

# Chronic Diarrhea Primary Care Pathway

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## 1. Suspected chronic diarrhea

- 3 or more loose/watery stools per day
- Onset at least 4 weeks ago

## 2. 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)
- Nocturnal symptoms or significant incontinence
- Visible blood in stool
- Iron deficiency anemia (see Iron Primer)

Yes

[8. Refer for consultation/ endoscopy](#)

No

Initial investigation and management (dependent on history)

## 3. Baseline investigations

- **Blood:** CBC, electrolytes, ferritin, CRP, celiac disease screen
- **Stool:** *C. difficile*, ova and parasites
- \*If high clinical suspicion of IBD, do fecal calprotectin test (see Expanded Details)

Consider based on history

If fecal cal test > 200 mcg/g or positive for celiac

## 4. Optimize management of secondary causes

- Medical history and physical examination
- Medication-induced diarrhea: optimize or discontinue use
- History of cholecystectomy
- Identify common triggers like sugar alcohols (mannitol, sorbitol), lactose, fructose, and gluten/wheat

## 5. General principles for treatment and management of chronic diarrhea

- Education on normal stool form and bowel movement frequency
- Patient reassurance and management of expectations
- Modify diet, remove trigger foods, and space small meals throughout the day
- Soluble fibre supplementation and ensure adequate water intake
- Lifestyle modification: physical activity and psychological therapy (e.g. sleep disorder and stress management)

## 6. Pharmacological options for treating chronic diarrhea

- Anti-diarrheals/anti-motility agents (Loperamide, Diphenoxylate-atropine)
- Tricyclic antidepressants (TCA)
- Bile acid sequestrants
- Antibiotics (Rifaximin)
- Mixed opioid agonists/antagonists (Eluxadolone)

If unsatisfactory response, consider using an advice service before referring

## 7. Consider alternative diagnoses

- Microscopic colitis
- Irritable bowel syndrome-diarrhea predominant (IBS-D)
- Bile acid induced diarrhea (BAD)
- Small intestinal bacterial overgrowth (SIBO)
- Pancreatic exocrine insufficiency (PEI)

If IBS suspected

[Follow IBS pathway](#)

Yes

[Treat or refer for consultation](#)

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](#).

## CHRONIC DIARRHEA PATHWAY PRIMER

- Chronic diarrhea is defined as 3 or more loose or watery stools/day (Type 6-7 on the [Bristol Stool Chart](#)) often associated with an increase in frequency, but not always, and persisting for more than 4 weeks in duration. Symptoms can also include an urgent need to pass stool and occasional incontinence, with significant impact on the patient's quality of life.
- **This clinical pathway focuses only on the investigation and management of chronic diarrhea.**
  - Acute diarrhea is defined as 30 days or less. In Canada, acute diarrhea is most often infectious and often requires only self-limited symptom management.
- Chronic diarrhea is common gastrointestinal disorder, affecting approximately 3-5% of the general population.<sup>1</sup>
- Chronic diarrhea is more common among women than men and those with a body mass index > 30.
- Challenges may exist distinguishing between chronic diarrhea and irritable bowel syndrome diarrhea-predominant (IBS-D) as there is overlap in symptoms.
  - Pathogenic mechanisms of chronic diarrhea may be common to that of IBS, including underlying motility disruption.
  - Chronic diarrhea is distinct from IBS-D as it occurs characteristically in the absence of abdominal pain, thus visceral hypersensitivity is less of a feature.

<b>Checklist to guide in-clinic review of your patient with Chronic Diarrhea</b>	
<input type="checkbox"/>	Confirm absence of alarm features (see algorithm Box 2). If alarm features identified, refer for specialist consultation.
<input type="checkbox"/>	Assess Rome IV criteria for IBS – recurrent abdominal pain > 1 day per week in the last three months related to defecation or associated with change of frequency and/or form (appearance) in stool. If present, refer to the <a href="#">IBS pathway</a> .
<input type="checkbox"/>	Complete baseline investigations confirming no abnormal results (CBC, electrolytes, ferritin, celiac disease screen, and stool testing for <i>C.difficile</i> and ova and parasites).
<input type="checkbox"/>	Address other causes of diarrhea – medical conditions, culprit medications (see <a href="#">Table 1</a> ), alternative diagnoses, and dietary triggers.

## EXPANDED DETAILS

### 1. Suspected chronic diarrhea

A careful history will provide significant insight into the etiology of chronic diarrhea. There are two main categories to consider:

- **Functional causes**
  - Functional diarrhea without abdominal pain, not associated with inflammation or alteration to the gastrointestinal tract. It is distinct from IBS-D and post-infectious IBS, which is classically associated with pain/abdominal discomfort.
- **Organic causes**
  - Irritable bowel disease (IBD), celiac disease, microscopic colitis, medication-induced diarrhea, bile acid induced diarrhea (BAD), or other rare causes of diarrhea (e.g. radiation induced).

