Enhanced Primary Care Pathway: Chronic Diarrhea

1. Focused summary of chronic diarrhea relevant to primary care

Chronic diarrhea is a common disorder typically characterized by frequent loose bowel movements that often have significant impact on patient function and quality of life. Fecal urgency and even incontinence can occur and have further impact on patients. The most common causes of chronic diarrhea seen in clinical practice are medication-induced diarrhea, and functional bowel disorders, including diarrhea-predominant irritable bowel syndrome (IBS-D) and functional diarrhea (FDr).

Medication-induced diarrhea

Medications are a common cause of diarrhea missed by health care practitioners. Careful attention should be paid to medication lists to identify potential culprits (see Table 1 on next page). One should note the date of onset (or worsening) of symptoms correlated to dates for medication initiation, discontinuation, and dosage changes. A trial of empiric discontinuation or dosage reduction of the possible offending medication can also be helpful.

Functional bowel disorders

Functional bowel disorders such as IBS-D and FDr are caused by a number of mechanisms including altered GI motility, brain-gut disturbances, genetic and environmental factors, prior infections, alterations in the microbiota and psychosocial factors.

The confident diagnosis of IBS and FDr relies on the presence of foundational symptoms, recognition of intestinal and extra-intestinal symptoms and psychological stressors that support the diagnosis, detailed medical history and physical examination as well as judicious use of investigations to identify red flag features and exclude organic conditions that mimic functional bowel disorders.

Treatment of functional bowel disorders involves initial reassurance, dietary, psychological, behavioral interventions, pharmacotherapy based on dominant symptoms, and scheduled patient clinical review, reappraisal, support, and guidance.

Irritable bowel syndrome is a common symptom complex characterized by chronic abdominal pain and abnormal bowel function in absence of organic cause. These key features of IBS can be widely variable in severity and may remit and recur, often being affected by dietary factors and various stressors.

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**Diagnostic Criteria for Irritable Bowel Syndrome (Rome IV)**

Recurrent abdominal pain, on average, ≥ 1 day per week in the last 3 months, associated with ≥ 2 of the following criteria:

1. Related to defecation
2. Associated with a change in frequency of stool
3. 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.

These diagnostic criteria were developed for uniformity of patient recruitment in clinical trials. In clinical practice, such criteria only provide a framework for assessing patients with suspected IBS; indeed these criteria alone are far better for ruling out IBS than ruling it in.

IBS is frequently associated with other gastrointestinal symptoms including bloating, flatulence, nausea, burping, gastroesophageal reflux, and dyspepsia. Extra-intestinal symptoms also frequently occur in IBS patients including dysuria and frequent, urgent urination, widespread musculoskeletal pain, dysmenorrhea, dyspareunia, fatigue, anxiety, and depression. A long-standing duration of symptoms is also predictive of a functional bowel disorder.

Isolated functional diarrhea is another functional bowel disorder defined by Rome IV criteria. It is not as common as IBS. FDr causes loose or watery stools in the absence of prominent abdominal pain and bloating.
## Table 1. Common drugs that may cause diarrhea

