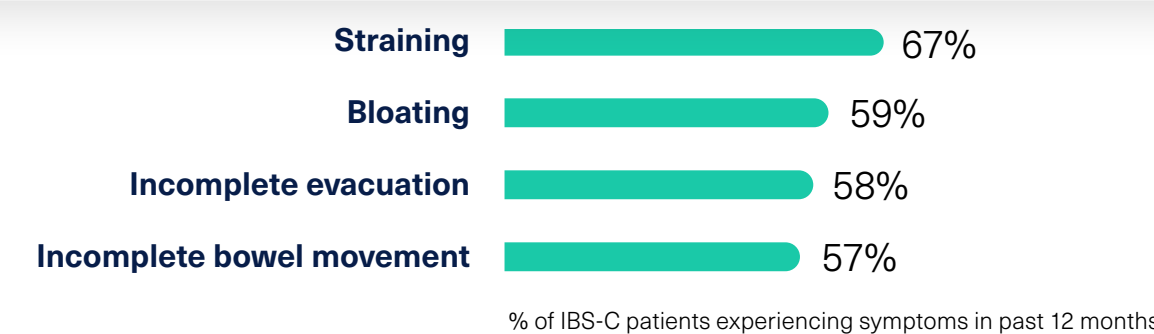


Patients with IBS:

- Use more diagnostic tests and medications
- Miss work more often
- Have lower work productivity
- Are hospitalized more often



- IBS symptoms affect productivity an average of 8.0 days out of the month, and those with the condition miss ~1.5 days of work/school per month
- In exchange for 1 month of relief from IBS, more than half of IBS patients reported they would be willing to give up caffeine or alcohol, 40% would give up sex, 25% would give up cell phones, and 21.5% would give up the internet for 1 month



% of IBS-C patients experiencing symptoms in past 12 months

1. Taylor, DCA, Abel JL, Martin C, et al. *J Med Econ.* 2020; 23(10):1072-1083. 2. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc.

1. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc. 2. International Foundation for Functional Gastrointestinal Disorders. <https://aboutibs.org/what-is-ibs/facts-about-ibs/> 3. International Foundation for Functional Gastrointestinal Disorders. <https://aboutibs.org/what-is-ibs/facts-about-ibs/statistics/> 4. Lacy BE, Rosemore J, Robertson D, et al. *Scand J Gastroenterol.* 2006;8:892-902. 5. American Gastroenterological Association. <https://www.multivu.com/players/English/7634451-aga-ibs-in-america-survey/> 6. Oka P, Parr H, Barberio, et al. *Lancet Gastroenterol Hepatol.* 2020;5(10):908-917. 7. Ballou S, McMahon C, Lee HN, et al. *Clin Gastroenterol Hepatol.* 2019; 17(12):2471-2478.

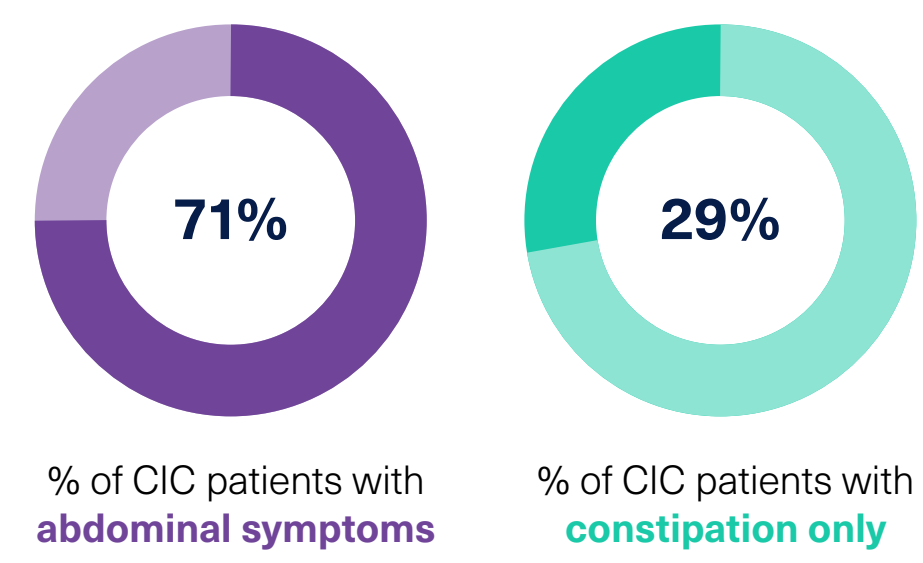
CIC=chronic idiopathic constipation. GI=gastrointestinal. IBS-C=irritable bowel syndrome with constipation. IBS=irritable bowel syndrome. IBS-D=irritable bowel syndrome with diarrhea.