<sup>1</sup> Scallan, E., Majowicz, S. E., Hall, G., Banerjee, A., Bowman, C. L., Daly, L., ... & Angulo, F. J. (2005). Prevalence of diarrhea in the community in Australia, Canada, Ireland, and the United States. *International journal of epidemiology*, 34(2), 454-460.



Chronic diarrhea can also be described as one of, or a combination of, the following pathophysiologic processes:

- **Watery Diarrhea:**
  - **Osmotic**
    - The amount of water present in the stool is dependent upon the presence of solutes/effective osmoles (e.g. lactose, fructose).
    - The presence of poorly absorbed solutes (e.g. maldigested sugars) in the bowel inhibit normal water and electrolyte absorption and may lead to diarrhea (presence of higher water content in the stool).
    - Some laxatives (e.g. lactulose, citrate of magnesium) or foods/nutrients (e.g. lactose, sorbitol, and fructose) may not be well absorbed, leading to osmotic diarrhea.
    - When the solute is removed (excluded from the diet), the diarrhea typically resolves.
  - **Secretory**
    - Caused by excessive electrolyte secretions in the colon, leading to increased fluid.
    - One characteristic feature is the persistence of secretion during fasting/removal of food.
    - Medications (e.g. antibiotics, proton pump inhibitors (PPIs)), poorly reabsorbed bile acids or fatty acids in the colon, and microscopic colitis are possible causes; and rarely, hormone-producing tumors, excessive prostaglandin production, and other intestinal diseases (e.g. IBD and acquired immune deficiency syndrome (AIDS)).
- **Inflammatory Diarrhea**
  - The presence of blood and mucous in the stool can occur from inflammation and this may be immune-mediated. This occurs with chronic conditions, including IBD and other rare chronic infections (e.g. amoebiasis, tuberculosis (TB)).
  - Mucous can be a normal presence in stool and does not necessarily reflect inflammation. The key difference is the presence of blood. **This is a red flag and necessitates referral.**
- **Overflow Diarrhea**
  - A history of antecedent chronic constipation, particularly in the elderly, necessitates consideration of overflow diarrhea as a source of new onset/ poorly controlled watery stools in this context.
  - Plain x-ray imaging of the abdomen to identify fecal loading may be helpful to direct management (see [Chronic Constipation pathway](#)).

**Additional history:**

- **Medication review**
  - Many medications can cause chronic diarrhea, including over the counter medications (see [Table 1](#)).
- **Travel history and associated illness (gastroenteritis)**
  - IBS associated with prior short-term, self-limited gastroenteritis is common and can lead to longer-term altered bowel habit (post-infectious changes or IBS). This can occur in conjunction with pain (see [IBS pathway](#)).
- **Personal or significant family history of immune-mediated disease** (e.g. thyroid disease, IBD, or celiac disease).
- **Diet**
  - A dietary review can be helpful to identify easily avoidable contributing factors, such as excessive caffeine, dairy products (e.g. high lactose foods, like milk and ice cream), sugar sweetened beverages, gluten/wheat, etc.

## 2. 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 appropriate 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)
- Nocturnal symptoms or significant incontinence
- Visible blood in stool
- Iron deficiency anemia (see [Iron Primer](#))

Although alarm features are important to recognize, they have not been shown to be highly predictive of colon cancer.

### 3. Baseline investigations

- **Blood**
  - CBC, electrolytes, ferritin
  - C Reactive Protein (CRP): a non-specific marker of inflammation with modest accuracy for detecting inflammation. The sensitivity or false negative rate is approximately 70-75% with limitations as non-specific. If elevated, it can be helpful, but if normal, does not definitively exclude an inflammatory condition. A very low CRP value is however, reassuring.<sup>2</sup>
  - Celiac disease screen: a highly accurate (sensitivity is ~95%) antibody screen for this immune-mediated condition. Ensure diet is gluten inclusive for at least two weeks prior to testing to ensure no false negatives.
- **Stool**
  - *C. difficile*, stool for ova and parasites
  - In Alberta, the most common parasites are *Giardia*, *Cryptosporidium*, and *Entamoeba histolytica*, but others may be indicated if there has been travel history. If there is a relevant travel history or other relevant factors, provide this information in the details of the ova and parasites requisition.
  - **Note:** Tests such as stool leukocytes and fat globules are generally **not** recommended. Fecal immunochemical testing (FIT) has NOT been validated for investigation of chronic diarrhea-like symptoms. Ordering FIT in this circumstance is inappropriate given the presence of symptoms.
  - Further investigation using fecal calprotectin - consider ordering a fecal calprotectin if there is a high clinical suspicion of inflammation.
  - Fecal calprotectin is a stool-based test used to detect a protein released into the gastrointestinal tract from inflammatory cells (neutrophils) when present. Fecal calprotectin may be elevated and useful when there is a high clinical suspicion of IBD.

Fecal calprotectin < 100 mcg/g = Unlikely the patient has IBD  
 Fecal calprotectin 100-200 mcg/g = Test again in 4-6 weeks and order a CRP test as well  
 Fecal calprotectin > 200 mcg/g = Higher risk of IBD. Refer for specialist consultation.