<table>
<thead>
<tr>
<th>System</th>
<th>Class</th>
<th>Common culprits</th>
</tr>
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<tbody>
<tr>
<td>Cardiovascular</td>
<td>Anti-platelets</td>
<td>ASA</td>
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<tr>
<td></td>
<td>Antiarrhythmics</td>
<td>Digoxin, Procainamide</td>
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<td></td>
<td>Anti-hypertensives</td>
<td>ACEi, ARBs*, Beta-blockers</td>
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<td></td>
<td>Cholesterol/lipid-lowering agents</td>
<td>Statins, Ezetimibe, Orlistat</td>
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<tr>
<td></td>
<td>Diuretics</td>
<td>Furosemide</td>
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<tr>
<td>CNS</td>
<td>Anxiolytics</td>
<td>Benzodiazepines</td>
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<tr>
<td></td>
<td>Antidepressants</td>
<td>SSRIs</td>
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<tr>
<td></td>
<td>Anti-parkinsonian drugs</td>
<td>Levodopa</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>Anticholinergic agents, Lithium</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Oral hypoglycemic agents</td>
<td>Metformin, Acarbose</td>
</tr>
<tr>
<td></td>
<td>Thyroid replacement</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Anti-secretory agents / antacids</td>
<td>H2RAs, PPIs, Magnesium-containing antacids</td>
</tr>
<tr>
<td></td>
<td>Laxatives</td>
<td><em>(Any)</em></td>
</tr>
<tr>
<td></td>
<td>IBD therapy</td>
<td>5-aminosalicylates</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>NSAIDs</td>
<td>ASA, Ibuprofen, Naproxen</td>
</tr>
<tr>
<td></td>
<td>Gout therapy</td>
<td>Colchicine</td>
</tr>
<tr>
<td>Other</td>
<td>Antibiotics</td>
<td><em>(Most)</em>†</td>
</tr>
<tr>
<td></td>
<td>Antineoplastic agents</td>
<td>Several</td>
</tr>
<tr>
<td></td>
<td>Dietary culprits</td>
<td>Alcohol, Artificial sweeteners (eg. sorbitol)</td>
</tr>
<tr>
<td></td>
<td>Supplements</td>
<td>Iron, Magnesium, Vitamin C, Herbals <em>(Many)</em></td>
</tr>
</tbody>
</table>

ACEi: angiotensin converting enzyme inhibitor  
ARB: angiotensin receptor blocker  
ASA: acetylsalicylic acid  
H2RA: histamine H2 receptor antagonist  
NSAID: non-steroidal anti-inflammatory drug  
PPI: proton-pump inhibitor  
SSRI: selective serotonin reuptake inhibitor

* Olmesartan has been associated with sprue-like enteropathy  
† Clindamycin is a common cause of *C. difficile*-associated diarrhea
2. Checklist to guide your in-clinic review of this patient with chronic diarrhea symptoms

- Ensure absence of red flag features
  - Bleeding, iron deficiency anemia, > 5% weight loss, nocturnal symptoms, onset after age 50
- No family history of inflammatory bowel disease or colorectal cancer
- Address other causes of diarrhea
  - Medical conditions, culprit medications (see Table 1 above), and dietary factors
- Meets 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) of stool

3. Links to additional resources for patients

- Canadian Digestive Health Foundation Understanding Irritable Bowel Syndrome
- UpToDate® - Beyond the Basics Patient Information about IBS (freely accessible)
- Bad Gut
  [https://www.badgut.org/information-centre/a-z-digestive-topics/ibs/](https://www.badgut.org/information-centre/a-z-digestive-topics/ibs/)
- American College of Gastroenterology Patient Resource Center

4. Clinical flow diagram with expanded detail

This AHS Calgary Zone pathway incorporates the most current evidence-based clinical guidelines for diagnosis and management of IBS, from both Gastroenterology and Primary Care literature:

- Drossman DA and Hasler WL. Rome IV—Functional GI disorders: Disorders of gut-brain interaction
  Gastroenterology 2016;150:1257-61
- Weinberg et al. AGA Institute Guideline on the pharmacological management of irritable bowel syndrome.
  Gastroenterology 2015;147:1146-8
  [http://www.gastrojournal.org/article/S0016-5085(14)01089-0/abstract](http://www.gastrojournal.org/article/S0016-5085(14)01089-0/abstract)
- Kuritzky L. Individualizing Pharmacologic Management of Irritable Bowel Syndrome.
- Wilkins et al. Diagnosis and management of IBS in adults.
  American Family Physician 2012;86:419-426
  [http://www.aafp.org/afp/2012/0901/p419.html](http://www.aafp.org/afp/2012/0901/p419.html)
Flow Diagram: Chronic Diarrhea

