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# April is Irritable Bowel Syndrome Awareness Month!

Key Inforbits

- What is IBS?
- How many patients suffer from IBS?
- What are the subcategories of IBS?
- Non-pharmacologic treatment options.
- Guideline recommended treatment options.
- New and emerging treatments for IBS.

# What is Irritable Bowel Syndrome (IBS)?

Irritable bowel syndrome (IBS) is a common condition that affects the digestive system and requires long term management. Symptoms of irritable bowel syndrome (IBS) vary widely between individuals and can include abdominal pain, cramping, gas, bloating, diarrhea, constipation, and fatigue. IBS does not cause changes in bowel tissue or increase the risk of developing colorectal cancer.<sup>1</sup>

# Prevalence and Impact:2,17

- IBS is one of the most common gastrointestinal disorders affecting up to 15% of the global population
- This condition can have a significant impact on quality of life due to the discomfort, pain, and disruption of daily activities it can cause.
- Although IBS does not cause changes in bowel tissue or increase the risk of developing colorectal cancer, its chronic nature and variability in symptoms can result in psychological distress and diminished quality of life.

# Approaches to Management:<sup>1,2</sup>

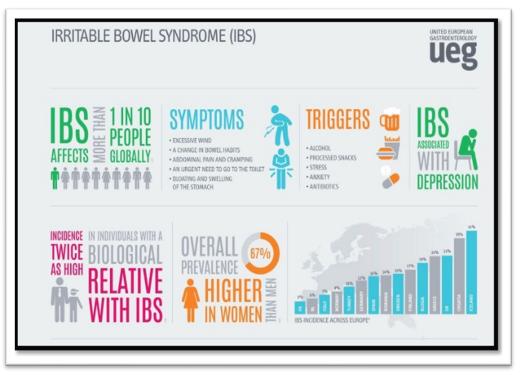
- Management of IBS typically involves a combination of lifestyle modifications, dietary changes, medication, and stress management techniques.
- Dietary changes begin by identifying and avoiding triggers that exacerbate symptoms.

- o Common triggers
  - Foods high in FODMAP (fermentable carbohydrates)
  - Spicy foods
  - Fatty foods
  - Caffeinated and carbonated drinks
  - Alcohol
  - Artificial sweeteners
- Medications used to manage IBS symptoms include antispasmodics, laxatives, antidiarrheal agents, and medications targeting visceral hypersensitivity or gut motility.
- Cognitive-behavioral therapy (CBT), relaxation techniques, and stress management strategies can also play a role in managing IBS symptoms.

#### Long-Term Management:<sup>2,3</sup>

- Since IBS is a chronic condition, long-term management is key to minimizing symptom flare-ups and improving quality of life.
- Patients may benefit from keeping symptom journals to track triggers, symptoms, and response to treatment.
- Regular communication and collaboration between patients and healthcare providers are essential for developing individualized treatment plans and adjusting treatment strategies when needed.

# How many patients suffer from IBS?



Taken From: <u>https://www.prnewswire.com/news-releases/new-breakthrough-for-ibs-patients-597427691.html</u>

# What are the subcategories of IBS?<sup>1,4,17</sup>

- Individuals with IBS-C experience predominantly constipation as their primary symptom.
- Common symptoms include:
  - Infrequent bowel movements
  - Difficulty passing stools
  - Feeling of incomplete evacuation.
- Abdominal discomfort and bloating may also be present but are typically less severe compared to other subtypes.

#### **IBS with Diarrhea (IBS-D)**:

- IBS-D has the highest prevalence at 40%
- Individuals with IBS-D experience frequent episodes of diarrhea as their primary symptom.
- Common symptoms include:
  - Loose or watery stools
  - Urgency to have a bowel movement
  - Frequent trips to pass a bowel movement
- Abdominal pain, cramping, and bloating may also be present but these symptoms can be overshadowed by diarrhea.

#### Mixed IBS (IBS-M):

- Individuals with IBS-M experience periods of constipation followed by episodes of diarrhea, or vice versa.
- Common symptoms include abdominal discomfort, bloating, and gas.