- Elevated levels of fecal calprotectin are found in inflammatory bowel disease (Crohn's disease and ulcerative colitis). However, 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. By contrast, in functional disorders such as IBS, fecal calprotectin levels are normal.<sup>3</sup>
- Cost: \$102 (this includes collection and shipping & handling)

### 4. Optimize management of secondary causes

- A detailed medical history and physical examination should be performed at presentation to assess for a multitude of other conditions that mimic functional diarrhea.
- A careful review of medications should be performed to identify ones that may be causing GI side effects. Some common medications include PPIs, acetylsalicylic acid (ASA), NSAIDs, laxatives/antacids,

<sup>2</sup> Menees, S. B., Powell, C., Kurlander, J., Goel, A., & Chey, W. D. (2015). A meta-analysis of the utility of C-reactive protein, erythrocyte sedimentation rate, fecal calprotectin, and fecal lactoferrin to exclude inflammatory bowel disease in adults with IBS. *American Journal of Gastroenterology*, 110(3), 444-454.

<sup>3</sup> York Teaching Hospital – NHS Foundation Trust & Yorkshire and Humber Academic Health Sciences Network (2016, July) *The York Fecal Calprotection Care Pathway Information for GPs*. <https://www.yorkhospitals.nhs.uk/seecmsfile/?id=941>



magnesium supplements, metformin, antidepressants, antidiarrheal agents, anti-hypertensives, and herbal products (see [Table 1](#)).

- Optimization of underlying medical conditions, including diabetes and thyroid disorders
- Discontinue use or reduce dosage of culprit medications
- Ask about a history of cholecystectomy and whether this coincided with onset or worsening of symptoms. Post-cholecystectomy diarrhea, due to BAD, can be treated with cholestyramine.
- Ask about a history of bariatric surgery and whether this coincided with onset or worsening of symptoms.
- Ask about history of COVID-19 infection.
- Assess common dietary triggers - excessive intake of sugar sweetened beverages, juice, alcohol, caffeine (e.g. coffee, tea), artificial sweetener (e.g. sorbitol, diet pop), dairy (e.g. high lactose content in milk and ice cream), and gluten/wheat.

Table 1: Common medications that may cause diarrhea

System	Class	Common culprits
Cardiovascular	Anti-platelets	ASA
	Antiarrhythmics	digoxin, procainamide
	Antihypertensives	angiotensin converting enzyme inhibitor (ACEi), angiotensin receptor blocker (ARBs)*, beta-blockers
	Cholesterol/lipid-lowering agents	statins
Central nervous system	Antidepressants	selective serotonin reuptake inhibitor (SSRIs)
	Anti-parkinsonian medications	levodopa, pramipexole, entacapone
	Others	lithium
Endocrine	Oral hypoglycemic agents	metformin, acarbose, GLP-1 receptor agonists
	Thyroid replacement	levothyroxine
Gastrointestinal	Anti-secretory agents / antacids	proton pump inhibitors (PPIs), magnesium-containing antacids
	Laxatives	any
	Other	orlistat
Musculoskeletal	NSAIDs	ASA, ibuprofen, naproxen
	Gout therapy	colchicine, allopurinol
Other	Antibiotics	most**
	Antineoplastic agents	several
	Immunosuppressants	mycophenolate, cyclosporine, tacrolimus, sirolimus
	Vitamin supplements	vitamin C - doses over the upper limit of 2000 mg/day magnesium - doses over the upper limit of elemental Mg 350 mg/day potassium chloride
	Herbal supplements	

\*Olmesartan has been associated with sprue-like enteropathy

\*\*Clindamycin, fluoroquinolones, and 3<sup>rd</sup>-generation cephalosporins are common causes of *C. difficile*-associated diarrhea

## 5. General principles for treatment and management of chronic diarrhea

Patients with functional bowel disorders will benefit from lifestyle and dietary modifications. These simple modifications may be all that is required in those with mild or intermittent symptoms where quality of life is not significantly impacted. Connecting patients with resources for diet, exercise, stress reduction, and psychological counseling, where available, may be helpful. Initial assessment should include screening for underlying sleep and/or mood disorders. Patients with mental health issues such as depression and anxiety may have refractory symptoms unless mental health issues are addressed.