Suspected functional bowel disorder causing Chronic Diarrhea
- 3 or more loose/watery stools per day
- Onset at least 4 weeks ago

Alarm features?
- Unintended weight loss ≥ 5%
- GI bleeding / iron deficiency anemia
- Onset of symptoms after age 50
- Nocturnal symptoms
- Family history of colorectal cancer or inflammatory bowel disease

Yes
Refer for specialist consultation through GI Central Access & Triage

No alarm features

Address secondary causes
- Optimization of underlying medical conditions, including diabetes and thyroid disorders
- Discontinuation or dose reduction of culprit medications (see Table 1 for details)
- Elimination of obvious dietary triggers (eg. excessive intake of pop, juice, sorbitol, alcohol)

No improvement after optimization

Further investigation
Blood:
- CBC, electrolytes, ferritin, albumin, CRP, TSH, celiac serology

Stool:
- C. difficile, parasite antigen screen
  The parasite (protozoal) screen tests for Giardia, Cryptosporidium, and Entamoeba. Order full microscopic examination for Ova & Parasites instead if compatible history of travel to endemic areas
- Fecal leukocytes, pH, fat globules, elastase
  Request these special stool tests only in the context of appropriate clinical suspicion (see text for details)

No organic cause identified

Appropriate work-up and management of underlying cause

Iron deficiency anemia, suspected celiac disease, suspected IBD

General principles of treating diarrhea associated with functional bowel disorders
- Education about a wide range of normal stool form and bowel motion frequency
- Patient reassurance and management of expectations
- Dietary review, journaling, and intervention (check for FODMAP, gluten, and dairy product sensitivities)
- Lifestyle modification and complementary therapies addressing exercise, sleep hygiene, and stress management
- Establishment of a therapeutic relationship to allow for longitudinal monitoring and review

Treatment options for IBS (all subtypes)
- Regular exercise
- Low FODMAPs diet, gluten avoidance, lactose avoidance
- Increase soluble fiber intake
- Probiotics
- Antispasmodics
- Low-dose tricyclic antidepressants
- Complementary therapies

See IBS Pathway for further details

Treatment options for diarrhea-predominant IBS and functional diarrhea
- Anti-diarrheals / anti-motility agents
- Mixed opioid agonists/antagonists (Eluxadoline)
- Bile acid sequestrants
- Rifaximin
1. **Diagnosis:** The diagnosis of functional bowel disorders such as functional diarrhea (FDr) and diarrhea predominant irritable bowel syndrome (IBS-D) are based on Rome IV criteria. Both FDr and IBS-D are associated with change in stool frequency or form. The definition for IBS-D also includes recurrent abdominal pain. Suspected functional bowel disorders require very little initial laboratory investigation – CBC, ferritin, and celiac disease screen according to most guidelines. Special stool testing should only be requested within the appropriate clinical context.

**Special stool testing:** In patients in whom an infectious or inflammatory cause is suspected (fevers, severe cramping, blood or mucous in stools), stool can be sent to test for elevated fecal leukocytes. Stool is normally alkaline. In the setting of carbohydrate malabsorption (including lactose malabsorption), stool pH tends to be acidic with pH < 6. Fat-laden stools are often foul smelling, float in the toilet, and are difficult to flush. Diarrhea of this quality should be investigated for the presence of fecal fat globules to test for fat malabsorption. Fecal elastase is requested in patients with a history of pancreatitis or imaging suggestive of chronic pancreatitis; low levels of fecal elastase suggest pancreatic exocrine insufficiency. Fecal immunochemical testing (FIT) has not been validated for investigation of IBS-like symptoms; ordering FIT in this circumstance is inappropriate.