Burden

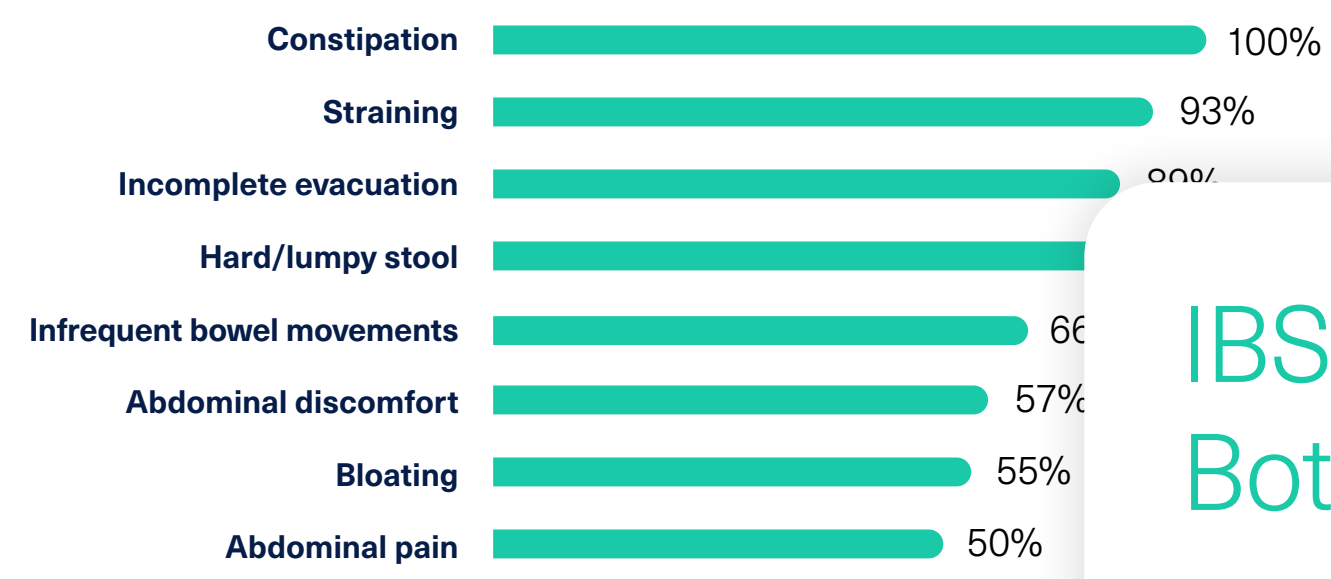
CIC

CIC Patients Experience Symptoms Beyond Constipation¹

Patient Symptom Overview i

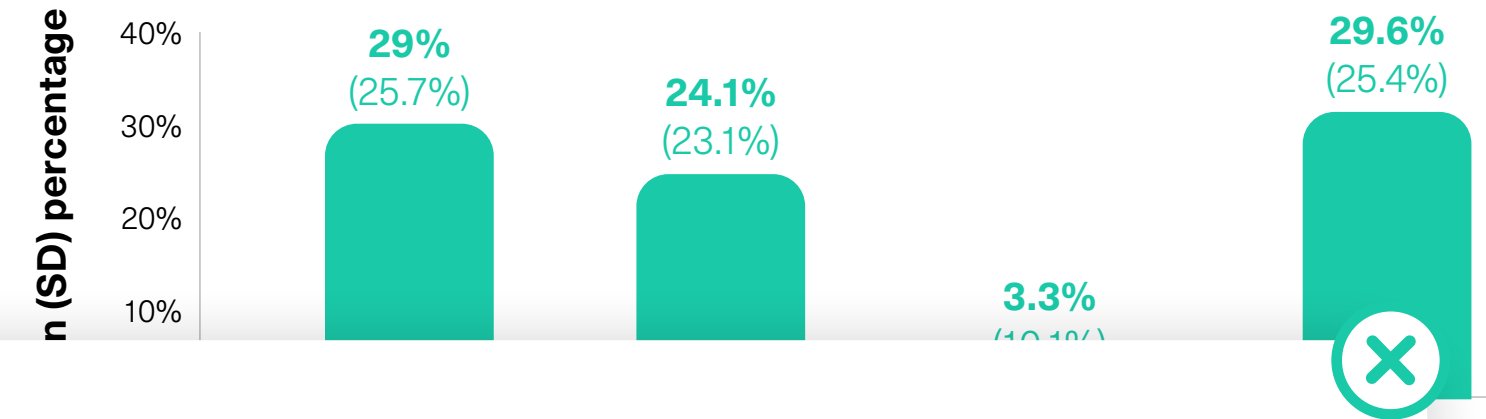


Most Frequent CIC Symptoms



IBS

Impact of IBS-C and CIC on Patients' Quality of Life and Work Productivity¹

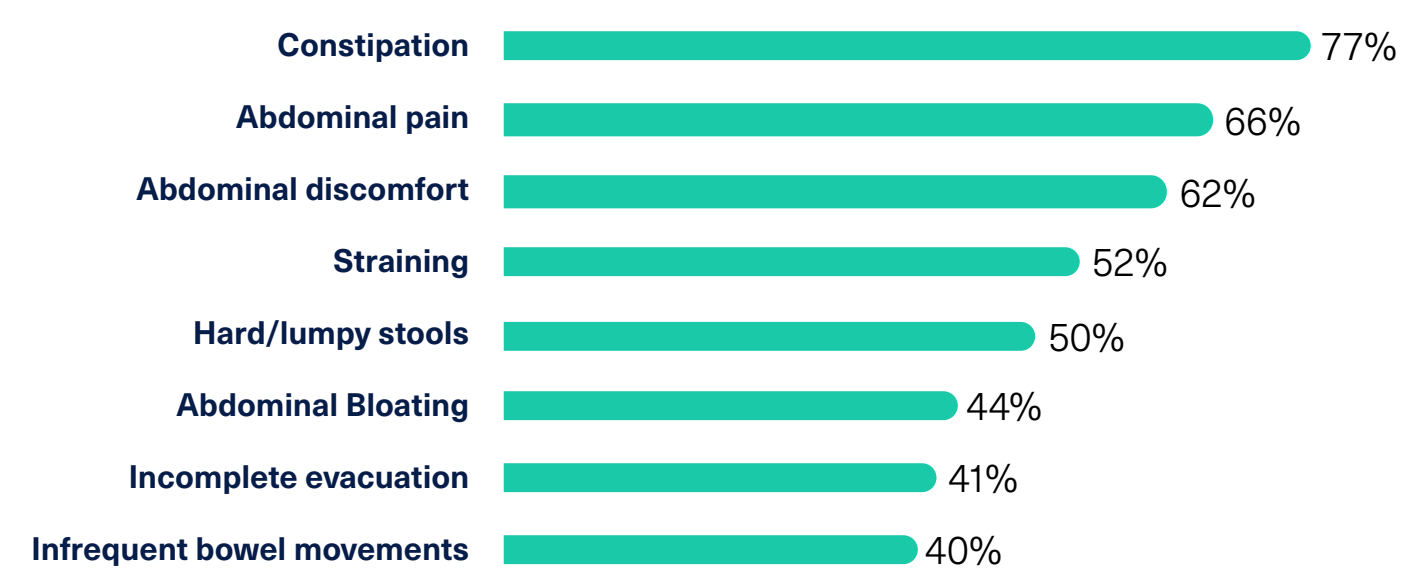


- IBS-C and CIC have a substantial impact on work productivity and daily activity interpreted as the proportion of time that work or non-work activity is affected
- Overall work impairment was due more to presenteeism (impairment while working) than absenteeism (work time missed)

IBS-C Is Associated With Bothersome Symptoms

The symptoms of IBS-C are among the most common reasons for primary care visits, and patients may experience a long road from recognition of symptoms to diagnosis.

Symptoms Rated as Very Bothersome



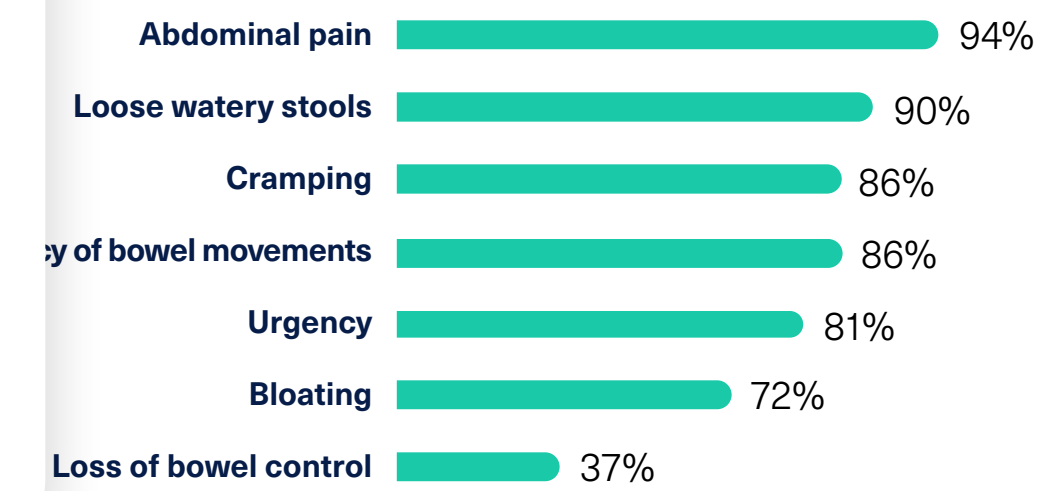
1. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc.

Associated With Altered Bowel Habits

Is a Common GI Syndrome Characterized by Abdominal Pain Associated With Loose Stool and Frequent Bowel Movement

Abdominal pain and abdominal symptoms are chronically associated with IBS-D and cause significant disease burden.

Common Symptoms of IBS-D² i



% of diagnosed IBS-D patients experiencing symptoms in the past 12 months

BURDEN OF IBS

IBS Is Among the Most Common Reasons for a Physician Visit and Is Associated With Significant Burden

IBS accounts for:

- 12% of primary care visits
- 20-40% of gastroenterologist visits

IBS in the United States:

- Is the 7th most common diagnosis by physicians
- Represents >\$20 billion/year in healthcare spending

Patients with IBS:

- Use more diagnostic tests and medications
- Miss work more often
- Have lower work productivity
- Are hospitalized more often

- IBS symptoms affect productivity an average of 8.0 days out of the month, and those with the condition miss ~1.5 days of work/school per month
- In exchange for 1 month of relief from IBS, more than half of IBS patients reported they would be willing to give up caffeine or alcohol, 40% would give up sex, 25% would give up cell phones, and 21.5% would give up the internet for 1 month

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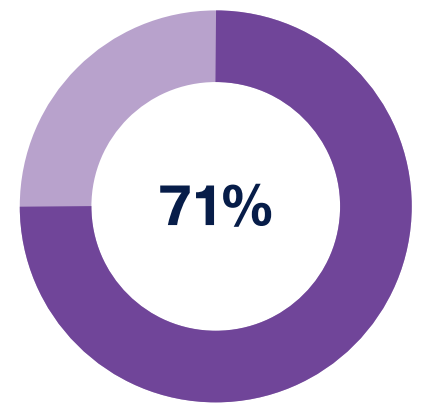
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Burden