Treatment options (non-pharmacological)	
Education on normal stool form and bowel movement frequency	<ul style="list-style-type: none"> <li>• Details on variable frequency and form that is part of a normal spectrum of bowel habit.</li> <li>• There is marked variation in what is considered a normal bowel habit. In a study of healthy individuals, stool frequency varied from a low of 3 to a high of 21 bowel movements per week as being in the normal range.<sup>4</sup> Similarly, there is some normal variation in stool consistency as measured by the <a href="#">Bristol Stool Chart</a>.</li> <li>• If stool habit changes substantially, and persists, further investigations may be needed.</li> </ul>
Patient reassurance and management of expectations	<ul style="list-style-type: none"> <li>• A key to long-term, effective management is to provide patients reassurance after their initial diagnosis and offer points of reassessment and reappraisal to establish a therapeutic relationship.</li> <li>• Reassessment is recommended if there is a significant increase in diarrhea or signs and symptoms of dehydration.</li> </ul>
Modify diet, remove trigger foods, and space small meals throughout the day	<ul style="list-style-type: none"> <li>• Referral to a dietitian can be helpful.</li> <li>• Eat smaller meals spaced over the day to reduce gastric load.</li> <li>• Diets high in lactose, fructose, sugar sweetened beverages and juices, diet beverages, sugar free gum, sorbitol, caffeine, and gluten/wheat can increase symptoms.</li> <li>• Water is the best choice for hydration.</li> <li>• Assess common food triggers. Follow a systematic approach of removing triggers and assessing symptoms before permanent elimination.</li> <li>• It may be helpful for patients to use the <a href="#">Bowel and Symptom Journal</a> to understand their symptoms, food triggers, and stressors. Use the diary to determine how dietary modifications, psychological, and pharmacological therapies impact their symptoms.</li> </ul>
Fibre and fluids	<ul style="list-style-type: none"> <li>• <b>Total fibre:</b> Adults are recommended to consume 14 g/1000 kcal of fibre per day. Suggest about 21-38 g/day for most adults.</li> <li>• <b>Two types of fibre:</b> <ul style="list-style-type: none"> <li>○ 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.</li> <li>○ 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.</li> <li>○ There is a dose-response relationship between fibre plus fluid intake and stool output. This is important to quantify, as patients whose fibre and fluid intake is inadequate are most likely to benefit from this intervention. Fibre acts as a sponge, so it is important to <b>combine</b> fluid and fibre. Increased fluid intake on its own will only result in increased urination.</li> </ul> </li> <li>• <b>Soluble fibre supplementation:</b> <ul style="list-style-type: none"> <li>○ 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: <ul style="list-style-type: none"> <li>▪ 1 tbsp. psyllium husk or powder supplement - 3.0 grams</li> <li>▪ 2 tbsp. ground flaxseed - 1.8 grams</li> <li>▪ ½ cup kidney beans - 2.8 grams</li> <li>▪ 1 pear - 2.2 grams</li> </ul> </li> </ul> </li> </ul>

<sup>4</sup> Mitsuhashi, S., Ballou, S., Jiang, Z. G., Hirsch, W., Nee, J., Iturrino, J., ... & Lembo, A. (2018). Characterizing normal bowel frequency and consistency in a representative sample of adults in the United States (NHANES). *American Journal of Gastroenterology*, 113(1), 115-123.



Fibre and fluids cont'd	<ul style="list-style-type: none"> <li>• <b>General care:</b> <ul style="list-style-type: none"> <li>○ Increasing fibre intake may result in negative side-effects that can be minimized or avoided. <ul style="list-style-type: none"> <li>▪ Slowly increase fibre to prevent gas, abdominal pain, and bloating. Start with a third of a dose and determine tolerance.</li> <li>▪ Drink additional fluid (water) to compliment a high fibre diet. Inadequate fluid may lead to constipation, hardening of stool, bloating, and abdominal pain.</li> <li>▪ Caution soluble fibre intake for people with or at risk of a bowel obstruction or narrowing of the esophagus, stomach, or intestine.</li> <li>▪ Fibre supplements may reduce or delay absorption of certain medications.</li> </ul> </li> <li>○ See <a href="#">Patient Resources</a> section for more information on fibre supplementation.</li> </ul> </li> <li>• <b>Ensure adequate fluids:</b> 2 L/day for females, 3 L/day for males</li> </ul>
Physical activity	<ul style="list-style-type: none"> <li>• 20+ minutes of physical activity/day, aiming for 150 min/week is known to be an effective strategy for stress reduction.</li> <li>• See the <a href="#">Canadian 24-Hour Movement Guidelines</a>.</li> </ul>
Psychological therapy	<ul style="list-style-type: none"> <li>• <b>Cognitive-Behavioral Therapy</b> and <b>hypnotherapy</b> may help with stress management and gastrointestinal symptoms.<sup>5</sup> It is recommended that therapy be provided by a regulated health professional such as a registered psychologist.</li> <li>• <b>Screening for, and treating, any underlying sleep or mood disorders</b> may be important.</li> </ul>

## 6. Pharmacological options for treating chronic diarrhea

Treatment options (pharmacological)	
The use of pharmaceuticals in functional bowel disorders 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.	
Loperamide (Imodium®)	<ul style="list-style-type: none"> <li>• <b>Evidence:</b> Effective for improved diarrheal symptoms, but has not been shown to consistently improve IBS-D symptoms.</li> <li>• <b>Mechanism of action:</b> Through <math>\mu</math> (mu) opioid receptor agonist, thus decreasing GI motility.</li> <li>• <b>Place in therapy:</b> Effective antidiarrheal for prophylaxis for social situations or travel, however should not be prescribed for continuous use.</li> <li>• <b>Adverse effects:</b> Sedation, nausea, abdominal cramps.<sup>6</sup> Lowest addiction potential of all opioids.</li> <li>• <b>Dose:</b> 4 mg initially, followed by 2 mg after each loose bowel movement. Max 16 mg/day.</li> <li>• Clinical improvement usually seen within 48 hours, if no clinical improvement after at least 10 days on maximum dose, symptoms unlikely to be controlled by further administration.<sup>7</sup></li> </ul>
Diphenoxylate - Atropine (Lomotil®)	<ul style="list-style-type: none"> <li>• <b>Evidence:</b> Adjunctive therapy in management of moderate to severe diarrhea.</li> <li>• <b>Mechanism of action:</b> Through <math>\mu</math> (mu) opioid receptor agonist, thus decreasing GI motility. Atropine is an anticholinergic that further decreases GI motility and also discourages abuse.</li> <li>• <b>Place in therapy:</b> Less effective than loperamide, but may be used for intermittent symptoms for some patients.</li> <li>• <b>Adverse effects:</b> Sedation, nausea, abdominal cramps, dry skin, and mucous membranes (from atropine). Some addiction potential.<sup>5</sup></li> </ul>

<sup>5</sup> DynaMed Plus. (2018, September 10). *Confidence in Practice. Irritable bowel syndrome (IBS)*. <https://www.dynamed-com.ahs.idm.oclc.org/>

<sup>6</sup> 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>

<sup>7</sup> DynaMed. Chronic Diarrhea. EBSCO Information Services. Accessed June 15, 2021. [www.dynamed-com.ahs.idm.oclc.org/condition/chronic-diarrhea](https://www.dynamed-com.ahs.idm.oclc.org/condition/chronic-diarrhea)





Diphenoxylate - Atropine (Lomotil®) cont'd	<ul style="list-style-type: none"> <li>• <b>Dose:</b> 5 mg PO initially, then 2.5 mg PO after each loose bowel movement. Max 20 mg/day.</li> <li>• Elderly are more susceptible to anticholinergic effects.</li> <li>• Avoid concomitant use with monoamine oxidase inhibitors as this may precipitate hypertensive crisis.</li> </ul>
Tricyclic antidepressants (TCA)	<ul style="list-style-type: none"> <li>• <b>Evidence:</b> The most studied antidepressant class for treatment of abdominal pain.<sup>8</sup></li> <li>• <b>Mechanism of action:</b> 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.<sup>9</sup> Their anticholinergic properties also slow GI transit time.</li> <li>• <b>Place in therapy:</b> Recommended for overall symptom improvement in patients with IBS, as well as sleep issues, anxiety, or depression.</li> <li>• <b>Adverse effects:</b> Anticholinergic and antihistaminic (drowsiness/insomnia, xerostomia, palpitations, weight gain, constipation, urinary retention).<sup>9</sup></li> <li>• Use with caution in patients at risk of prolonged QT.</li> <li>• It can take 2-3 months to reach maximum effect.</li> <li>• The lowest effective dose should be used. Reassess therapy after 6-12 months.</li> <li>• Dose should be gradually reduced if discontinuing.</li> </ul> <p><b>Recommended Medications</b></p> <ul style="list-style-type: none"> <li>• 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).</li> <li>• 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).</li> <li>• Desipramine - 25 mg qhs, increase based on response and tolerability. Doses up to 150 mg daily have been evaluated for IBS (~\$25/month).</li> </ul>
Bile acid sequestrants	<ul style="list-style-type: none"> <li>• <b>Evidence:</b> An empiric trial may be considered for suspected bile acid induced diarrhea (BAD). May result in significant clinical improvement in approximately 25% of people. Binds and removes bile acids in the intestine.</li> <li>• <b>Mechanism of action:</b> Through the formation of a non-absorbable complex with bile acids in the intestine.</li> <li>• <b>Place in therapy:</b> Use gradual daily dose titration to minimize adverse effects and use at the lowest dose needed to minimize symptoms for BAD.<sup>5</sup></li> <li>• <b>Adverse effects:</b> Nausea, fat-soluble vitamin deficiency with long-term use, constipation.</li> <li>• Take other medications 1 hour before or 4-6 hours after.</li> <li>• <b>Dose:</b> A 2-4 week titration trial is reasonable to see effects. Intermittent, on-demand use may also be trialed.</li> <li>• Relief usually occurs within 3 days of initiation of therapy. If no relief occurs, alternative therapy should be initiated.<sup>5</sup></li> </ul> <p><b>Recommended Medications</b></p> <ul style="list-style-type: none"> <li>• Cholestyramine resin - 4 g PO Q12H, take with fluids. (\$30/month). Pouch can be divided into a smaller dose and mixed with water or juice (tomato or orange juice) starting at 2-4 g once/day, titrating to effect.</li> <li>• Colestipol (Colestid®) or Colesevelam (Lodalis®) available as tablets if patient is unable to tolerate powder.</li> </ul>

<sup>8</sup> Törnblom, H., & Drossman, D. A. (2016). Centrally targeted pharmacotherapy for chronic abdominal pain: understanding and management. *Gastrointestinal Pharmacology*, 417-440.

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





## Second line therapies

Consider consulting a GI using Specialist Link, Connect MD, or e-Referral Advice Request for guidance on these treatments.

Rifaximin (Zaxine®)	<ul style="list-style-type: none"> <li>• A non-systemically absorbed antibiotic.</li> <li>• <b>Mechanism of action:</b> Not clearly identified, but may alter the microbiome, thus reducing gas production.</li> <li>• <b>Dose:</b> 550 mg 3x/daily for 2 weeks. This is a safe drug, but tends to require multiple recurrent courses. There is no long-term safety or efficacy data over 3 courses. (~\$325, not covered by public insurers).</li> </ul>
Eluxadoline (Viberzi™)	<ul style="list-style-type: none"> <li>• <b>Mechanism of action:</b> Belongs to the class of medications called opioid receptor agonists/antagonists. Works in the bowel to regulate muscle activity and slow the rate that material passes through the digestive system, thus improving diarrhea.</li> <li>• <b>Dose:</b> Take 100 mg PO BID with food. (~\$135/month, not covered by insurance).</li> <li>• Not recommended for patients over age 65, given limited evidence for safety. Contraindicated in patients with significant alcohol use (more than 3 drinks/day), pancreatitis, prior cholecystectomy, and severe liver impairment.</li> </ul>

## 7. Consider alternative diagnoses

- **Microscopic Colitis** (see [Microscopic Colitis Primer](#))

- **Irritable Bowel Syndrome-diarrhea predominant (IBS-D)**

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. For patients with suspected IBS-D, the Rome IV diagnostic criteria may provide a guide.

**Recurrent abdominal pain**, on average,  $\geq 1$  day per week in the last 3 months, associated with  $\geq 2$  of the following criteria where pain is:

- Related to defecation
- Associated with a change in frequency of stool
- Associated with a change in form (appearance) of stool
- Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

If the patient assessment identifies predominant symptoms of pain and/or bloating, refer to the [IBS pathway](#).

- **Bile acid induced diarrhea (BAD)**

Bile acids produced in the liver and stored in the gallbladder are normally secreted into the small bowel in response to a meal, and then reabsorbed in the distal ileum (also known as enterohepatic circulation). Bile acid overproduction or poor/ ineffective ileal reabsorption (bile acid malabsorption/ bile acid diarrhea or BAM/BAD) can dysregulate this process. Subsequent unabsorbed bile acids stimulate sodium and water secretion in the colon, increase motility, and stimulate defecation, thereby contributing to chronic diarrhea.<sup>10</sup>

**There are several subtypes:**

- Idiopathic: contributing to 25-35% of patients with chronic diarrhea-predominant IBS-D or chronic functional diarrhea
- Post-cholecystectomy
- Other: e.g. secondary to small bowel resection (Crohn's disease) or radiation therapy affecting the ileum

<sup>10</sup> Sadowski, D. C., Camilleri, M., Chey, W. D., Leontiadis, G. I., Marshall, J. K., Shaffer, E. A., ... & Walters, J. R. (2020). Canadian association of gastroenterology clinical practice guideline on the management of bile acid diarrhea. *Journal of the Canadian Association of Gastroenterology*, 3(1), e10-e27.



### Diagnosis and treatment:

Diagnosis may be challenging. Giving an empiric trial of bile acid sequestrants is reasonable, easy, and inexpensive. See [Treatment options - Bile acid sequestrants](#).

- **Small Intestinal Bacterial Overgrowth (SIBO)**

Unlike the colon, a significant number of bacteria do not normally reside in the small bowel. Small intestinal bacterial overgrowth (SIBO) is a condition where dysbiosis or increased bacteria are present proximal to the ileocecal valve and within the small bowel where there is normally less bacteria. SIBO is a **rare** cause of gastrointestinal symptoms.

SIBO should only be considered in patients who have:<sup>11</sup>

- Severe diabetic neuropathy
- Advanced scleroderma
- Anatomic alterations such as surgery for Crohn's disease, Crohn's strictures, and/or radiation
- Immune deficiency (e.g. common variable immunodeficiency)
- **Note:** The accuracy of the breath test for SIBO is highly variable and may be unreliable. Routine testing for SIBO is not currently recommended.<sup>12,13</sup>
- The use of hydrogen breath testing has been used in the past to make a diagnosis of SIBO. However, the accuracy is not consistent, therefore; should not be ordered in primary care.

Empiric antibiotic treatment for SIBO should only be considered for symptomatic patients with at least one of the above considered risk factors. See [Second line therapies - Rifaximin](#).