Anemia or other red flag features increase the likelihood of organic disease and mandate referral to GI. Absence of red flags, however, does not completely exclude the possibility of organic disease. Various other intestinal and extra-intestinal features often co-exist with functional bowel disorders and provide support to the diagnosis. It is estimated that unrecognized organic disorders will be present in about 15% of patients who meet Rome IV criteria for IBS and do not have alarm features. The most common diseases that are mislabeled as IBS are celiac disease, Crohn's disease, and microscopic colitis. **If C-reactive protein is ≤ 1.0 mg/dL, the probability of IBD is ≤1%.** GI cancers are very unlikely in patients that meet usual criteria for IBS.

A detailed medical history and physical examination should be performed at presentation to assess for a multitude of other conditions that mimic FDr and IBS-D. A careful review of medications should be performed to identify ones that may be causing GI side effects. Some common ones include PPIs, ASA/NSAIDs, laxatives/antacids, magnesium supplements, metformin, antidepressants, anti-hypertensives, diuretics, and herbal products (see Table 1 for details).

2. **General principles of treatment:** All 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 that do not significantly affect quality of life. The key to effective long-term management is to provide patient reassurance at the initial diagnosis and offer points of reassessment and reappraisal to establish a therapeutic relationship. Connecting patients with resources for diet, exercise, stress reduction, and psychological counseling is important. Initial assessment should also include screening for underlying sleep or mood disorders. Patients with mental health issues such as depression and anxiety will often have refractory symptoms unless mental health issues are addressed. It is important however to note that stress can contribute to functional bowel disorder symptoms but does NOT cause them.

3. **Specific Treatments:** 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. Pain and bloating is a defining feature of IBS and, in some patients, these features are severe or frequent enough to affect quality of life. Antispasmodics may be beneficial in managing or aborting acute episodes of pain, and patients often take reassurance in having these on-demand treatments available. For chronic IBS pain, tricyclic antidepressants have shown benefit, and may have added benefits in those patients with mood or sleep issues.

**In absence of alarm features, what would prompt referral for GI consultation and possible colonoscopy?** Colonoscopy may be helpful in patients with diarrhea predominance who have persistent symptoms or limited benefit from usual treatments. This is mainly to assess for Crohn's disease and microscopic colitis (important to note that microscopic colitis is generally a benign condition that is most often treated with anti-diarrheal or binding agents thus diagnosis by colonoscopy is not essential for most patients). In patients with constipation predominance or alternating diarrhea and constipation, colonoscopy is very unlikely to yield relevant findings.
## Principles and Specifics of Chronic Diarrhea Management

<table>
<thead>
<tr>
<th>All subtypes of IBS/Functional GI disorders</th>
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<tbody>
<tr>
<td><strong>Exercise</strong></td>
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<td><strong>Soluble Fibre</strong></td>
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</table>
| **Probiotics** | Bifidobacterium infantis (Align®) 1 capsule/d ($40/mo.)  
* Lactobacillus plantarum 229v (TuZen®) 1-2 capsules/d ($40-80/mo.)  
Visbiome® ½ to 1 sachet/day ($100/mo.) Available online only |
| **Antispasmodics** | Peppermint oil (0.2 to 0.275mL caps, enteric coated) 2 capsules BID ($20-25/mo.)  
Hyoscine Butylbromide (Buscopan®) 10mg TID-QID ($25-40/mo.)  
Dicyclomine hydrochloride (Bentylol®) 20mg TID-QID ($25-40/mo.)  
Pinaverium Bromide (Dicetel®) 50-100mg TID ($50-75/mo.)  
Trimebutine (Modulon®) 100-200mg TID ($40-80/mo.)  
All prescribed antispasmodic medications should be fully discussed with the patient in terms of specific risks and side effects and appropriateness of use in context of their full medical history |
| **Antidepressants** | Nortriptyline or amitriptyline 10-25 mg qhs, dose escalate by 10-25 mg/wk  
May require 2.5-150mg/d ($20-60/mo.); usually takes 2-3 mos. for peak effect  
Particularly useful in patients with diarrhea and pain predominance or sleep issues/anxiety/depression  
Use with caution in patients at risk of prolonged QT; note somnolence and anticholinergic side effects  
Latest IBS technical review **does not** endorse use of SSRIs |
| **Complementary Therapies** | Psychological treatments  
Mindfulness-based stress reduction (www.thebreathproject.org)  
Hypnotherapy  
Acupuncture  
Yoga (www.yogacalgary.ca) |
| **Healthy Living/Self Management** | Alberta Healthy Living Program (ahs.ca/info/cdmcalgaryzone.asp) |

