

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 <a href="mailto:short video">short video</a>.

#### DYSPEPSIA PATHWAY PRIMER

- Although the causes of dyspepsia include esophagitis, peptic ulcer disease, Helicobacter pylori (H. pylori)
  infection, celiac disease, and rarely neoplasia, most patients with dyspepsia have no organic disease with
  a normal battery of investigations, including endoscopy. Dyspeptic symptoms in the general population
  are common. Estimates are that as high as 30% of individuals experience dyspeptic symptoms, while few
  seek medical care.
- The mechanism of this symptom complex isn't completely understood, but likely involves a combination of visceral hypersensitivity, alterations in gastric accommodation and emptying, and altered central pain processing.
- Differential diagnosis
  - o There is frequent overlap between dyspepsia and gastroesophageal reflux disease (GERD). If the patient has predominant heartburn symptoms, refer to the GERD pathway.
  - Dyspepsia also overlaps with irritable bowel syndrome (IBS), especially if upper abdominal bloating is a dominant symptom. In IBS, the predominant symptom complex includes bloating and relief after defecation.
  - Biliary tract pain should also be considered, with classic presentation being a post-prandial deepseated crescendo-decrescendo right upper quadrant pain (particularly after a fatty meal) that builds over several hours and then dissipates. Often, it radiates to the right side towards the right scapula and may be associated with nausea and vomiting.
- To learn more about deprescribing PPIs, refer to the six vignettes in the <a href="Provider Resources">Provider Resources</a> section.

Checklist to guide in-clinic review of your patient with Dyspepsia				
	Diagnostic criteria - Predominant (> 1 month):  • Epigastric discomfort/pain  • Upper abdominal bloating			
	Confirm absence of alarm features (see algorithm Box 3).  If alarm features identified, refer for specialist consultation.			
	Identification and adjustment of medication and lifestyle factors that may cause/contribute to dyspepsia			
	Complete baseline investigations confirming no underlying medical condition causing dyspepsia (see algorithm Box 5).			
	Confirm negative <i>H. pylori</i> testing. If positive, refer to the <i>H. pylori</i> pathway.			
	If unsatisfactory response to management and / or inclusion of pharmacological therapy (see algorithm Box 7), consider using an advice service before referring. Otherwise, continue care in the Patient Medical Home.			

### **EXPANDED DETAILS**

## 1. Suspected dyspepsia

• Dyspepsia is characterized by epigastric pain or upper abdominal discomfort. It may be accompanied by a sense of abdominal distension or "bloating," early satiety, belching, nausea, and/or loss of appetite.

- The Rome IV committee on functional GI disorders defines dyspepsia as one or more of the following symptoms for three months prior, with symptom onset ≥ six months prior:
  - o Postprandial fullness
  - Epigastric pain
  - Epigastric burning
  - Early satiety

#### 2. Is it GERD?

If the patient's predominant symptom is heartburn ± regurgitation, refer to the GERD pathway.

#### 3. Alarm features

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

- Family history (first-degree relative) of esophageal or gastric cancer
- Personal history of peptic ulcer disease
- Age > 60 with new and persistent symptoms (> 3 months)<sup>1</sup>
- Unintended weight loss (> 5% over 6-12 months)
- Progressive dysphagia
- Persistent vomiting (not associated with cannabis use)
- Black stool or blood in vomit (see Primer on Black Stool)
- Iron deficiency anemia (see <u>Iron Primer</u>)
- Note: FIT testing is not required or suggested. It has only been validated for screening in asymptomatic individuals

Stronger consideration should be given for symptoms that are > 3 months in duration and have failed a trial of PPI. Evidence suggests that alarm features poorly predict clinically significant pathology and should be factored into the entire patient presentation, not in isolation.

# 4. Medication and lifestyle review

#### Medication review

- Common culprits include ASA/NSAIDs/COX-2 inhibitors, corticosteroids, bisphosphonates, antibiotics, dabigatran, metformin, and iron or magnesium supplements.
- Any new or recently prescribed or over the counter medications or herbal/natural products may be implicated, as virtually all medications can cause GI upset in some patients.