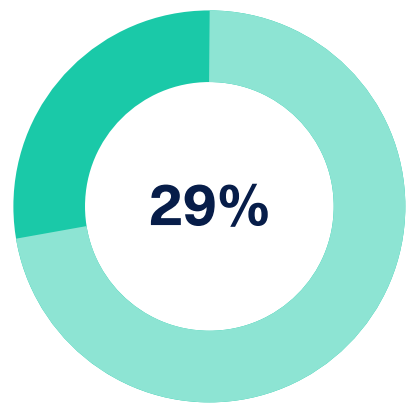
CIC

CIC Patients Experience Symptoms Beyond Constipation¹

Patient Symptom Overview i

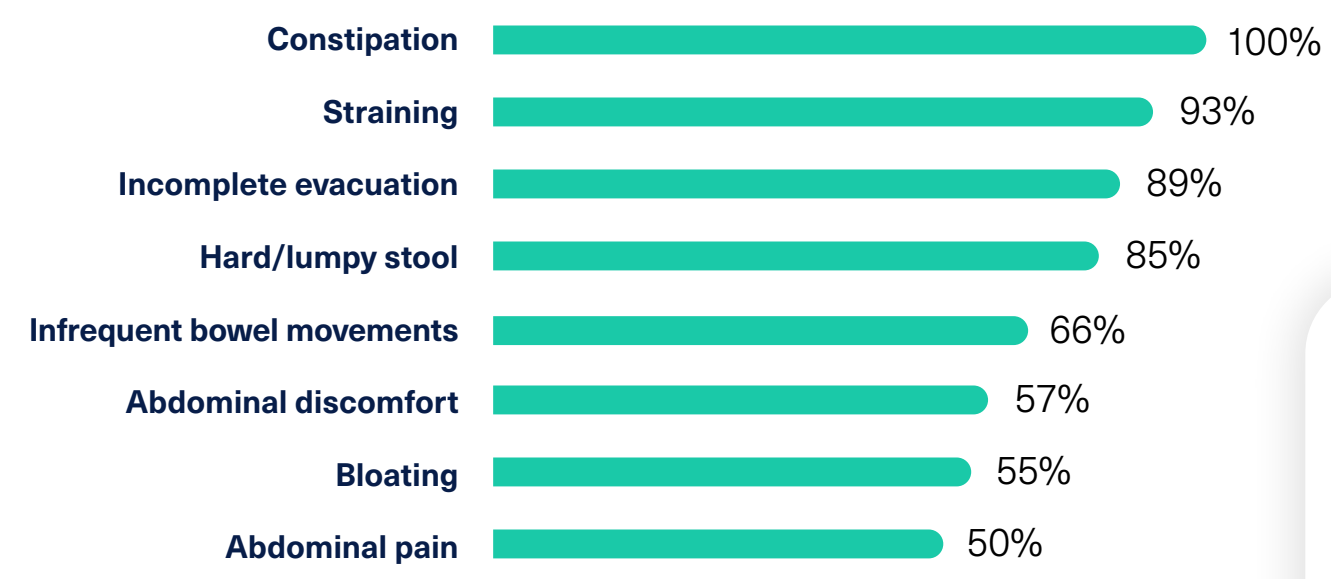


% of CIC patients with abdominal symptoms



% of CIC patients with constipation only

Most Frequent CIC Symptoms



BURDEN OF IBS

IBS Is Among the Most Common Reasons for a Physician Visit and Is Associated With Significant Costs²⁻⁷



IBS accounts for:

- 12% of primary care visits
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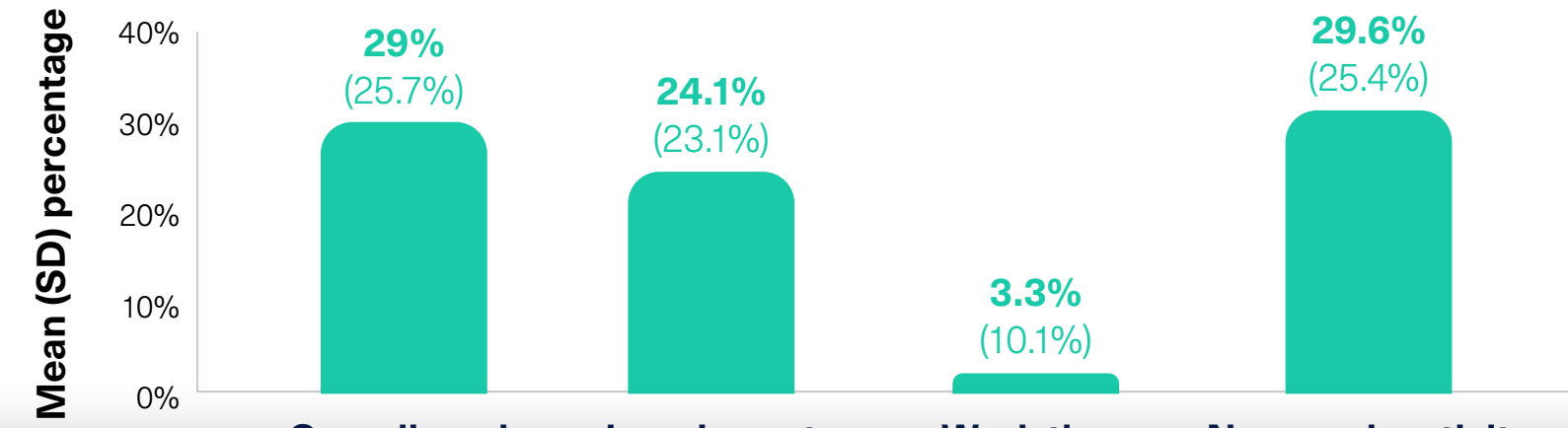
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- Have lower work productivity
- Are hospitalized more often



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IBS

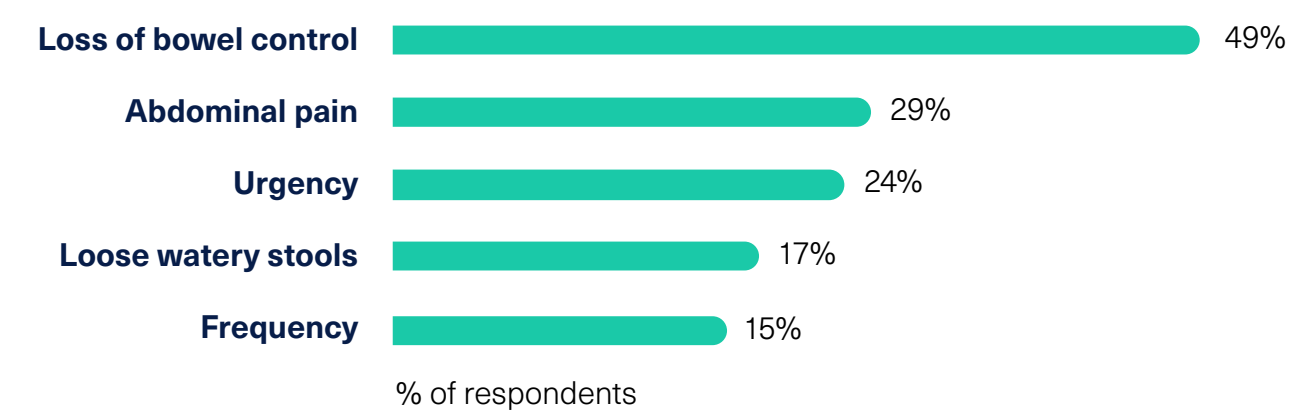
Impact of IBS-C and CIC on Patients' Quality of Life and Work Productivity¹