### Diarrhea-Predominant IBS and Functional Diarrhea

| Anti-diarrheals | Eluxalodine (Viberzi®) 75-100 mg BID with food ($2.21/tab=$132.60/mo.)  
**Contraindicated in patients with EtOH abuse, prior pancreatitis, sphincter of Oddi dysfunction, prior cholecystectomy and established liver cirrhosis of any cause**  
Loperamide (Imodium®) 2-4mg BID-QID ($25-50/mo. OTC)  
Diphenoxylate-atropine (Lomotil®) 2.5 – 5mg BID-QID ($25-50/mo.)  
Cholestyramine powder (Olestryl® $0.40/g); colestipol (Colestid® $0.25/g) tablets or powder 1-4g OD-TID; colesveelam (Lodalis® $1.80/g) tablets or powder 1-4g OD-TID  
Especially useful post-cholecystectomy; advise regarding timing with other medications to avoid interaction; if long term use, risk of fat soluble vitamin deficiencies |
| Low FODMAPs | Canadian Digestive Health Foundation  
| Gluten Avoidance | Non-celiac gluten sensitivity |
| Antibiotics | Rifaximin (Zaxine®) 550mg TID for 2 weeks (~$325!)  
*currently off-label indication for IBS-D and FDr; expected Health Canada approval late 2018
**Enhanced Primary Care Pathway: Chronic Diarrhea**

To ensure that your referral is triaged appropriately, please review this quality referral checklist as you create the referral. Free pocket sized copies of this checklist are available through Quality Referral Evolution (QuRE) at www.ahs.ca/QuRE.

### PATIENT INFORMATION
- Name, DOB, PHN, Address, Phone, Alternate contact, Translator required

### PRIMARY CARE PROVIDER INFORMATION
- Name, Phone, Fax, cc/indicate if different from family physician

### REFERRING PHYSICIAN INFORMATION
- Name, Phone, Fax

### REASON FOR REFERRAL
- Diagnosis, management and/or treatment
- Procedure issue / care transfer

### PATIENT’S CURRENT STATUS
- Stable, worsening or urgent/emergent
- Understanding of situation
- Key symptoms and findings
- Symptom onset / duration
- Red flags

### FINDINGS AND/OR INVESTIGATIONS
- What has been done & is available
- What has been ordered & is pending

### CURRENT & PAST MANAGEMENT
- (LIST WITH OUTCOMES)
  - None
  - Unsuccessful / successful treatment(s)
  - Previous or concurrent consultations for this issue

### COMORBIDITIES
- Medical history
- Pertinent concurrent medical problems
- Current & recent medications (name, dosage, PRN basis)
- Allergies
- Warnings & challenges

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**IMPORTANT INFORMATION REGARDING YOUR RECENT REFERRAL**

TIPS:

- Assist with patient communication by indicating patient's preferred method of contact and if they will be unavailable (holiday, etc)

- Don't forget that the referring physician isn't always the family physician. Keep everyone in the loop with a cc.

- Make sure to express clear expectations for the consult and, when possible, outline a specific question.

- Current status is must-know clinical information that has direct impact on triage of the referral.

- Ensure you have listed all ordered tests so the receiving consultant does not unknowingly order the same tests again.

- Provide information on what has been tried previously and why a consult is required.

- A complete medical history can help the consultant determine the complexity and urgency of the referral.