#### Lifestyle review

- Review and address lifestyle factors that may contribute to symptoms, including obvious dietary triggers, alcohol intake, weight management, stress, caffeine intake, and smoking. Use the <u>Gut</u> <u>Health Patient Journal</u> as a resource for patients to track symptoms, diet, and lifestyle factors.
- o Engage other health professionals, as appropriate (nurse, dietitian, pharmacist, etc.).
- Heavy cannabis use can be associated with persistent vomiting/other GI symptoms and should be considered and addressed, if appropriate.

### 5. Baseline investigations

 Baseline investigations to identify concerning features or clear etiologies include CBC, INR, BUN (blood urea nitrogen), ferritin, and celiac disease screen.

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<sup>&</sup>lt;sup>1</sup> There is some variation between guidelines about the age at which dyspepsia symptoms are more concerning and warrant stronger consideration of gastroscopy. Choosing Wisely Canada now uses age 65. However, age is only one element of a risk assessment related to the need for gastroscopy to investigate dyspepsia symptoms.

- Upper GI series is not recommended for investigation of dyspepsia due to high rates of false positives and false negatives.
- If hepatobiliary or pancreatic disease is suspected, consider abdominal ultrasound, ALT, ALP, bilirubin, and lipase (lipase ≥ 3 times upper normal limit may be indicative of acute pancreatic disease).
- Pancreatic cancer should be considered in patients with dyspepsia and weight loss, especially if there is evidence of jaundice. The investigation of choice for suspected pancreatic cancer is an **urgent CT scan**.

#### 6. Test and treat for *H. pylori* Infection

See H. pylori pathway

### 7. Pharmacological therapy

# Treatment options (pharmacological) • Evidence: In the absence of H. pylori infection, or if symptoms continue despite H. pylori eradication, a trial of PPI may benefit some patients. • Mechanism of action: Suppresses gastric acid secretion by inhibiting the parietal cell H+/K+ ATP • Initial PPI therapy should be once daily, 30 minutes before breakfast on an empty stomach. • If there is inadequate response after 4-8 weeks, step up to BID dosing for another 4-8 weeks. • If symptoms are controlled, it is advisable for most patients to titrate the PPI down to the lowest Proton pump effective dose and attempt once yearly to taper or stop PPI use. inhibitors (PPIs) PPI deprescribing resources are available on the Digestive Health Strategic Clinical Network website • There are no major differences in efficacy between PPIs. • Commonly prescribed agents: o Rabeprazole - 10 mg o Pantoprazole - 40 mg o Dexlansoprazole - 30 mg Omeprazole - 20 mg Lansoprazole - 30 mg Esomeprazole - 40 mg • See Table 1 for PPI pricing. Optional or while awaiting specialist consultation • Evidence: Shown to reduce dyspepsia symptoms in RCTs for IBS.<sup>2</sup> • 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 antiinflammatory effects.3 • Place in therapy: If patient has no response to PPI therapy, the Canadian Association of Gastroenterology guidelines suggest a trial of a TCA prior to a prokinetic based on superior evidence Tricyclic available.2 antidepressants • Adverse effects: Anticholinergic and antihistaminic (drowsiness/insomnia, xerostomia, palpitations, (TCAs) weight gain, constipation, urinary retention).3 • Use with caution in patients at risk of prolonged QT. • It can take 2-3 months to reach maximum effect.

• The lowest effective dose should be used.

· Dose should be gradually reduced if discontinuing.

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<sup>&</sup>lt;sup>2</sup> Canadian Association of Gastroenterology. (2017). ACG and CAG Clinical Guideline: Management of Dyspepsia. Retrieved from: https://www.cag-acg.org/images/publications/CAG\_CPG\_Dyspepsia\_AJG\_Aug2017.pdf

<sup>&</sup>lt;sup>3</sup> Lexicomp, Inc., