# Irritable Bowel Syndrome (IBS) Primary Care Pathway

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## 1. Suspected IBS

Recurrent abdominal pain at least one day per week (on average) in the last 3 months, with two or more of the following:
- Related to defecation (either increasing or improving pain)
- Associated with a change in frequency of stool
- Associated with a change in form (appearance) of stool

- Typical symtoms - bloating, flatulence, nausea, burping, early satiety, dyspepsia
- Other symptoms - dysuria, frequent/urgent urination, widespread musculoskeletal pain, dysmenorrhea, dyspareunia, fatigue, anxiety, depression, headaches

## 2. Baseline investigations

- Medical history, physical exam, assess secondary causes of symptoms
- CBC, ferritin
- Celiac disease screen

Positive for celiac

## 6. Refer for consultation/ endoscopy

## 3. Alarm features

- Family history (first degree relative) of IBD or colorectal cancer
- Onset of symptoms after age 50
- Unintended weight loss (> 5% over 6-12 months)
- Visible blood in stool
- Nocturnal symptoms
- Iron deficiency anemia (see Iron Primer)

Yes

No

If unsatisfactory response to treatment, consider using an advice service

## Presumed Diagnosis of IBS

## 4. Potential approaches to IBS treament (all subtypes)

- Dietary modifications: assess common food triggers, soluble fibre supplementation, ensure adequate fluids
- Physical activity: 20+ minutes of physical activity/day, aiming for 150 min/week
- Psychological treatment: patient counselling and reassurance, Cognitive-Behavioural Therapy and hypnotherapy, screen and treat underlying sleep or mood disorders
- Pharmacological therapy: antispasmodics, enteric coated peppermint oil

## 5. Specific approaches based on IBS subtypes

| IBS-D (diarrhea predominant) | | IBS-M/U (mixed/undefined) | IBS-C (constipation predominant) |
|---|---|---|---|
| Further testing for patients with high suspicion of IBD. Do fecal calprotectin test. | • Loperamide<br>• Tricyclic antidepressants<br>• Probiotics<br>• Low FODMAP diet | • Pay particular attention to lifestyle & dietary principles<br>• Probiotics<br>• Low FODMAP diet<br>• Tricyclic antidepressants | • Adequate fibre and water intake<br>• Osmotic laxatives<br>• Linaclotide<br>• Prucalopride<br>• Tenapanor<br>• Plecanatide<br>• SSRIs |
| **If fecal cal test > 120 ug/g, refer to consultation/ endoscopy.** *See expanded details | Second line therapies*:<br>• Rifamixin<br>*See expanded details | | |

This primary care pathway was co-developed by primary and specialty care and includes input from multidisciplinary teams. It is intended to be used in conjunction with specialty advice services, when required, to support care within the medical home. Wide adoption of primary care pathways can facilitate timely, evidence-based support to physicians and their teams who care for patients with common low-risk GI conditions and improve appropriate access to specialty care, when needed. To learn more about primary care pathways, check out this short video.

## IRRITABLE BOWEL SYNDROME (IBS) PATHWAY PRIMER

- IBS is a brain-gut disorder characterized by recurrent abdominal pain/discomfort and altered bowel habits (constipation, diarrhea, or both). It is often associated with bloating or abdominal distention. These key symptoms can vary in severity and tend to remit and recur, often affected by dietary exposures and stress.
- IBS is a manifestation of bidirectional disordered communication within the brain-gut axis that influences gastrointestinal motility, secretion, and sensation.[1]
    - Contributing factors include visceral hypersensitivity, altered gastrointestinal (GI) motility, post-infectious diarrhea, chronic stress, altered brain networks, and the microbiome. Alterations in the colonic immune system, neuronal activity, and gut permeability also play a role.
- It is one of the most common GI disorders affecting approximately 10% of the general population and can have significant impact on a patient's quality of life.[2,3]
- Historically, many providers believe it is a diagnosis of **exclusion**, but this notion is changing and moving towards a positive, symptom-based diagnosis.
    - The current recommended diagnostic criteria for IBS are the **Rome IV criteria**:
        - Recurrent abdominal pain (≥ 1 day/week for ≥ 3 months) associated with two or more of the following: related to defecation, associated with a change in the frequency of stool, associated with a change in the form (appearance) of stool.
    - Typical associated lower GI symptoms include bloating and flatulence. Upper GI symptoms include nausea, burping, early satiety, and dyspepsia.
    - Relief of abdominal discomfort after a bowel movement or in association with a change in stool form or frequency is a defining feature. Bowel dysfunction includes frequent bowel movements, fecal urgency, altered stool form (hard/lumpy or loose/watery), sense of or incomplete evacuation, straining with stool passage, and passage of mucous.
    - IBS correlates with other pain syndromes, so other symptoms such as dysuria, frequent/urgent urination, widespread musculoskeletal pain, dysmenorrhea, dyspareunia, fatigue, anxiety, depression, and headaches may also be present. Pain often is variable and may be related to the subtype.[4]
- IBS is subtyped according to stool consistency:
    - Constipation-predominant (IBS-C, > 25% hard stools and < 25% loose stools)
    - Diarrhea-predominant (IBS-D, > 25% loose stools and < 25% hard stools)
    - Mixed bowel habits (IBS-M, > 25% loose stools and > 25% hard stools)
    - Unclassified (IBS-U, < 25% loose stools and < 25% hard stools)

[1] Farmer, A. D., Wood, E., & Ruffle, J. K. (2020). An approach to the care of patients with irritable bowel syndrome. *CMAJ*, *192*(11), E275-E282.
[2] Moayyedi, P., Andrews, C. N., MacQueen, G., Korownyk, C., Marsiglio, M., Graff, L., ... & Sidani, S. (2019). Canadian Association of Gastroenterology clinical practice guideline for the management of irritable bowel syndrome (IBS). *Journal of the Canadian Association of Gastroenterology*, *2*(1), 6-29.
[3] Palsson, O. S., Whitehead, W., Törnblom, H., Sperber, A. D., & Simren, M. (2020). Prevalence of Rome IV Functional Bowel Disorders Among Adults in the United States, Canada, and the United Kingdom. *Gastroenterology*.
[4] Shah, E. D., Almario, C. V., Spiegel, B. M., & Chey, W. D. (2020). Presentation and Characteristics of Abdominal Pain Vary by Irritable Bowel Syndrome Subtype: Results of a Nationwide Population-Based Study. *American Journal of Gastroenterology*, *115*(2), 294-301.

- The most common diseases mislabeled as IBS are celiac disease, Crohn's disease, and microscopic colitis. GI cancers are unlikely in patients that meet usual criteria for IBS in the absence of red flags/abnormal blood work.

| Checklist to guide in-clinic review of your patient with IBS | |
|---|---|
| ☐ | Recurrent abdominal pain at least one day per week (on average) in the last three months, with two or more of the following:<br>• Related to defecation (either increasing or improving pain)<br>• Associated with a change in frequency of stool<br>• Associated with a change in form (appearance) of stool |
| ☐ | Complete detailed medical history, physical examination, and review of medications. |
| ☐ | Complete baseline investigations confirming no abnormal results (CBC, ferritin, serological testing to exclude celiac disease). |
| ☐ | Confirm absence of alarm features (see algorithm Box 3).<br>If alarm features are identified, refer for specialist consultation. |
| ☐ | In diarrhea predominant patients - review history of cholecystectomy and consider ordering fecal calprotectin if there is a high clinical suspicion of irritable bowel disease (IBD). |

## EXPANDED DETAILS

### 1. Suspected IBS

- Recurrent abdominal pain at least one day per week (on average) in the last three months, with two or more of the following:
    - Related to defecation (either increasing or improving pain)
    - Associated with a change in frequency of stool.
    - Associated with a change in form (appearance) of stool.
- Are symptoms consistent with IBS? Some important questions to guide the history.
    - Do you experience pain?
    - Does the pain improve/worsen/stay the same with bowel movements?
    - When the pain is present, is it often associated with a change in stool frequency or stool form?
    - Do these symptoms represent an acute change?
    - Typical associated lower GI symptoms include bloating and flatulence. Upper GI symptoms include nausea, burping, early satiety, and dyspepsia.
    - IBS correlates with other pain syndromes, so other symptoms such as dysuria, frequent/urgent urination, widespread musculoskeletal pain, dysmenorrhea, dyspareunia, fatigue, anxiety, depression, and headaches may also be present. Pain often is variable and may be related to the subtype.
- It is vital to understand a patient's predominant symptom (pain, constipation, or diarrhea) as this influence's treatment selection.

### 2. Baseline investigations

- A detailed medical history and physical examination should be performed at presentation to assess other conditions that mimic IBS. This should include a careful review of medications to identify those potentially causing GI side effects (e.g., PPI, ASA/NSAIDs, laxatives/antacids, iron/calcium/magnesium supplements, antidepressants, opioids, metformin, use of cannabis, and herbal products).
- In patients with diarrhea-predominant symptoms, ask about a history of cholecystectomy and whether this coincided with onset or worsening of symptoms. Post-cholecystectomy diarrhea, due to bile acid diarrhea (BAD), can be treated with cholestyramine.
- IBS requires few standard initial laboratory investigations.
    - CBC and ferritin should be tested.

- Serological testing is suggested to exclude celiac disease, but **routine testing** for inflammation using C-reactive protein (CRP) or food allergies is not generally recommended.
- Anemia or other alarm features (see Section 3) increase the likelihood of organic disease. If present, the patient will require further investigation.
- Patients often ask about small intestinal bacterial overgrowth (SIBO) as a cause of symptoms. Although there may be a link between SIBO and IBS, the quality of the existing evidence is low. The accuracy of the breath test for SIBO is highly variable and may be unreliable. Routine testing for SIBO is not currently recommended.[1,5]

- Additional testing can be considered based on patient history.
  - *C.difficile* or ova and parasites if there has been recent travel and diarrhea is the main concern.
- A significant percentage of patients with chronic abdominal pain or other functional GI disorders have a history of trauma (e.g., sexual assault or physical and psychological abuse) or PTSD. This type of trauma may contribute to symptoms through the brain-gut axis, so it is important to explore this in a compassionate manner. Undergoing endoscopy may trigger a negative response in survivors of trauma. Addressing this possibility may be appropriate if considering a referral for endoscopy when the clinician is aware of a history of trauma. For additional information, see Abuse, Trauma, and GI Illness: Is There a Link? and Trauma-informed care.

## 3. Alarm features

If any of the following alarm features are identified, refer for consultation/endoscopy. Include any and all identified alarm features in the referral to ensure proper triage.

- Family history (first degree relative) of IBD or colorectal cancer
- Onset of symptoms after age 50
- Unintended weight loss (> 5% over 6-12 months)
- Visible blood in stool (see High Risk Rectal Bleeding Pathway and/or Iron Deficiency Anemia Pathway)
- Nocturnal symptoms
- Iron deficiency anemia (see Iron Primer)

## 4. Potential approaches to IBS treatment (overview for all subtypes)

| **Treatment options – all IBS subtypes** | |
|---|---|
| Patients with IBS will benefit from a multipronged, individualized approach to treatment, including dietary modifications, psychological, and pharmacological therapies.[1,6] | |
| Dietary modifications | • All subtypes of patients with IBS are likely to benefit from dietary modifications.<br>• **Assess common food triggers:** Follow a systematic approach to effectively guide modifications and understand the impact changes make on symptoms.<br>• Diets high in processed foods, fatty foods, caffeine, sugar alcohols, alcohol, and insoluble fibre (e.g., wheat bran, raw vegetables, the skin of fruits, and cruciferous vegetables such as broccoli, cauliflower, Brussels sprouts, and legumes) can increase IBS symptoms.<br>• It may be helpful for patients to use the Food and Lifestyle Symptom Diary to understand their symptoms, food triggers, and stressors. Use the diary to determine how dietary modifications and psychological and pharmacological therapies impact their symptoms.<br>• Assess dietary intake compared to Canada's Food Guide.<br>• Referral to a Registered Dietitian can be helpful to support dietary changes. |

[5] Shah, A., Talley, N. J., Jones, M., Kendall, B. J., Koloski, N., Walker, M. M., ... & Holtmann, G. J. (2020). Small intestinal bacterial overgrowth in irritable bowel syndrome: a systematic review and meta-analysis of case-control studies. *American Journal of Gastroenterology*, *115*(2), 190-201.
[6] Black, C. J., Yuan, Y., Selinger, C. P., Camilleri, M., Quigley, E. M., Moayyedi, P., & Ford, A. C. (2020). Efficacy of soluble fibre, antispasmodic drugs, and gut–brain neuromodulators in irritable bowel syndrome: a systematic review and network meta-analysis. *The Lancet Gastroenterology & Hepatology*, *5*(2), 117-131.

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|---|---|
| Dietary modifications cont'd | • **Total fibre:** Adults are recommended to consume 14 g/1000 kcal of fibre per day. Suggest about 21-38 g/day for most adults.<br>• **Two Types of fibre:**<br>  ○ Insoluble fibre is found in wheat bran, the skin of fruits, and many raw vegetables. It adds bulk to the stool and contributes greatly to daily total fibre requirements. It may not add therapeutic health benefits like soluble fibre.<br>  ○ Soluble fibre is found in psyllium, oats, barley, fruit, and seeds. It absorbs water in the intestine to form a viscous gel that thickens the stool and stimulates peristalsis.<br>• **Soluble Fibre Supplementation:**<br>  ○ May provide symptom relief for patients with IBD, IBS, constipation, and diarrhea. The therapeutic goal is 5-10 g/day of soluble fibre from foods and supplements including:<br>  ▪ 1 tbsp. psyllium husk or powder supplement - 3.0 grams<br>  ▪ 2 tbsp. ground flaxseed - 1.8 grams<br>  ▪ ½ cup kidney beans - 2.8 grams<br>  ▪ 1 pear - 2.2 grams<br>• **General Care:**<br>  ○ Increasing fibre intake may result in negative side-effects that can be minimized or avoided.<br>  ▪ Slowly increase fibre to prevent gas, abdominal pain, and bloating. Start with a third of a dose and determine tolerance.<br>  ▪ Drink additional fluid (water) to compliment a high fibre diet. Inadequate fluid may lead to constipation, hardening of stool, bloating, and abdominal pain.<br>  ▪ Caution soluble fibre intake for people with, or at risk of, a bowel obstruction or narrowing of the esophagus, stomach, or intestine.<br>  ▪ Fibre supplements may reduce or delay absorption of certain medications.<br>  ○ See Patient Resources section for more information on fibre supplementation.<br>• **Ensure adequate fluids:** 2 L/day for females, 3 L/day for males. |
| Physical activity | • 20+ minutes of physical activity/day, aiming for 150 min/week is known to be an effective strategy for stress reduction.<br>• See the Canadian 24-Hour Movement Guidelines. |
| Psychological therapy | • **Patient counselling and reassurance.** A key to effective long-term management of IBS is to provide patients reassurance after their initial diagnosis and offer points of reassessment and reappraisal to establish a therapeutic relationship.<br>  ○ Reassurance about potential inconsistency in the pattern of symptoms in response to triggers may be necessary. Not all elimination/avoidance of food triggers consistently or predictably improves symptoms. The contribution from food is complex and symptoms are often the result of multiple contributing factors (e.g., "I tried cheese last week and felt fine. Today, I have terrible bloating and diarrhea!").<br>• **Cognitive-Behavioral Therapy** and **hypnotherapy** may help with stress management and gastrointestinal symptoms.[7] It is recommended that therapy be provided by a regulated health professional such as a registered psychologist.<br>• **Screening for, and treating, any underlying sleep or mood disorders** may be important. |

[7] DynaMed Plus. (2018, September 10). *Confidence in Practice. Irritable bowel syndrome (IBS)*. https://www-dynamed-com.ahs.idm.oclc.org/results?q=ibs&lang=en

| Pharmacological therapy – all IBS subtypes | |
|---|---|
| The use of pharmaceuticals in IBS is generally reserved for those who have not adequately responded to dietary and lifestyle interventions, or in those with moderate or severe symptoms that impair quality of life. These often need to be tailored to the patient's predominant subtype presentation (e.g., pain vs. diarrhea vs. constipation). | |
| Antispasmodics | • **Evidence:** May reduce symptoms of abdominal pain, however, it is not clear if one agent is more effective than another.[8]<br>• **Place in therapy:** May provide symptom relief. Consider peppermint oil as first line as it is generally well tolerated and appears to be effective.<br>• **Mechanism of action:** Smooth muscle relaxation by various mechanisms.<br>• **Adverse effects:** Anticholinergic reactions with some agents (CNS depression, xerostomia), dyspepsia (peppermint oil).[9]<br>• **Dose:** A reasonable trial is 1-2 agents (not at once) given for 4 weeks as listed below. Could use regularly or PRN.<br>**Recommended Medications:**<br>• Trimebutine (Modulon®) - 100-200 mg TID ($40-80/month).<br>• Pinaverium Bromide (Dicetel®) - 50-100 mg TID ($50-75/month).<br>• Hyoscine Butylbromide (Buscopan®) - 10 mg TID-QID ($25-40/month).<br>• Dicyclomine hydrochloride (Bentylol®) - 20 mg TID-QID ($25-40/month). |
| Enteric coated peppermint oil | • **Place in therapy:** Shown benefit for reducing abdominal pain[10,11]<br>• **Adverse effects:** May interact with medications. It is important to discuss use with their pharmacist and/or healthcare team.[9]<br>**Recommended Medications:**<br>• Enteric coated peppermint oil capsules (0.2-0.275 mL caps) - 2 capsules BID ($20-25/month, unlikely to be covered by insurance providers).<br>• IBgard® - 80 mg/capsule. Max dose is 6 capsules/day or 480 mg/day ($70-100/month). Take 2 capsules 30-90 minutes before meals. |

## 5. Specific approaches based on IBS subtypes

| IBS-D (diarrhea-predominant) | |
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| Categorizing IBS by dominant subtype guides specific treatment approaches. | |
| **Fecal calprotectin** | • Consider ordering fecal calprotectin in IBS-D patients if there is a high clinical suspicion of IBD.<br>• Calprotectin is a protein released into the gastrointestinal tract when it is inflamed and can be detected in the stool by laboratory assay.<br>• Elevated levels of fecal calprotectin are found in inflammatory bowel disease (Crohn's disease and ulcerative colitis). Mid-range levels can also be found in several benign conditions, such as in patients on NSAIDs or PPIs or those with GI infections, celiac disease, and microscopic colitis (see Microscopic Colitis Primer). By contrast, in functional disorders such as IBS, fecal calprotectin levels are normal.[12] |

[8] Ruepert, L., Quartero, A. O., de Wit, N. J., van der Heijden, G. J., Rubin, G., & Muris, J. W. (2011). Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome. *Cochrane database of systematic reviews*, (8).

[9] Lexicomp, Inc., Lexi-Drugs Online, Hudson, Ohio: UpToDate, Inc; 2013; [cited 27 Apr 2021].

[10] Khanna, R., MacDonald, J. K., & Levesque, B. G. (2014). Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *Journal of clinical gastroenterology*, *48*(6), 505-512.

[11] Cappello, G., Spezzaferro, M., Grossi, L., Manzoli, L., & Marzio, L. (2007). Peppermint oil (Mintoil®) in the treatment of irritable bowel syndrome: A prospective double-blind placebo-controlled randomized trial. *Digestive and liver disease*, *39*(6), 530-536.

[12] York Teaching Hospital – NHS Foundation Trust & Yorkshire and Humber Academic Health Sciences Network (2016, July) *The York Faecal Calprotectin Care Pathway Information for GPs*. https://www.yorkhospitals.nhs.uk/seecmsfile/?id=941

- FCP methods are not standardized, so numerical FCP results tested by DynaLIFE should **NOT** be compared to previous FCP results from the referral laboratory.

