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.

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

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

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**
cdhf.ca/en/disorders/details/id/12

UpToDate® – *Beyond the Basics* Patient Information about **IBS** (freely accessible)
uptodate.com/contents/irritable-bowel-syndrome-beyond-the-basics?source=search_result&search=ibs&selectedTitle=2%7E150

Bad Gut
badgut.org/information-centre/a-z-digestive-topics/ibs/

American College of Gastroenterology Patient Resource Center
patients.gi.org/topics/irritable-bowel-syndrome/

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
gastrojournal.org/issue/S0016-5085(15)X0019-9

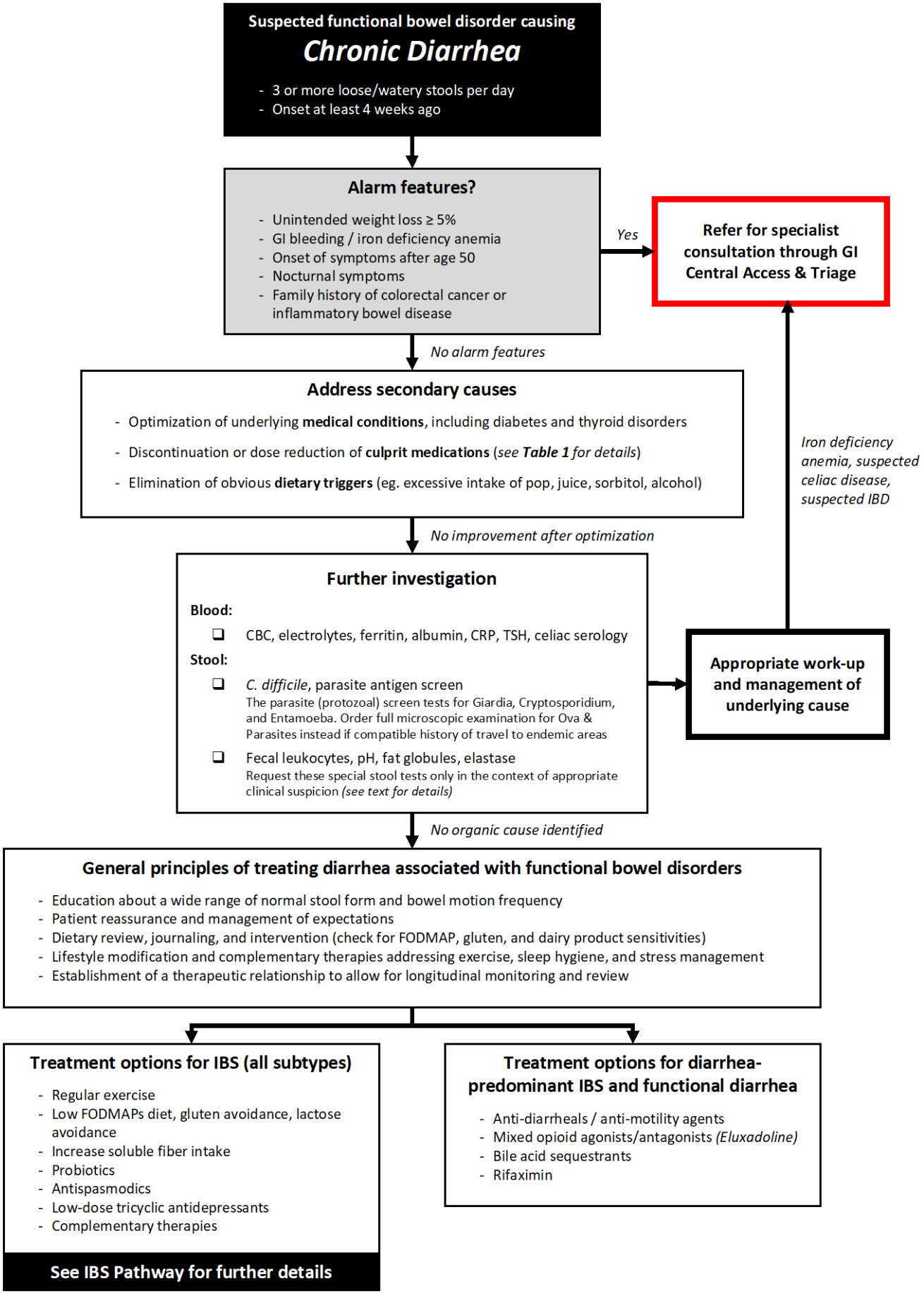
Weinberg *et al.* AGA Institute Guideline on the pharmacological management of irritable bowel syndrome.
Gastroenterology 2015;147:1146-8
gastrojournal.org/article/S0016-5085(14)01089-0/abstract

Ford *et al*. American College of Gastroenterology Monograph on the Management of Irritable Bowel Syndrome and Chronic Idiopathic Constipation Am J Gastroenterol 2014; 109:S2 – S26; doi: 10.1038/ajg.2014.187
gi.org/wp-content/uploads/2014/08/IBS_CIC_Monograph_AJG_Aug_2014.pdf

Kuritzky L. Individualizing Pharmacologic Management of Irritable Bowel Syndrome.
J Fam Pract. 2015;64:S16-21.
admin.imng.com/fileadmin/qhi/jfp/pdfs/CME_-_Hot_Topics_IBS_article_2.19.16.pdf

Wilkins *et al.* Diagnosis and management of IBS in adults.
American Family Physician 2012;86:419-426
aafp.org/afp/2012/0901/p419.html

Flow Diagram: Chronic Diarrhea



Flow Diagram: Chronic Diarrhea Expanded Detail

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.

   <u>In absence of alarm features</u>, 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

All subtypes of IBS/Functional GI disorders	
Exercise	Moderate to vigorous exercise for 20-60 minutes 3-5x per week
Soluble Fibre	Use in IBS remains controversial, as may be beneficial in some but detrimental in others. Reasonable to try psyllium husk one-half to one tablespoon daily. Insoluble fibre is not beneficial.
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 25-150mg/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 (thebreathproject.org) Hypnotherapy Acupuncture Yoga (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 (Olestyr® $0.40/g); colestipol (Colestid® $0.25/g) tablets or powder 1-4g OD-TID; colesevelam (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 cdhf.ca/bank/document_en/32-fodmaps.pdf
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**

IMPORTANT INFORMATION REGARDING YOUR RECENT REFERRAL

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
(RELEVANT RESULTS ATTACHED)
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

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 unknowlingly 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.

Alberta Health Services