#### Unspecified IBS (IBS-U):

- Individuals with IBS-U do not fit clearly into any of the above subtypes.
- Symptoms may vary widely between individuals and may include a combination of constipation, diarrhea, and mixed bowel habits.

#### **Post-Infectious IBS (PI-IBS):**

- PI-IBS can develop after an acute gastrointestinal infection like gastroenteritis.
- Post-Infectious IBS is often characterized by the sudden onset of symptoms that can persist for months or years.
- Symptoms of PI-IBS include diarrhea, constipation, alternating bowel habits, abdominal pain and discomfort.

# Non-pharmacological Treatments for IBS:

# Exercise

Consistent daily exercise can reduce the symptoms of IBS and chronic constipation.<sup>3</sup> In a randomized controlled trial (RCT) of 102 patients with IBS, those assigned to engage in physical

activity experienced a lower prevalence of IBS symptoms compared to the control group (8% versus 23%).<sup>5</sup>

Activities such as walking, jogging, low-impact aerobics, bodyweight exercises, cycling, swimming, and yoga can alleviate symptoms associated with IBS. A study published in the World Journal of Gastroenterology found that engaging in an average of 5.2 hours of exercise per week can improve both the physical and psychological symptoms of IBS.<sup>6</sup>



Adapted from: <u>https://aboutibs.org/treatment/ibs-diet/ibs-diet-what-to-do-and-what-to-avoid/</u>

#### Diet

Patients with IBS should prioritize eating balanced meals in moderation while ensuring they consume moderate amounts fiber. It's important to reduce intake of fatty and spicy foods, while avoiding caffeine, soft drinks, carbonated beverages, and artificial sweeteners. These steps can be effective before resorting to stricter elimination diets.<sup>7</sup>

The low FODMAP diet is a strict dietary approach designed to help manage symptoms of irritable bowel syndrome (IBS) and other gastrointestinal disorders. FODMAPs are types of carbohydrates that are poorly absorbed in the small intestine and can ferment in the colon, leading to symptoms such as gas, bloating, abdominal pain, and diarrhea in some individuals. The diet involves restricting foods high in FODMAPs, including certain fruits, vegetables, grains, dairy products, and sweeteners, and then gradually reintroducing them to identify specific triggers.<sup>8</sup> By reducing FODMAP intake, many people with IBS experience a reduction in symptoms. The low FODMAP diet shows promise for managing IBS symptoms, but there are still uncertainties regarding its long-term safety, effectiveness, and feasibility. If patients choose to follow this diet, it is advisable to do so under the supervision of a qualified dietitian.<sup>7,8</sup>

The gluten-free diet is another strict dietary approach that provides benefits for patients with celiac disease, as gluten triggers an immune response in these individuals. Some patients without markers of celiac disease also report improvement, possibly due to the reduction of fructans found in wheat, which can be problematic for those with IBS. However, the long-term effects of a gluten-free diet on the microbiome and overall nutrition are not well understood.<sup>7,8</sup>

# **Cognitive Behavioral Therapy (CBT)**:

Treatment guidelines for IBS suggest psychological interventions for patients who do not respond to standard pharmacotherapy.<sup>18</sup> CBT for IBS is a non-pharmacological therapy that typically involves a combination of cognitive restructuring, relaxation techniques, and behavioral strategies with the goal to adjust patient's thoughts and behaviors that contribute to symptom exacerbation. It teaches patients to recognize and challenge negative thoughts that make symptoms worse. They also learn ways to manage stress and anxiety and slowly start doing activities or eating foods they avoided before. Studies show that CBT can greatly improve IBS symptoms, quality of life, and mental health, making it a helpful addition to standard medical treatments for IBS.