- **Pancreatic exocrine insufficiency (PEI)**

The normal functioning pancreas produces enzymes responsible for facilitating macronutrient digestion (enzymatic cleavage) so absorption can occur. Pancreatic insufficiency is not a common cause of chronic diarrhea, but may be a contributing component in the context of known pancreatic disease (e.g. chronic pancreatitis, cystic fibrosis, or prior surgical resection of the small bowel or stomach). If you suspect pancreatic insufficiency in someone with pancreatic disease, consider testing stool for fecal elastase (low levels suggest pancreatic insufficiency). Routine use of pancreatic enzymes to support digestion are **not** supported by evidence and are costly.

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

- If alarm features are identified
- If investigation reveals a positive celiac disease screen
- If the fecal calprotectin result is > 200 mcg/g
- Colonoscopy may be helpful in patients with chronic diarrhea who have persistent symptoms or limited benefit from usual treatments.
  - The purpose of endoscopic examination is to exclude chronic immune-mediated conditions including Crohn's disease and microscopic colitis
  - **Note:** Microscopic colitis is generally a benign condition that is most often treated with anti-diarrheal or binding agents).
- 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.

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<sup>11</sup> Bull-Henry, K. (2020). Continuing Medical Education Questions: February 2020: ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth. *American Journal of Gastroenterology*, 115(2), 164.

<sup>12</sup> 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.

<sup>13</sup> 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.



## 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.<sup>14</sup>

When a "gut feeling" persists in spite of 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 low, 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 (< 10%) 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

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<sup>14</sup> 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.



- 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/Entorcort® 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 provide evidence-based guidance to support primary care providers in caring for patients with common digestive health conditions within the 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 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 Digestive Health Strategic Clinical Network in 2021, by a multi-disciplinary team led by family physicians and gastroenterologists. Names of participating reviewers and their conflict of interest declarations are available on request.

### 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 May 2024. However, we welcome feedback at any time. Please email comments to [Digestivehealth.SCN@ahs.ca](mailto:Digestivehealth.SCN@ahs.ca).

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### Disclaimer

This pathway represents evidence-based best practice but does not override the individual responsibility of health care 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 health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care 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](http://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](http://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.

References	
Ma, C., Battat, R., Parker, C. E., Khanna, R., Jairath, V., & Feagan, B. G. (2019). Update on C-reactive protein and fecal calprotectin: are they accurate measures of disease activity in Crohn's disease? <i>Expert review of gastroenterology &amp; hepatology</i> , 13(4), 319-330.	
Resources	
Poverty: A Clinical Tool for Primary Care Providers (AB)	<a href="http://cep.health/media/uploaded/Poverty_flowAB-2016-Oct-28.pdf">cep.health/media/uploaded/Poverty_flowAB-2016-Oct-28.pdf</a>
Nutrition Guideline: Household Food Insecurity	<a href="http://ahs.ca/assets/info/nutrition/if-nfs-ng-household-food-insecurity.pdf">ahs.ca/assets/info/nutrition/if-nfs-ng-household-food-insecurity.pdf</a>



## PATIENT RESOURCES

### Information

Description	Website
General information on diarrhea (MyHealth.Alberta.ca)	<a href="http://myhealth.alberta.ca/health/pages/conditions.aspx?Hwid=diar4">myhealth.alberta.ca/health/pages/conditions.aspx?Hwid=diar4</a>
General information on diarrhea (Canadian Digestive Health Foundation)	<a href="http://cdhf.ca/digestive-disorders/diarrhea/">cdhf.ca/digestive-disorders/diarrhea/</a>
Diarrhea and Diet (GI Society & Canadian Society of Intestinal Research)	<a href="http://badgut.org/information-centre/health-nutrition/diarrhea-and-diet/">badgut.org/information-centre/health-nutrition/diarrhea-and-diet/</a>
Fibre Facts	<a href="http://ahs.ca/assets/info/nutrition/if-nfs-fibre-facts.pdf">ahs.ca/assets/info/nutrition/if-nfs-fibre-facts.pdf</a>
Bowel and Symptom Journal	<a href="http://ahs.ca/assets/info/nutrition/if-nfs-bowel-symptom-journal.pdf">ahs.ca/assets/info/nutrition/if-nfs-bowel-symptom-journal.pdf</a>
Nutrition Education Material	<a href="http://ahs.ca/NutritionResources">ahs.ca/NutritionResources</a>
Gut Health Patient Journal (Physician Learning Program)	<a href="http://9c849905-3a37-465a-9612-7db1b9a0a69c.filesusr.com/ugd/7b74c1_81f1695f08214a66bc339462c52cd011.pdf">9c849905-3a37-465a-9612-7db1b9a0a69c.filesusr.com/ugd/7b74c1_81f1695f08214a66bc339462c52cd011.pdf</a>