| Indication for testing | Result | Interpretive Guidance |
|---|---|---|
| **Investigation of patients with GI symptoms*** | **<50 µg/g** | **Normal** (no detectable inflammation). |
| | **50-120 µg/g** | **Indeterminate** (If symptoms persist, consider repeating the test in 4-6 weeks). |
| | **>120 µg/g** | **Elevated** (refer for specialist consultation or physician advice). |
| **Monitoring of known IBD patients** | **>250 µg/g** | Result suggests active inflammation. |
| *For Patient <4 years of age | | |
| • High levels of fecal calprotectin are commonly observed in pediatric patients less than 4 years of age. Robust pediatric reference intervals have not been established for this age group. | | |

| Treatment options | |
|---|---|
| All prescribed medications should be fully discussed with the patients in terms of specific risks and side effects and appropriateness of use in context of their full medical history. | |
| Loperamide (Imodium®) | • **Evidence:** Does not affect global IBS symptoms but may help with frequency and consistency of bowel movements. Suggested against for overall symptom improvement.[13]<br>• **Mechanism of action:** Through µ (mu) opioid receptor agonist, thus decreasing GI motility.<br>• **Place in therapy:** Effective antidiarrheal. Does not lead to overall symptom improvement in patients with IBS.<br>• **Adverse effects**: Sedation, nausea, abdominal cramps.[11] Lowest addiction potential of all opioids.<br>• **Dose:** 4 mg initially, followed by 2 mg after each loose bowel movement. Max 16 mg/day. |
| Tricyclic antidepressants (TCAs) | • **Evidence:** The most studied antidepressant class for treatment of abdominal pain.[14]<br>• **Mechanism of action:** Suggested to be beyond serotonin and norepinephrine, and as a result of blocking voltage-gated ion channels, opioid receptor activation and potential neuro-immunologic anti-inflammatory effects.[9] Their anticholinergic properties also slow GI transit time.<br>• **Place in therapy:** Recommended for overall symptom improvement in patients with IBS, as well as sleep issues, anxiety, or depression.<br>• **Adverse effects:** Anticholinergic and antihistaminic (drowsiness/insomnia, xerostomia, palpitations, weight gain, constipation, urinary retention).[13]<br>• Use with caution in patients at risk of prolonged QT.<br>• It can take 2-3 months to reach maximum effect.<br>• The lowest effective dose should be used. Reassess therapy after 6-12 months.<br>• Dose should be gradually reduced if discontinuing.<br>**Recommended Medications**<br>• Nortriptyline - 10-25 mg qhs. Increase dose by 10-25 mg every 3-4 weeks (due to delayed onset). May require 25-75 mg/day. Often takes 2-3 months for peak effect. ($20-60/month).<br>• Amitriptyline - 10-25 mg qhs. Increase dose by 10-25 mg every 3-4 weeks (due to delayed onset). May require 25-75 mg/day. Often takes 2-3 months for peak effect. ($15-20/month).<br>• Desipramine - 25 mg qhs. Increase based on response and tolerability. Doses up to 150 mg daily have been evaluated for IBS (~$25/month). |
| Probiotics | • **Evidence:** May improve symptoms in patients with IBS, but overall conclusions are limited by inconsistency in specific probiotics studied. |

[13] DynaMed. Irritable Bowel Syndrome (IBS). EBSCO Information Services. Accessed June 10, 2021. https://www-dynamed-com.ahs.idm.oclc.org/condition/irritable-bowel-syndrome-ibs

[14] Törnblom, H., & Drossman, D. A. (2016). Centrally targeted pharmacotherapy for chronic abdominal pain: understanding and management. *Gastrointestinal Pharmacology*, 417-440.

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|---|---|
| | • **Place in therapy:** May improve global symptoms, bloating, and flatulence.<br>• The most effective probiotic strain is unknown. Patients should be encouraged to select products that are licensed by Health Canada's Natural and Non-prescription Health Products Database. Refer to Probiotic Chart for up to date evidence. These strains have the most evidence to support benefits (a one-month trial is reasonable). Probiotics have not been conclusively shown to improve symptoms of IBS.[15] |
| Probiotics cont'd | **Recommended Strains with the Most Evidence**<br>• Align® - 1 capsule/day ($40/month)<br>• TuZen® - 1-2 capsules/day ($40-80/month)<br>• Visbiome® - 0.5-1 sachet/day ($50-100/month) |
| Low FODMAP Diet | • A trial of a low fermentable oligosaccharides, disaccharides, monosaccharides, polyols (FODMAP) diet is suggested, while an exclusive gluten-free diet is not. Some patients may wish to trial the elimination of a single nutrient/food (e.g., lactose, fructans, fructose, sugar alcohols) or an elimination of multiple nutrients/foods using this diet. Referral to a dietitian should be considered if this diet is planned.<br>• A single nutrient/food elimination trial is the removal of a nutrient/food for 2-4 weeks. Use a symptom diary to note the impact of the dietary modification. If no improvement, the nutrient/food can be added back, and a second single nutrient/food elimination trial can be tested.<br>• A low FODMAP diet trial is the removal of multiple nutrients/food all at once for 2-6 weeks (max) until symptoms have improved. A single nutrient/food is then added back into the diet, using a food diary to test for tolerance. |

| **Second line therapies** | |
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| Consider consulting a GI using Specialist Link, Connect MD, or e-Referral Advice Request for guidance on these treatments. | |
| Rifaximin (Zaxine®) | • A non-systemically absorbed antibiotic.<br>• **Mechanism of action:** Not clearly identified, but may alter the microbiome, thus reducing gas production.<br>• **Dose:** 550 mg 3 x/day for 2 weeks. This is a safe medication but tends to require multiple recurrent courses. There is no long-term safety or efficacy data over 3 courses. (~$325/month, not covered by public insurers). |