# Pharmacological Treatments for IBS:

Pharmacological treatments for IBS can help patients by reducing symptoms and improving quality of life. Antispasmodics such as dicyclomine or hyoscyamine are commonly used because they promote relaxation of the smooth muscle in the intestines, helping with digestion and reducing pain.<sup>9</sup> In patients with IBS-C, laxatives such as polyethylene glycol can be helpful. In patients with IBS-D, medications such as loperamide can reduce the frequency of bowel movements. Low-dose antidepressants, such as tricyclic antidepressants or selective serotonin reuptake inhibitors, can provide relief for many IBS patients because they modulate pain signaling in the gut.<sup>9,10,11</sup> The role of gut microbiota in IBS is gaining more attention meaning that probiotics could also have a role to play in restoring the balance of gut microbiota and treating IBS symptoms.

Table 1: Pharmacological Treatments for IBS <sup>9,10,11</sup>				
Category	Examples	Type of IBS*	Efficacy/Clinical Applications	Comments
Over-the-counter laxatives	Polyethylene glycol (Miralax)	Constipation- predominant	Improves stool frequency, but not abdominal pain; scant evidence of effectiveness. <sup>A</sup>	Always advise patients to take with plenty of water.

	Table 1: Pha	ırmacological Tre	eatments for IBS <sup>9,10,11</sup>	
Antidiarrheals	Loperamide (Imodium)	Diarrhea- predominant	Effectively decreases stool frequency and increases stool consistency. <sup>A</sup>	Intended for short- term use for no more than 2 days. Unique ADRs: Dry mouth Dizziness
Probiotics	Lactobacillus, Bifidobacterium, Streptococcus	All types	NNT = 4 to prevent worsening global IBS symptoms. <sup>B</sup>	Always consult a medical provider before starting.
Antibiotics	Rifaximin (Xifaxan) Neomycin	Diarrhea- predominant, Mixed presentation, & Constipation- predominant	NNT = 11 to prevent worsening global IBS symptoms over four weeks Improves constipation and bloating. <sup>B</sup>	Take with or without food (taking with food can decrease GI side effects).
Antispasmodics	Hyoscyamine (Levsin), dicyclomine (Bentyl)	All types	NNT = 7 for improvement of abdominal pain NNT = 5 for improvement of global assessment NNT = 3 for improvement in symptom score. <sup>B</sup>	Take 30 minutes before meals. Avoid driving or operating any heavy machinery. Unique ADRs: Blurry vision Dry mouth Tachycardia Difficulty urinating
Selective C-2 chloride channel activators	Lubiprostone (Amitiza)	Constipation- predominant	Improves global IBS symptoms. <sup>A</sup>	Take with food and water to maximize absorption and reduce the risk for GI side effects.

Table 1: Pharmacological Treatments for IBS <sup>9,10,11</sup>					
Antidepressants	SSRIs: citalopram (Celexa), fluoxetine (Prozac), paroxetine (Paxil) TCAs: amitriptyline, desipramine (Norpramin), doxepin, imipramine (Tofranil), trimipramine (Surmontil)	All types	NNT = 5 for improvement in abdominal pain NNT = 4 for improvement in global assessment NNT = 4 for improvement in symptom score. <sup>B</sup>	<ul> <li>Unique ADRs:</li> <li>Insomnia</li> <li>Sexual side effects</li> <li>Agitation/rest lessness</li> </ul>	

\*\*\*Common side effects of all agents include nausea, gas, abdominal discomfort, and bloating.

\*\*\*Number needed to treat (NNT) measures the clinical significance of a treatment by expressing the number of people who need to receive a specific treatment for one person to benefit.

\*\*\*Table note: A- single B-composite outcome

# New and emerging treatments for IBS

New and emerging treatments for irritable bowel syndrome (IBS) are providing new options for patients. Medications such as tenapanor, rifaximin and soluble fiber combinations, and elobixibat are providing targeted relief for IBS symptoms.<sup>12-15</sup> Tenapanor, which inhibits sodium absorption, has been approved for IBS with constipation (IBS-C) and it reduces abdominal pain and improves bowel frequency. Rifaximin, often used with soluble fiber, has shown effectiveness in IBS-D. Additionally, elobixibat, a bile acid transporter inhibitor, increases bowel movements and relieves constipation. These developments, along with ongoing research into serotonin receptor agonists and microbiota-based therapies, indicate a growing understanding and more targeted treatment choices for IBS. These new therapies are bringing hope for better symptom management and improved quality of life for patients.