- IBS-C and CIC have a substantial impact on work productivity and daily activity interpreted as the proportion of time that work or non-work activity is affected
- Overall work impairment was due more to presenteeism (impairment while at work)

Most Bothersome IBS-D Symptoms and Consequences

Most Bothersome Symptoms of Diagnosed IBS-D Patients¹



On average, IBS leads to **2 missed days** of school/work and **9 days of impacted productivity** each month



Most IBS patients are only symptom-free **for a few days or less**



Nearly 1 in 4 patients report that they are "not at all" able to predict if they will experience symptoms on a given day



A majority of patients with IBS-D would assume a 10% risk of sudden death for a 99% chance of a cure for their condition²

1. Data on File, AbbVie Inc and Ironwood Pharmaceuticals Inc. 2. International Foundation for Functional Gastrointestinal Disorders. <https://aboutibs.org/what-is-ibs/facts-about-ibs/> 3. International Foundation for Functional Gastrointestinal Disorders. <https://aboutibs.org/what-is-ibs/facts-about-ibs/statistics/> 4. Lacy BE, Rosemore J, Robertson D, et al. *Scand J Gastroenterol*. 2006;8:892-902. 5. American Gastroenterological Association. <https://www.multivu.com/players/English/7634451-aga-ibs-in-america-survey/> 6. Oka P, Parr H, Barberio, et al. *Lancet Gastroenterol Hepatol*. 2020;5(10):908-917. 7. Ballou S, McMahon C, Lee HN, et al. *Clin Gastroenterol Hepatol*. 2019; 17(12):2471-2478.

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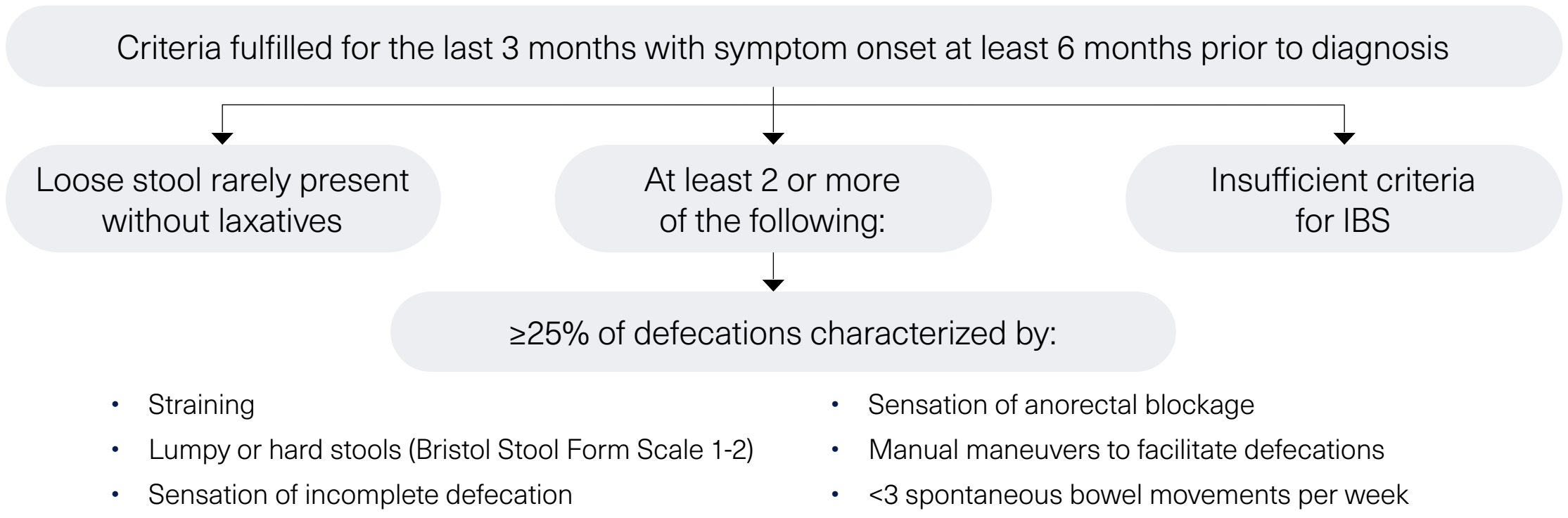
CIC=chronic idiopathic constipation. GI=gastrointestinal. IBS-C=irritable bowel syndrome with constipation. IBS=irritable bowel syndrome. IBS-D=irritable bowel syndrome with diarrhea.

Diagnosis

CIC

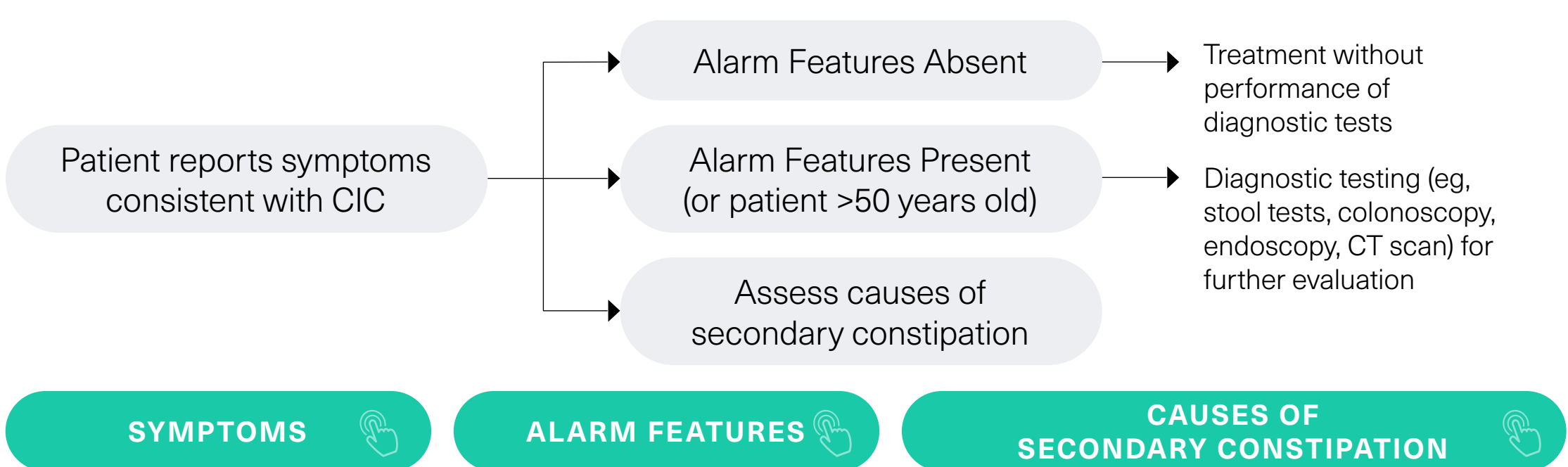
The Rome Diagnostic Criteria for CIC Diagnosis