**IBS M/U (mixed/undefined)**

| **Treatment options** | |
|---|---|
| Lifestyle and dietary principles | • Refer to Section 4 |
| Probiotics | • See IBS-D treatment recommendations |
| Low FODMAPS diet | • See IBS-D treatment recommendations |
| TCAs | • See IBS-D treatment recommendations |

**IBS-C (constipation predominant)**

| **Treatment options** | |
|---|---|
| Fibre and fluids | • See Patient Resources section |
| Osmotic laxatives | • **Evidence:** Laxatives do not affect global IBS symptoms but may help with frequency and consistency of bowel movements.[13]<br>• **Mechanism of action:** Drawing water into the colon to increase bowel movements and allow easier passage of stool. |

[15] Su, G. L., Ko, C. W., Bercik, P., Falck-Ytter, Y., Sultan, S., Weizman, A. V., & Morgan, R. L. (2020). AGA Clinical Practice Guidelines on the Role of Probiotics in the Management of Gastrointestinal Disorders. *Gastroenterology*.

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| | • **Place in therapy:** Consider use of laxatives in patients with constipation. Advise titration of dose to assure well-formed stool. Stepwise treatment with laxatives of increasing strength is recommended until constipation relief is reached.<br>• **Adverse effects:** Avoid use of lactulose due to common side-effects of bloating, distention, and cramps.<br>**Recommended Medications**<br>• Polyethylene Glycol (PEG 3350) – Start with 17 g at night dissolved in 250 mL of liquid. Titrate to effect or max 34 g/day. Onset of action 48-96 hours. Safe for long-term use. ($25-50/month). |
| Osmotic laxatives cont'd | • Milk of Magnesia - 30-60 mL/day. Onset of action 1-6 hours. Avoid in renal failure due to risk of hypermagnesemia. |
| Linaclotide (Constella®) | • **Mechanism of action:** A guanylate cyclase agonist which increases chloride and bicarbonate secretion from enterocytes and increases intestinal transit. May decrease visceral pain by reducing pain-sensing nerve activity.[13]<br>• **Place in therapy:** For persistent IBS symptoms with patients motivated for more intensive or expensive treatments.<br>• **Adverse effects:** Diarrhea, upper abdominal pain.<br>• **Dose:** 290 mcg daily PO 30 minutes before the first meal of the day ($160/month). |
| Prucalopride (Resotran®) | • **Evidence:** Shown to be effective in idiopathic constipation, there is less evidence of the effect of prucalopride in IBS-C. Has not been studied for use in men.[16]<br>• **Mechanism of action:** Through 5-$HT_4$ receptor agonism, leading to prokinetic activity.<br>• **Adverse effects:** Nausea, diarrhea, abdominal pain, headache.<br>• **For constipation:** 2 mg PO daily. Reduce dose to 1 mg PO daily if ($120/month):<br>  ○ > 65 years old<br>  ○ CrCl $\leq$ 30 mL/min<br>  ○ Severe hepatic impairment<br>• Discontinue therapy if no benefit provided with 4 weeks of treatment. |
| Tenapanor (Ibsrela®) | • **Evidence:** AGA Clinical Practice Guideline on the Pharmacological Management of IBS-C suggests using Tenapanor in patient with IBS-C (condition recommendation, moderate certainty).<br>• **Mechanism of action:** Sodium/hydrogen exchanger 3 inhibitor. Acts locally to reduce sodium absorption from the small intestine and colon. This results in increased lumen water secretion, accelerating intestinal transit time and softening stool consistency. It also decreases intestinal permeability and visceral hypersensitivity in animal models, which may reduce abdominal pain.<br>• **Adverse effects:** Diarrhea, abdominal distension, flatulence, rectal hemorrhage, dizziness.<br>• **Dose:** (adult, IBS-C) 50 mg po BID immediately prior to breakfast or the first meal of the day and immediately prior to dinner. No dosage adjustments for renal or hepatic impairment. |
| Plecanatide (Trulance®) | • **Evidence:** AGA Clinical Practice Guideline on the Pharmacological Management of IBS-C suggests using Plecanatide in patients with IBS-C (condition recommendation, moderate certainty).<br>• **Mechanism of action:** Plecanatide and its active metabolite bind and agonize guanylate cyclase-C on the luminal surface of the intestinal epithelium. Intracellular and extracellular cGMP concentrations are subsequently increased resulting in chloride and bicarbonate secretion into the intestinal lumen. Intestinal fluid increases and GI transit time is accelerated. |

[16] CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2015 [cited 2021 June 10]. Available from: http://www.e-therapeutics.ca

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|---|---|
| | • **Adverse effects:** Diarrhea, abdominal distention, abdominal tenderness, flatulence, nausea, UTI, increase liver enzymes, dizziness, URTI.<br>• **Dose:** (adult, IBS-C or CIC) 3 mg po daily. No dosage adjustments for renal or hepatic impairment. |
| Selective serotonin reuptake inhibitors (SSRIs) | • **Evidence:** Limited data to support use of SSRIs for IBS-C.<br>• **Place in therapy:** Can be helpful with abdominal pain and may loosen bowel movements for patients.<br>• **Adverse effects:** Nausea, diarrhea, weight gain, sexual dysfunction, tremor, insomnia.<br>• Caution with citalopram in patients with prolonged QT.<br>• Lowest effective dose should be used. It can take 2-3 months to reach maximum effect. Reassess therapy in 6-12 months. Dose should be gradually reduced if discontinuing.<br>**Recommended Medications**<br>• Fluoxetine (Prozac®) - 10 mg daily. May doses escalate up to 60 mg daily (~$25/month).<br>• Citalopram (Celexa®) - 10-20 mg daily. May doses escalate up to 40 mg daily (~$15/month). |

### NOTE: Alternative Remedies

Given the significant impact of IBS on quality of life, many patients pursue alternative, and often complementary, therapies to treat their symptoms (e.g., acupuncture, yoga, and reflexology). Although there are no evidence-based guidelines to support these alternative therapies, it is important to keep communication open.