Table 2: New and Emerging Treatments for IBS12-16					
Category	Examples	Type of IBS*	Efficacy/Clinical Applications	Comments	
5-HT3 antagonists	Alosetron (Lotronex)	Severe IBS-D (women only)	Improves global IBS symptoms and abdominal pain	Ischemic colitis, constipation, and death; restricted use in the United States	

Table 2: New and Emerging Treatments for IBS <sup>12-16</sup>				
			NNT = 7 to improve symptoms. <sup>A</sup>	
5-HT4 agonists	Tegaserod (Zelnorm)	IBS-C	NNT = 17 to improve constipation and stool frequency. <sup>A</sup>	Increased risk of myocardial infarction, unstable angina, and stroke (Available only for emergency use through the U.S. Food and Drug Administration).
NHE3 Inhibitors	Ibsrela (tenapanor)	IBS-C	Abdominal symptoms and global symptoms of IBS were significantly improved with tenapanor. <sup>A</sup>	Typically taken twice daily with food. Unique ADRs:
			Helps to reduce abdominal pain and improve bowel habits.	<ul> <li>Kidney problems</li> <li>Intestinal perforation due to severe diarrhea (rare)</li> </ul>
Bile Acid Transporter Inhibitor	Elobixibat (Goofice)	IBS-C	NNT= 3 for increasing bowel movements to > 4/ week. <sup>A</sup>	Taken once daily with food. Unique ADRs:
			Help to increase bowel movements and reduce constipation.	<ul><li>Electrolyte imbalances</li><li>Gallstones</li><li>Pancreatitis</li></ul>
Combinations	Rifaximin and Soluble Fiber Combination	IBS-D	This combination is not yet approved and still being studied.	Drink plenty of fluids while taking this medication.
Serotonin Receptor Agonists	Prucalopride (Resolor, Motegrity)	IBS-C	Reduced symptoms and increased the number of bowel movements. <sup>A</sup>	Take once daily with or without food. Drink plenty of fluids while taking this medication.

	Table 2	2: New and Em	erging Treatments for IBS	Unique ADRs:
				<ul> <li>Severe abdominal pair</li> <li>Irregular heartbeat</li> <li>Allergic reactions</li> </ul>
Fecal Microbiota Transplantation (FMT)	FMT (Rebyota) Potential for managing IBD by restoring gut microbial balance.	All Types	Did not show benefit in quality of life or symptom improvement. <sup>B</sup>	Unique ADRs: Infections Allergic reactions IBD flare up

\*\*\*Common side effects of all agents include nausea, gas, abdominal discomfort, and bloating.

\*\*\*Number needed to treat (NNT) measures the clinical significance of a treatment by expressing the number of people who need to receive a specific treatment for one person to benefit.

\*\*\*Table note: A- single B-composite outcome

IBS can be complex with many types. Many patients with IBS-M can experience both constipation and diarrhea making treatment difficult and dependent on current symptoms. Several factors such as diet, stress, and gut health have been shown to have a link to IBS. Treatment options for IBS should be individualized based on IBS type and presentation. Additionally, ongoing research is bringing new medications and improving the understanding and management of IBS in the future.