Rome IV Criteria^{1,2}



Diagnostic Steps for CIC

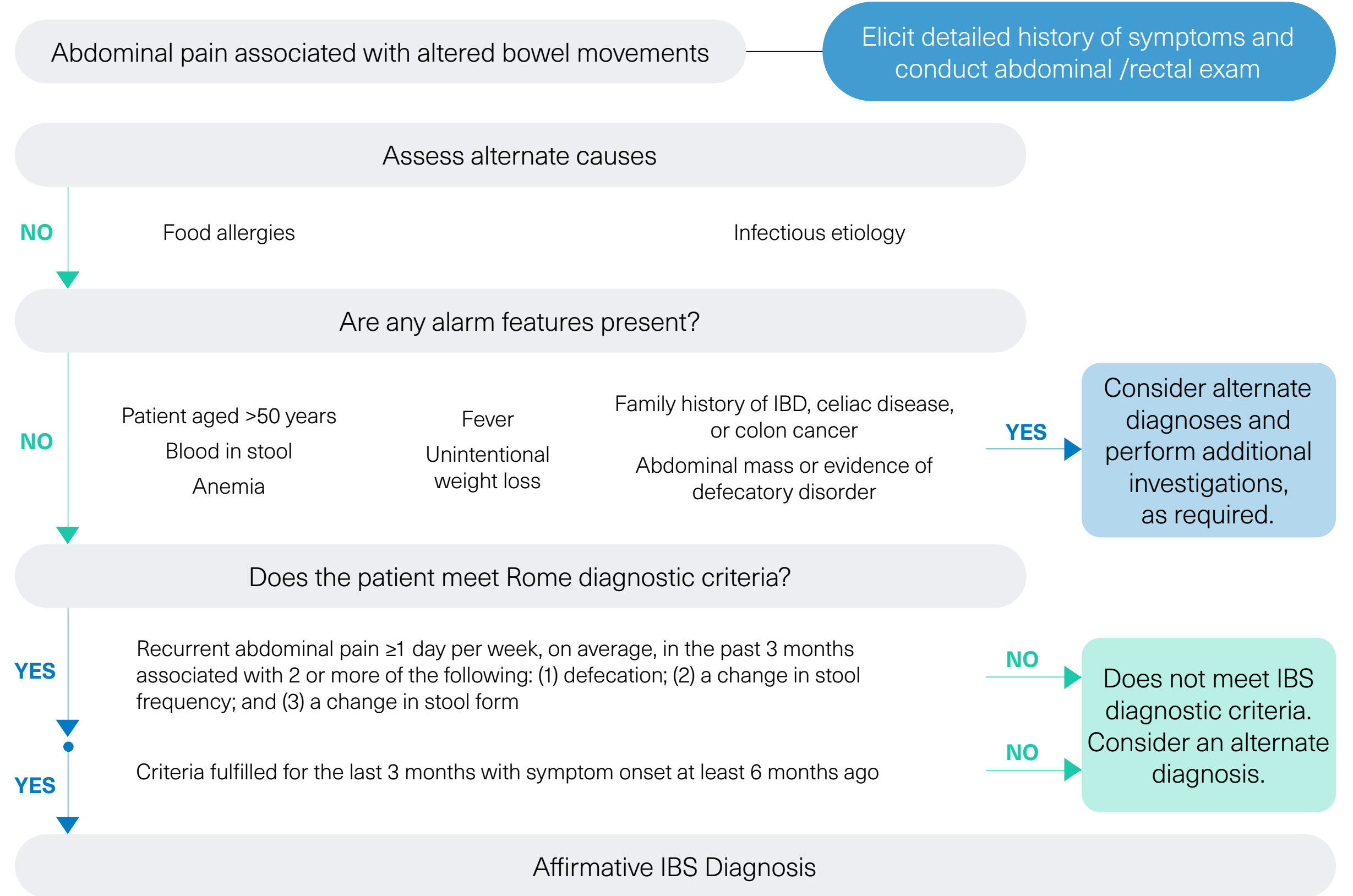
Diagnostic Paradigm³⁻⁵



IBS

IBS Diagnostic Pathway

IBS Is an Affirmative, Symptom-based Diagnosis, and Not a Diagnosis of Exclusion⁶⁻⁸



Diagnosis

Physiology/
MOD

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Pipeline Table

CIC

The Rome Diagnostic Criteria for CIC Diagnosis

Rome IV Criteria^{1,2}

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

Loose stool rarely present without laxatives

At least 2 or more of the following:

Insufficient criteria for IBS

≥25% of defecations characterized by:

- Straining
- Lumpy or hard stools (Bristol Stool Form Scale 1-2)
- Sensation of incomplete defecation
- Sensation of anorectal blockage
- Manual maneuvers to facilitate defecations
- <3 spontaneous bowel movements per week

Diagnostic Steps for CIC

Diagnostic Paradigm³⁻⁵



Symptoms

- Infrequent bowel movement (<3 per week)
- Difficult stool elimination
- Straining, hard/lumpy stools, prolonged time to stool (≥25% defecations)
- Chronically present symptoms
- Sensation of obstruction/blockage (≥25% defecations)
- Need for manual removal of stools (≥25% defecations)

...tment without
...formance of
...gnostic tests
...gnostic testing (eg,
...l tests, colonoscopy,
...oscopy, CT scan) for
...her evaluation

S OF
ONSTIPATION

IBS

IBS Diagnostic Pathway

IBS Is an Affirmative, Symptom-based Diagnosis, and Not a Diagnosis of Exclusion⁶⁻⁸

Abdominal pain associated with altered bowel movements

Elicit detailed history of symptoms and conduct abdominal /rectal exam

Assess alternate causes

NO

Food allergies

Infectious etiology

Are any alarm features present?

NO

Patient aged >50 years
Blood in stool
Anemia

Fever
Unintentional weight loss

Family history of IBD, celiac disease, or colon cancer
Abdominal mass or evidence of defecatory disorder

YES

Consider alternate diagnoses and perform additional investigations, as required.

Does the patient meet Rome diagnostic criteria?

YES

Recurrent abdominal pain ≥1 day per week, on average, in the past 3 months associated with 2 or more of the following: (1) defecation; (2) a change in stool frequency; and (3) a change in stool form

NO

Does not meet IBS diagnostic criteria. Consider an alternate diagnosis.

YES

Criteria fulfilled for the last 3 months with symptom onset at least 6 months ago