## 6. When to refer for consultation and/or endoscopy

- If alarm features are identified
- If investigations reveal a positive celiac disease screen
- If the fecal calprotectin result is > 120 mcg/g
- In patients with IBS-D who have persistent symptoms or limited benefits from treatments, a referral may be helpful to investigate for Crohn's disease and microscopic colitis.
- For patients with IBS-C or alternating diarrhea and constipation, colonoscopy is unlikely to yield relevant findings.
- If recommended strategies have led to unsatisfactory treatment or management of symptoms.
    - **Note**: Consider using an advice service before referring
- Provide as much information as possible on the referral form, including identified alarm feature(s), important findings, and treatment/management strategies trialed with the patient.
- In the absence of alarm features for patients under age 50, colonoscopy is unlikely to be additive for the diagnosis of IBS. Studies show that a colonoscopy does not provide reassurance to patients with IBS[17].

### Still concerned about your patient?

The primary care physician is typically the provider who is most familiar with their patient's overall health and knows how they tend to present. Changes in normal patterns, or onset of new or worrisome symptoms, may raise suspicion for a potentially serious diagnosis, even when investigations are normal and typical alarm features are not present.

There is evidence to support the importance of the family physician's intuition or "gut feeling" about patient symptoms, especially when the family physician is worried about a sinister cause such as cancer. A meta-analysis examining the predictive value of gut feelings showed that the odds of a patient being diagnosed with cancer, if a GP recorded a gut feeling, were 4.24 times higher than when no gut feeling was recorded.[18]

[17] Spiegel, B. M., Gralnek, I. M., Bolus, R., Chang, L., Dulai, G. S., Naliboff, B., & Mayer, E. A. (2005). Is a negative colonoscopy associated with reassurance or improved health-related quality of life in irritable bowel syndrome? *Gastrointestinal endoscopy*, *62*(6), 892-899.

[18] Friedemann Smith, C., Drew, S., Ziebland, S., & Nicholson, B. D. (2020). Understanding the role of General Practitioners' gut feelings in diagnosing cancer in primary care: A systematic review and meta-analysis of existing evidence. *British Journal of General Practice*, 70(698), e612-e621.

When a “gut feeling” persists despite normal investigations, and you decide to refer your patient for specialist consultation, document your concerns on the referral with as much detail as possible. Another option is to seek specialist advice (see Advice Options) to convey your concerns.

# PRIMERS

## Iron Primer

Evaluation of measures of iron storage can be challenging. Gastrointestinal (occult) blood loss is a common cause of iron deficiency and should be considered as a cause when iron deficiency anemia is present. Menstrual losses should also be considered.

There are two serological tests to best evaluate iron stores (ferritin, transferrin saturation) - neither of which are perfect.

The first step is to evaluate **ferritin**:

- If the ferritin is below the lower limit of normal (lower limit of normal is 30 µg/L for men and 20 µg/L for women), it is diagnostic of iron deficiency with high specificity (98% specificity).
- Ferritin is an acute phase reactant which may be elevated in the context of acute inflammation and infection. If ferritin is normal or increased, and you suspect it may be acting as an acute phase reactant, order a transferrin saturation test (see below).
    - However, if the ferritin is > 100 µg/L and there is no concurrent significant chronic renal insufficiency, iron deficiency is very unlikely - even in the context of acute inflammation/infection.

The second step is to evaluate **transferrin saturation**:

- The transferrin saturation is a calculated ratio using serum iron and total iron binding capacity. Serum iron alone does **NOT** reflect iron stores.
- Low values (< 16%) demonstrate low iron stores in conjunction with a ferritin < 100 µg/L.

In the absence of abnormal iron indices, anemia may be from other causes other than GI (occult) blood loss (e.g., bone marrow sources, thalassemia, and sickle cell anemia).

## Microscopic Colitis Primer

Microscopic colitis is a benign condition with a median age of onset in the mid-60s, more often in women than men. It is characterized by non-bloody, watery/secretory diarrhea having significant potential impact on quality of life. Atypical presentations can also occur.

- Examination by colonoscopy reveals normal findings, inflammation is present only histologically (on biopsy).
- Medications have been implicated in the pathophysiology. Common offenders include NSAIDs, proton pump inhibitors (PPIs), statins, topiramate, and SSRIs. Consideration should be given to stopping these medications, if possible.
- This condition is non-progressive, and therapy is directed to improving quality of life and stool habit regularity (<3 stools per day, minimal water content).
- Treatment for microscopic colitis is similar to those used in the treatment of IBS.
    - Increased soluble fibre (psyllium, inulin) can be helpful to regular stool habit in addition to loperamide, as needed.
    - For more significant manifestations (defecation at night, incontinence), corticosteroid therapy may be indicated (e.g., Budesonide/Entocort® or Cortiment® (little to no evidence exists for prednisone).
- Total treatment duration ranges on response from 6-8 weeks to 12 weeks.