#### **References:**

- Weaver KR, Melkus GD, Henderson WA. Irritable Bowel Syndrome. Am J Nurs. 2017 Jun;117(6):48-55. doi: 10.1097/01.NAJ.0000520253.57459.01. PMID: 28541989; PMCID: PMC5453305.
- Irritable bowel syndrome (IBS). Johns Hopkins Medicine. Accessed March 27, 2024. <u>https://www.hopkinsmedicine.org/health/conditions-and-diseases/irritable-bowel-syndrome-ibs</u>.
- 3. Wilkins T, Pepitone C, Alex B, Schade RR. Diagnosis and management of IBS in adults. Am Fam Physician. 2012;86(5):419-426.
- 4. Thabane M, Marshall JK. Post-infectious irritable bowel syndrome. World J Gastroenterol. 2009 Aug 7;15(29):3591-6. doi: 10.3748/wjg.15.3591. PMID: 19653335; PMCID: PMC2721231.
- 5. Johannesson E, Simrén M, Strid H, Bajor A, Sadik R. Physical activity improves symptoms in irritable bowel syndrome: a randomized controlled trial. Am J Gastroenterol. 2011;106(5):915-92.
- Johannesson E, Ringström G, Abrahamsson H, Sadik R. Intervention to increase physical activity in irritable bowel syndrome shows long-term positive effects. World J Gastroenterol. 2015;1421(2):600-8. doi:10.3748/wjg.v21.i2.600
- 7. Wilkinson JM, Gill MC. Irritable Bowel Syndrome: Questions and Answers for Effective Care. Am Fam Physician. 2021;103(12):727-736.
- Veloso HG. FODMAP diet: What you need to know. Johns Hopkins Medicine. December 29, 2021. Accessed March 27, 2024. <u>https://www.hopkinsmedicine.org/health/wellness-and-prevention/fodmap-diet-what-you-need-to-know</u>.
- Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, Moshiree B. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021 Jan;116(1):17-44. DOI: 10.14309/ajg.00000000001036
- 10. Irritable bowel syndrome. Mayo Clinic. May 12, 2023. Accessed March 26, 2024. <u>https://www.mayoclinic.org/diseases-conditions/irritable-bowel-syndrome/symptoms-causes/syc-20360016</u>.
- Masuy I, Pannemans J, Tack J. Irritable bowel syndrome: diagnosis and management. Minerva Gastroenterologica e Dietologica. 2020 Jun;66(2):136-150. DOI: 10.23736/s1121-421x.19.02640-0. PMID: 31820883.
- 12. About IBSRELA (tenapanor) & IBS-C treatment. Ibsrela. Waltham, MA: Ardelyx, Inc. December 15, 2023. Accessed April 1, 2024. <u>https://www.ibsrela.com</u>.
- Chey WD, Lembo AJ, Yang Y, Rosenbaum DP. Efficacy of tenapanor in treating patients with irritable bowel syndrome with constipation: a 26-week, placebo-controlled phase 3 trial (T3MPO-2). Am J Gastroenterol. 2021;116(6):1294-1303. doi:10.14309/ajg.00000000001056
- Rao SS, Manabe N, Karasawa Y, et al. Comparative profiles of lubiprostone, linaclotide, and elobixibat for chronic constipation: a systematic literature review with meta-analysis and number needed to treat/harm. BMC Gastroenterol. 2024;24(1):12. doi:10.1186/s12876-023-03104-8
- Malagelada C, Nieto A, Mendez S, et al. Effect of prucalopride on intestinal gas tolerance in patients with functional bowel disorders and constipation. J Gastroenterol Hepatol. 2017;32(8):1457-1462. doi:10.1111/jgh.13733
- Halkjær SI, Lo B, Cold F, et al. Fecal microbiota transplantation for the treatment of irritable bowel syndrome: A systematic review and meta-analysis. World J Gastroenterol. 2023;29(20):3185-3202. doi:10.3748/wjg.v29.i20.3185
- 17. Lacy BE. Diagnosis and treatment of diarrhea-predominant irritable bowel syndrome. Int J Gen Med. 2016 Feb 11;9:7-17. doi: 10.2147/IJGM.S93698. PMID: 26929659; PMCID: PMC4755466.
- 18. Sugaya N, Shirotsuki K, Nakao M. Cognitive behavioral treatment for irritable bowel syndrome: a recent literature review. Biopsychosoc Med. 2021;15(1):23. doi:10.1186/s13030-021-00226-x

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