### Services Available

Description	Website
Services for patients with chronic conditions (Alberta Healthy Living Program - AHS)	<a href="http://ahs.ca/info/page13984.aspx">ahs.ca/info/page13984.aspx</a>
Supports for working towards healthy lifestyle goals and weight management (Weight Management – AHS)	<a href="http://ahs.ca/info/Page15163.aspx">ahs.ca/info/Page15163.aspx</a>
Referral to a Registered Dietitian	<ul style="list-style-type: none"> <li>• Visit <a href="#">Alberta Referral Directory</a> and search for nutrition counselling.</li> <li>• To learn more about programs and services offered in your zone, visit <a href="#">Nutrition Services</a>.</li> <li>• <a href="#">Health Link</a> 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.</li> </ul>



# Your Pathway for Managing Chronic Diarrhea (adults)

## What is chronic diarrhea?

- Means loose or watery stool.
- Often associated with an increase in frequency.
- Symptoms can also include an urgent need to pass stool and occasional incontinence.
- It is normal to have up to 3 bowel movements per day.
- It affects approximately 3-5% of the population.
- It can affect your every day activities and have a negative impact on quality of life.
- Usually cared for by healthcare providers in your family doctor's office.

## What is the chronic diarrhea patient pathway?

It is a map for you and your healthcare providers to follow. It makes sure the care you are getting for chronic diarrhea is safe and helpful in managing your symptoms.

You and your healthcare providers may modify the pathway to best suit your healthcare needs.

If symptoms cannot be managed over time, you and your healthcare providers may decide a referral to a specialist would be helpful.

### 1. Check your symptoms

- Loose watery stools that last for more than 4 weeks

### 2. Make lifestyle changes to manage your symptoms (see over for details)

- Adjust or stop use of certain medicines
- Identify foods that cause symptoms and try to limit or avoid them
- Eat smaller meals throughout the day
- Increase your soluble fibre intake. Eat foods like oats, flax, chia, and barley.
- Make sure to get plenty of water daily
- Try to get at least 20 minutes of physical activity daily. Aim for 150 minutes each week.
- Identify what causes you stress and find ways to reduce it

### 3. Tests that may be done

- Blood or stool tests
- Test to rule out celiac disease
  - Make sure your diet includes gluten (e.g. white or whole wheat bread) for at least two weeks before testing

## Tell your healthcare providers if you have these symptoms:

- Family history of colon cancer
- Losing weight without meaning to
- Symptoms that often wake you up at night
- Stool that is black in colour or has blood in it

Talk to your healthcare providers if your symptoms don't improve, get worse, or keep interfering with your everyday activities

Once you find something that works for you, stick with it.

You may need to keep trying other options to find what works best to manage your symptoms.



### 4. Medicine that may be tried

- Many options can be used to improve your symptoms
- Talk with your healthcare providers about what medicines may be right for you





# What do I need to know about my symptoms and chronic diarrhea?

## Working through the chronic diarrhea patient pathway can take several months:

- Your healthcare providers will ask you questions about your health and do a physical exam. They will also review any medicines you are taking.
- They may suggest certain tests to learn more about possible causes of your symptoms.
- They will talk with you about possible lifestyle habits that may be causing your symptoms and how you can make changes that could help you feel better.
- You may find it helpful to write down your symptoms and what seems to cause them (e.g. certain food or stress). You and your healthcare providers can make a plan to help manage your symptoms using this information.
- Together, you may decide to try certain medicines to help in treating your symptoms.
- You may use medicines for a short amount of time (or possibly longer) depending on whether your symptoms improve.

## To manage your symptoms, try to:

- Identify foods that cause your symptoms. You may want to keep track of the foods you eat and how they affect your diarrhea.
- Get at least 20 minutes of physical activity daily. Aim for 150 minutes each week (e.g. walking, biking, gardening, stairs, or your favourite sports).
- Choose high soluble fibre foods like oats, flax, chia, and barley. Slowly increase the amount of fibre you eat. Target 25 g for females and 38 g for males.
- Consider the use of a psyllium fibre supplement (e.g. Metamucil).
- Drink plenty of water throughout the day.
- Identify what causes you stress and work on reducing it. You may want to try yoga, meditation, counselling, or a stress reduction program.

## Seeing a specialist is only recommended if:

- Your symptoms continue or get worse after following treatment and management options in the chronic diarrhea pathway.
- You and your healthcare providers identify concerning symptoms or test results.

## You can find more information in the great resources below:


- Canadian Digestive Health Foundation [cdhf.ca](http://cdhf.ca)  
\* search Diarrhea
- My Health Alberta [myhealth.alberta.ca](http://myhealth.alberta.ca)  
\* search Diarrhea
- Alberta Healthy Living Program [ahs.ca/info/page13984.aspx](http://ahs.ca/info/page13984.aspx)
  - Workshops on chronic pain and stress reduction
- Nutrition Education Materials [ahs.ca/NutritionResources](http://ahs.ca/NutritionResources)

## Write any notes or questions you may have here:

Please provide feedback about this patient pathway by completing a short [survey](https://bit.ly/DHSCNsurvey) (bit.ly/DHSCNsurvey) or email us at [Digestivehealth.SCN@ahs.ca](mailto:Digestivehealth.SCN@ahs.ca)



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