# BACKGROUND

## About this Pathway

- Digestive health primary care pathways were originally developed in 2015 as part of the Calgary Zone's Specialist LINK initiative. They were co-developed by the Department of Gastroenterology and the Calgary Zone's specialty integration group, which includes medical leadership and staff from Calgary and area Primary Care Networks, the Department of Family Medicine, and Alberta Health Services.
- The pathways were intended to provide evidence-based guidance to support primary care providers in caring for patients with common digestive health conditions within the patient medical home.
- Based on the successful adoption of the primary care pathways within the Calgary Zone, and their impact on timely access to quality care, in 2017 the Digestive Health Strategic Clinical Network (DHSCN) led an initiative to validate the applicability of the pathways for Alberta and to spread availability and foster adoption of the pathways across the province.

## Authors & Conflict of Interest Declaration

This pathway was reviewed and revised under the auspices of the DHSCN in 2021 by a multi-disciplinary team led by family physicians and gastroenterologists. For more information, contact the DHSCN at Digestivehealth.SCN@ahs.ca.

## Pathway Review Process

Primary care pathways undergo scheduled review every three years, or earlier, if there is a clinically significant change in knowledge or practice. The next scheduled review is April 2024; however, we welcome feedback at any time. Click on the Provide Feedback button to provide your feedback.

Provide Feedback >

## Copyright Information



## Disclaimer

This pathway represents evidence-based best practice but does not override the individual responsibility of healthcare professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified healthcare professional. It is expected that all users will seek advice of other appropriately qualified and regulated healthcare providers with any issues transcending their specific knowledge, scope of regulated practice, or professional competence.

## PROVIDER RESOURCES

### Advice Options

Non-urgent advice is available to support family physicians.

- Gastroenterology advice is available across the province via Alberta Netcare eReferral Advice Request (responses are received within five calendar days). View the Referring Provider - FAQ document for more information.
- Non-urgent telephone advice connects family physicians and specialists in real time via a tele-advice line. Family physicians can request non-urgent advice from a gastroenterologist:
    - In the Calgary Zone at specialistlink.ca or by calling 403-910-2551. This service is available from 8:00 a.m. to 5:00 p.m. Monday to Friday (excluding statutory holidays). Calls are returned within one (1) hour.
    - In the Edmonton and North Zones by calling 1-844-633-2263 or visiting pcnconnectmd.com. This service is available from 9:00 a.m. to 6:00 p.m. Monday to Thursday and from 9:00 a.m. to 4:00 p.m. Friday (excluding statutory holidays and Christmas break). Calls are returned within two (2) business days.

| Resources | |
|---|---|
| Poverty: A Clinical Tool for Primary Care Providers (AB) | cep.health/media/uploaded/Poverty_flowAB-2016-Oct-28.pdf |
| Nutrition Guideline: Household Food Insecurity | ahs.ca/assets/info/nutrition/if-nfs-ng-household-food-insecurity.pdf |

## PATIENT RESOURCES

### Information

| Description | Website |
|---|---|
| General information on IBS (MyHealth.Alberta.ca) | myhealth.alberta.ca/health/pages/conditions.aspx?Hwid=hw117851 |
| Understanding Irritable Bowel Syndrome (Canadian Digestive Health Foundation) | cdhf.ca/digestive-disorders/irritable-bowel-syndrome-ibs/ |
| Irritable Bowel Syndrome (UpToDate® – *Beyond the Basics* Patient education) | uptodate.com/contents/irritable-bowel-syndrome-beyond-the-basics |
| Managing Constipation | ahs.ca/assets/info/nutrition/if-nfs-managing-constipation.pdf |
| Fibre Facts | ahs.ca/assets/info/nutrition/if-nfs-fibre-facts.pdf |
| Food, Lifestyle, and Symptom Diary | https://www.albertahealthservices.ca/assets/info/nutrition/if-nfs-food-and-activity-journal.pdf |
| Nutrition Education Material | ahs.ca/NutritionResources |
| Gut Health Patient Journal (Physician Learning Program) | 9c849905-3a37-465a-9612-7db1b9a0a69c.filesusr.com/ugd/7b74c1_81f1695f08214a66bc339462c52cd011.pdf |

### Services available

| Description | Website |
|---|---|
| Services for patients, to prevent or to manage chronic conditions. (Alberta Healthy Living Program - AHS) | ahs.ca/ahlp |
| Supports for working towards healthy lifestyle goals and weight management. (Weight Management – AHS) | ahs.ca/info/Page15163.aspx |
| Referral to a Registered Dietitian | • Visit Alberta Referral Directory and search for nutrition counselling.<br>• To learn more about programs and services offered in your zone, visit Nutrition Services.<br>• Health Link has Registered Dietitians available to answer nutrition questions. If a patient has nutrition-related questions, they can call 8-1-1 and ask to talk to a Dietitian.<br>• Patients can also complete the Health Link Dietitian Self-Referral Form. |

## PATIENT PATHWAY

- IBS patient pathway