NO

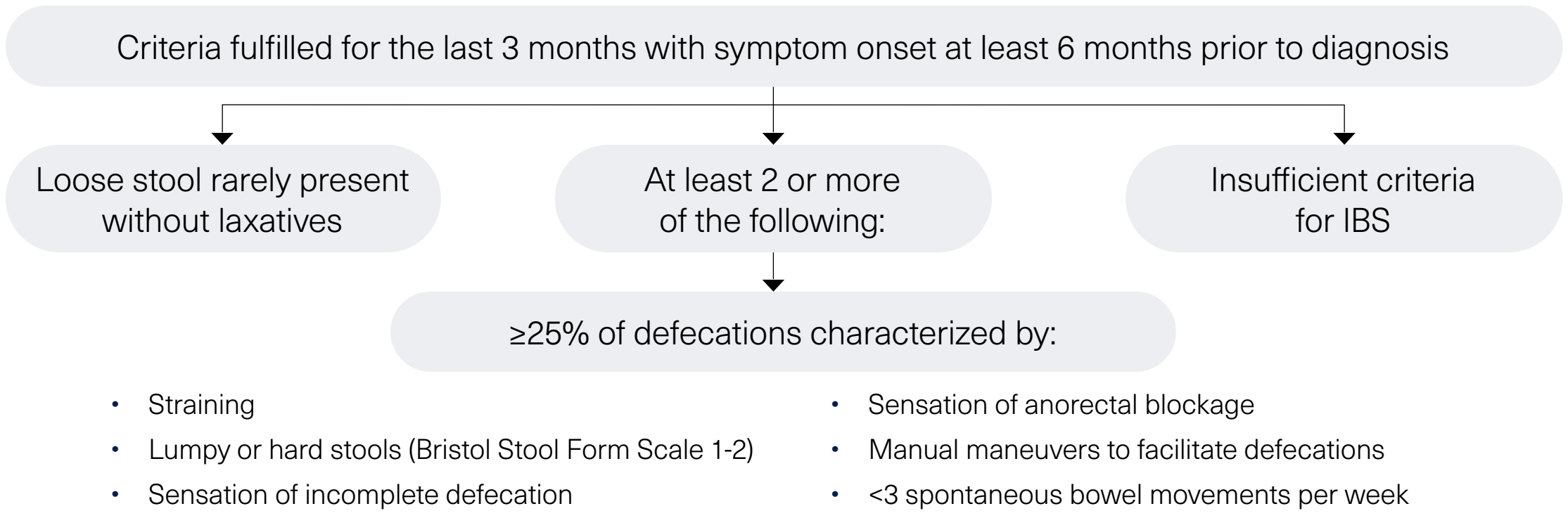
Affirmative IBS Diagnosis

Diagnosis

CIC

The Rome Diagnostic Criteria for CIC Diagnosis

Rome IV Criteria^{1,2}



Diagnostic Steps for CIC

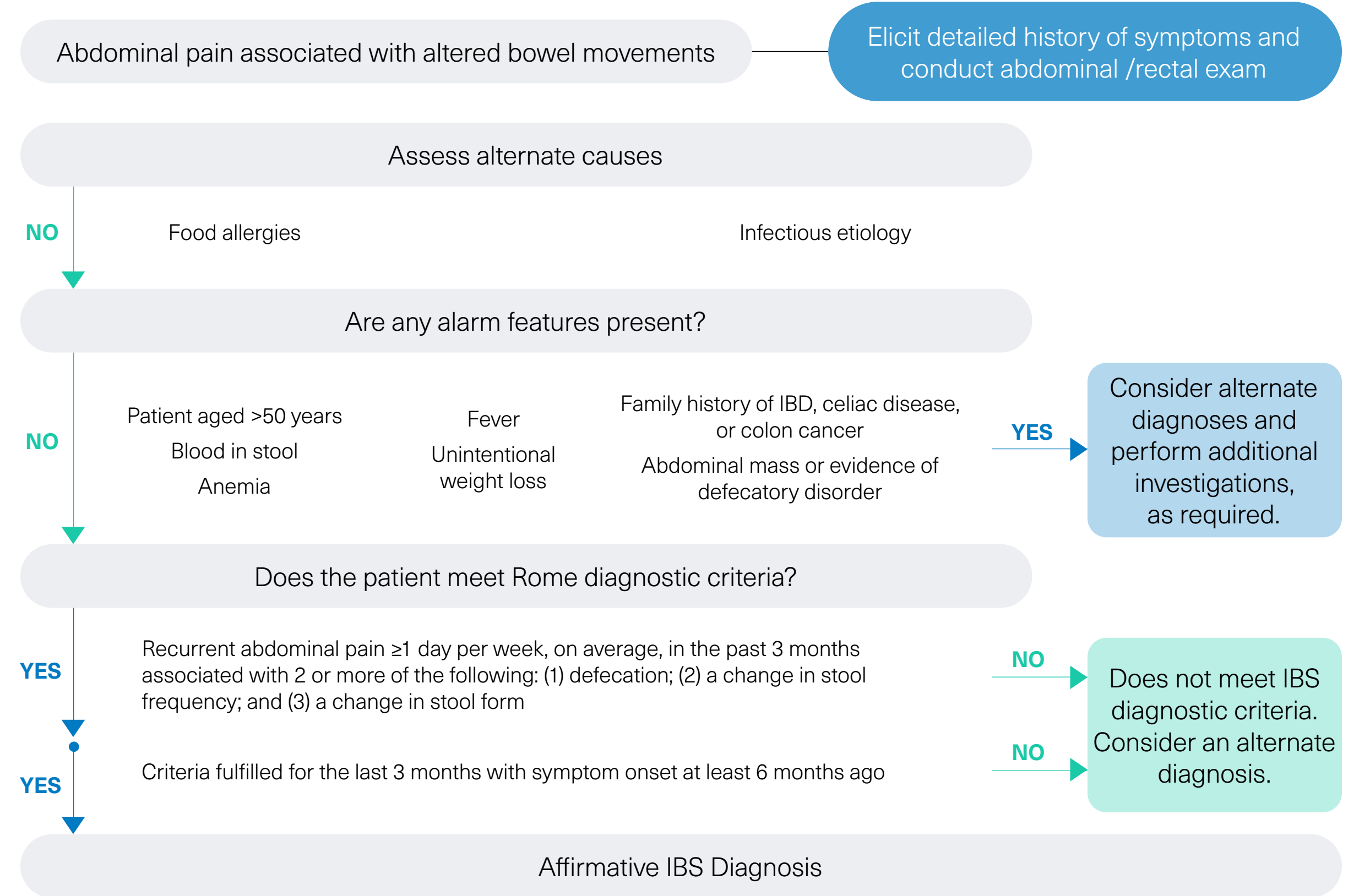
Alarm Features

- Rectal bleeding/blood in stool
- Anemia
- Unintentional weight loss of ≥10 pounds
- Family history of colon cancer or IBD
- Severe, persistent constipation non-responsive to treatment
- New onset of constipation in an elderly patient with no evidence of a potential cause of constipation

IBS

IBS Diagnostic Pathway

IBS Is an Affirmative, Symptom-based Diagnosis, and Not a Diagnosis of Exclusion⁶⁻⁸

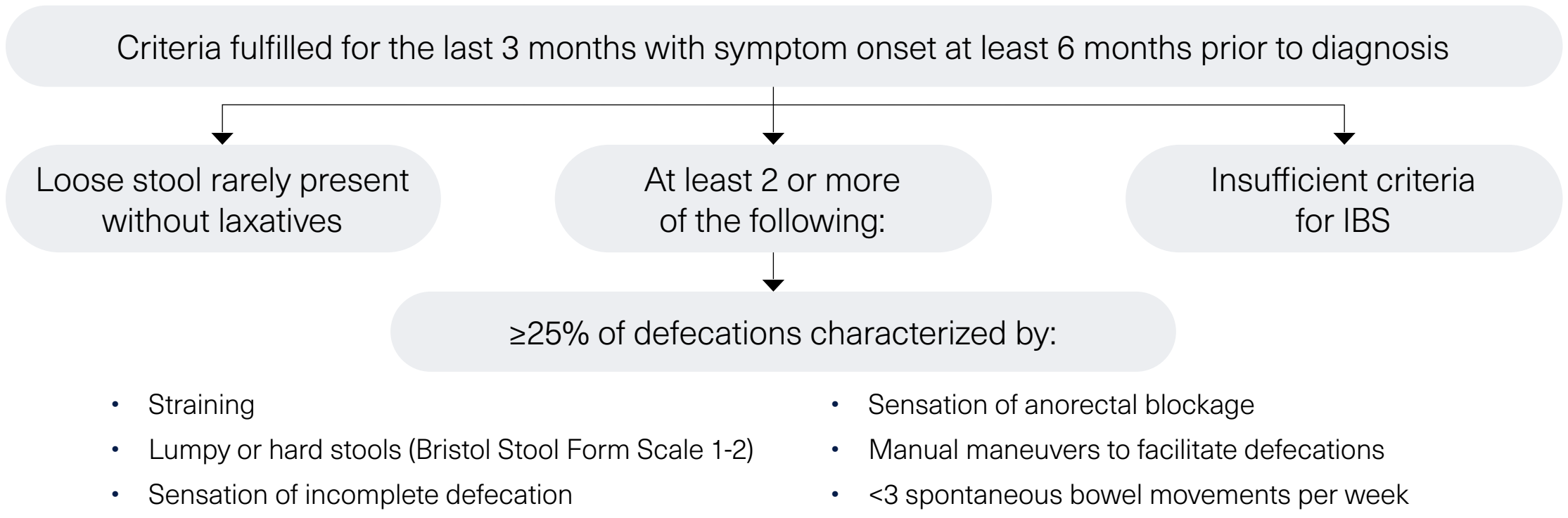


Diagnosis

CIC

The Rome Diagnostic Criteria for CIC Diagnosis

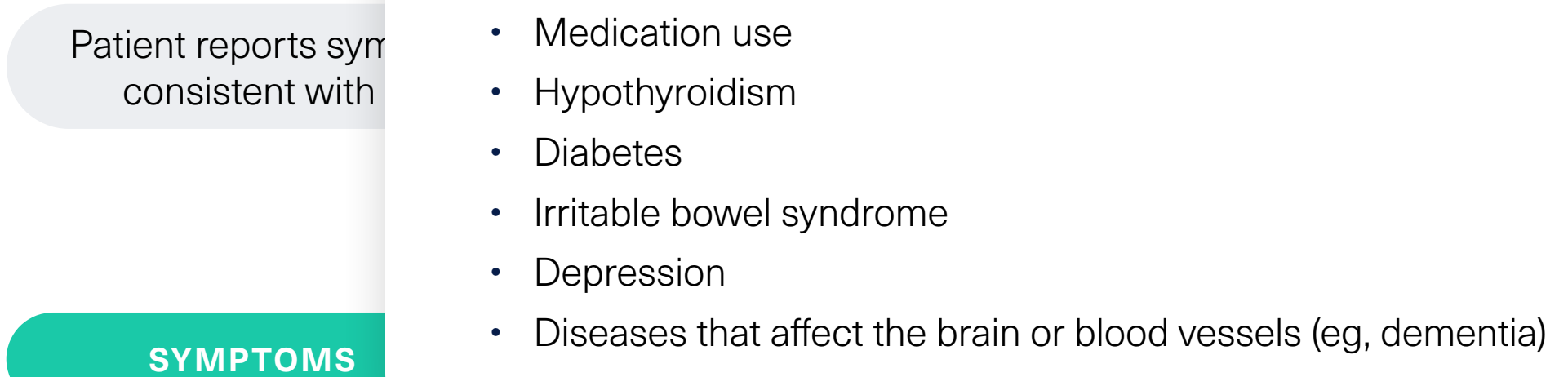
Rome IV Criteria^{1,2}



Diagnostic Steps for CIC

Diagnostic Paradigm³⁻⁵

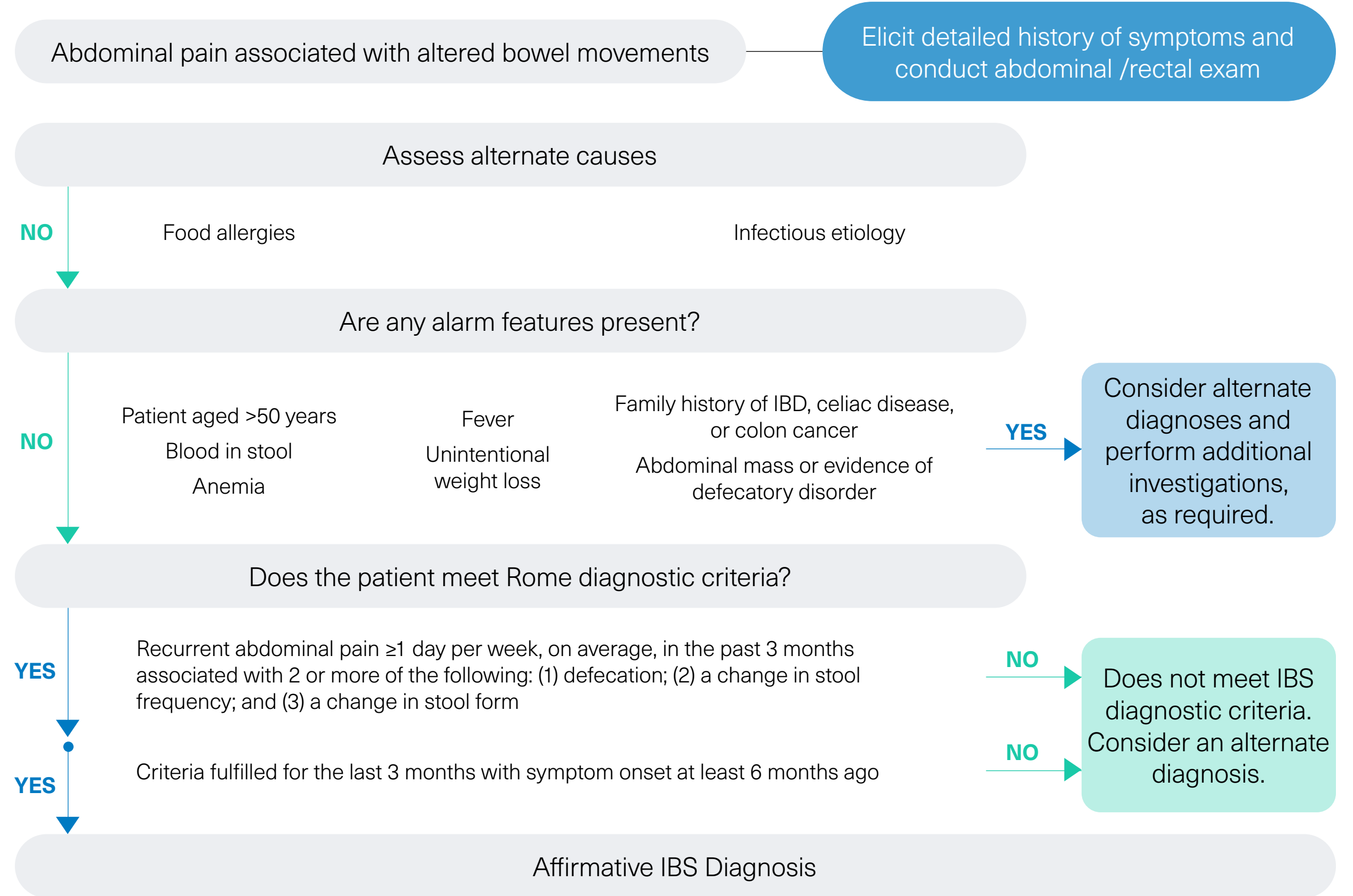
Causes of Secondary Constipation



IBS

IBS Diagnostic Pathway

IBS Is an Affirmative, Symptom-based Diagnosis, and Not a Diagnosis of Exclusion⁶⁻⁸



Treatment

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The ACG Recommendations for Management of IBS-C

Global IBS-C Symptoms

Treatment	Recommendation	Quality of Evidence	Notes
RECOMMENDED			
Guanylate cyclase activators	Strong	High	Treats global IBS-C symptoms
Chloride channel activators	Strong	Moderate	Treats global IBS-C symptoms
5-HT ₄ agonist	Conditional	Low	Use to treat IBS-C symptoms in women aged <65 years with ≤1 cardiovascular risk factors who have not adequately responded to secretagogues
NOT RECOMMENDED			
Polyethylene glycol	Conditional	Low	No evidence for the relief of abdominal pain

The ACG Recommendations for Management of IBS-D

Global IBS-D Symptoms

Treatment	Recommendation	Quality of Evidence	Notes
RECOMMENDED			
Non-absorbable antibiotic	Strong	Moderate	Treats global IBS-D symptoms
Mixed opioid agonists/antagonists	Conditional	Moderate	Treats global IBS-D symptoms
Opioid agonist	Not recommended as first-line therapy	N/A	May improve diarrhea, but not global IBS symptoms
5-HT ₃ antagonist	Conditional	Low	Use to treat IBS-D symptoms in women with severe symptoms who have failed conventional therapy
NOT RECOMMENDED			
Bile acid sequestrants	Conditional	Very Low	An option if bile acid malabsorption is suspected

Global IBS-D symptoms include recurrent and episodic abdominal pain, diarrhea, and other gastrointestinal or extraintestinal symptoms.

- ACG **recommends** a positive diagnostic strategy as compared to a diagnostic strategy of exclusion for patients with symptoms of IBS
- ACG **recommends** that serologic testing be performed to rule out celiac disease and diarrhea symptoms
- ACG **suggests** that fecal calprotectin (or fecal lactoferrin) and C reactive protein be checked in patients without alarm features and with suspected IBS and diarrhea symptoms

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Pipeline Table

LIN-MD-64 – Now Enrolling Adolescent (6-17 Years of Age) Subjects With Functional Constipation (FC) or Irritable Bowel Syndrome with Constipation (IBS-C) in the US

Study Design

A phase 3 multicenter, randomized, double-blind, parallel-group study to evaluate linaclotide in pediatric subjects with Functional Constipation or IBS-C

NCT # NCT04026113

Endpoints

Primary:

- Functional Constipation: Change from baseline in 12-week SBMs/week
- IBS-C: 6/12 week APS + 2 responder rate

Secondary:

- FC: Change from baseline in 12-week stool consistency
- IBS-C
 - Change from baseline in 12-week SBMs/week
 - Change from baseline in 12-week abdominal pain
 - Change from baseline in 12-week stool consistency
 - 6/12 weeks SBM + 2 responder
 - 6/12 weeks abdominal pain responder

Study Arms

- Placebo
- Linaclotide 72 µg
- Linaclotide 145 µg
- Linaclotide 290 µg

Patient Population & Key Inclusion Criteria

Male and female participants, 6-17 years, who meet the modified Rome III criteria for child/adolescent FC and

- Meets one or more of the following at least once per week for at least 2 months before the screening visit:
 - History of retentive posturing or excessive volitional stool retention
 - History of painful or hard BMs
 - History of large diameter stools that may obstruct the toilet
 - Presence of a large fecal mass in the rectum
 - At least 1 episode of fecal incontinence per week
- IBS-C: meets Rome III criteria for child/adolescent IBS. Participant has an average daytime abdominal pain score of ≥ 1 (at least "a tiny bit") during the 14 days before Visit 3

This use is investigational and not approved, and that safety and efficacy have not been established.

Contact
Information

ABBVIE CALL CENTER: 844-663-3742
abbvieclinicaltrials@abbvie.com

LINACLOTIDE INDICATION
AND SAFETY CONSIDERATIONS

abbvie

SBM=spontaneous bowel movement, APS=abdominal pain scale, FC=functional constipation, BM=bowel movement, IBS=irritable bowel syndrome.
1. ClinicalTrials.gov Identifier: NCT04026113. Accessed April 18, 2022. <https://www.clinicaltrials.gov/ct2/show/NCT04026113>



Clinical Trial Summaries

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MOD

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Clinical Trial
Summaries

Pipeline Table

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- IBS-C
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 - Change from baseline in 12-week abdominal pain
 - Change from baseline in 12-week stool consistency
 - 6/12 weeks SBM + 2 responder
 - 6/12 weeks abdominal pain responder

**Contact
Information**

ABBVIE CALL CENTER: 844-663-3742
abbvieclinicaltrials@abbvie.com

Study Arms

- Placebo
- Linaclotide 72 µg
- Linaclotide 145 µg
- Linaclotide 290 µg

Patient Population & Key Inclusion Criteria

Linaclotide Indication and Safety Considerations

USE: Linaclotide is indicated in adults for the treatment of both IBS-C and CIC

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS LESS THAN 2 YEARS OF AGE

Linaclotide is contraindicated in patients less than 2 years of age; in nonclinical studies in neonatal mice, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths due to dehydration.

CONTRAINDICATED: in patients less than 2 years of age due to risk of serious dehydration and in patients with know or suspected mechanical gastrointestinal obstruction.

WARNINGS: Risk of serious dehydration in patients less than 2 years of age. Contraindicated in patients less than 2 years of age. The safety and effectiveness has not been evaluated in patients less than 18 years of age. Diarrhea was the most common adverse reaction and was sometimes severe. If severe diarrhea occurs, dosing should be suspended and the patient rehydrated.



All criteria for child/adolescent FC and IBS-C must be met at least 2 months before the screening visit: on

as an average daytime abdominal pain

/ have not been established.

Clinical Trial Summaries

Physiology/
MOD

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Pipeline Table

3030-202-002 – Now Enrolling Adolescent (6-17 Years of Age) Subjects With Irritable Bowel Syndrome with Diarrhea (IBS-D)

Study Design

A phase 2, randomized, double-blind, placebo-controlled, dose-ranging study to evaluate the safety and efficacy of eluxadoline in pediatric subjects with IBS-D

NCT # NCT03339128

Endpoints

Primary:

- Change from baseline in stool consistency averaged over the 4-week treatment period

Secondary:

- Change from baseline in stool consistency for daily daytime and nighttime stool consistency scores
- Change from baseline for daytime, nighttime, and 24-hour abdominal pain scores
- Change from baseline for daytime, nighttime, and 24-hour bowel movement
- Change from baseline in the number of bowel movements
- Change from baseline for daytime, nighttime, and 24-hour urgency-free days
- Change from baseline in the number urgency free days in a week
- Change from baseline for daytime, nighttime, and 24-hour number of fecal incontinence-free days
- Change from baseline in the number of fecal incontinence-free days in a week

**Contact
Information**

ABBVIE CALL CENTER: 844-663-3742
abbvieclinicaltrials@abbvie.com

Study Arms

- Eluxadoline 25 mg twice daily
- Eluxadoline 50 mg twice daily
- Eluxadoline 100 mg twice daily
- Placebo

Patient Population & Key Inclusion Criteria

- Male and female participants, 6-17 years (inclusive), with a IBS-D diagnosis (child/adolescent Rome IV criteria)
- At least 1 daytime bowel movement with a consistency of Type 6 or Type 7 on the pediatric Bristol Stool Form Scale (p-BSFS) on at least 2 days per week during the 2 weeks prior to randomization that occurs in the absence of laxatives

Key Exclusion Criteria

- Participant has no gallbladder (ie, agenesis of the gallbladder or cholecystectomy)
- Child/adolescent Rome IV criteria of IBS with constipation, IBS with constipation and diarrhea (mixed), unspecified IBS, or functional constipation

This use is investigational and not approved, and that safety and efficacy have not been established.

ELUXADOLINE INDICATION
AND SAFETY CONSIDERATIONS

Clinical Trial Summaries

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Pipeline Table

3030-202-002 – Now Enrolling Adolescent (6-17 Years of Age) Subjects With Irritable Bowel Syndrome with Diarrhea (IBS-D)

Study Design

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NCT # NCT03339128

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- Change from baseline in stool consistency for daily daytime and nighttime stool consistency scores
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- Change from baseline for daytime, nighttime, and 24-hour number of fecal incontinence-free days
- Change from baseline in the number of fecal incontinence-free days in a week

**Contact
Information**

ABBVIE CALL CENTER: 844-663-3742
abbvieclinicaltrials@abbvie.com

Study Arms

- Eluxadoline 25 mg twice daily

Eluxadoline Indication and Safety Considerations

USE: Eluxadoline is indicated for treatment of IBS-D in adults

CONTRAINDICATED: Eluxadoline is contraindicated in patients:

- Without a gallbladder
- With known or suspected biliary duct obstruction, or sphincter of Oddi disease or dysfunction; a history of pancreatitis; or structural diseases of the pancreas.
- With alcoholism, alcohol abuse, alcohol addiction, or who drink more than 3 alcoholic beverages per day.
- With a known hypersensitivity reaction to eluxadoline
- With severe hepatic impairment
- With a history of chronic or severe constipation or sequelae from constipation, or known or suspected mechanical gastrointestinal obstruction

WARNINGS:

- Pancreatitis and Sphincter of Oddi Spasm: Monitor patients for new or worsening abdominal pain, with or without nausea and vomiting, or acute biliary pain with liver or pancreatic enzyme elevations; immediately discontinue use and seek medical attention if symptoms develop
- Hypersensitivity Reactions, including anaphylaxis: Immediately discontinue use and seek medical attention if symptoms develop
- Constipation: Instruct patients to stop use and immediately contact their healthcare provider if they develop severe constipation. Avoid use with other drugs that may cause constipation

Pipeline Table

Ongoing Pediatric Clinical Trials

	FC	IBS-C	IBS-D
LIN-MD-64	●	●	
LIN-MD-66	●	●	
3030-202-002			●
3030-302-002			●

FC=functional constipation

IBS-C=irritable bowel syndrome with constipation

IBS-D=irritable bowel syndrome with diarrhea

● Phase 2

● Phase 3

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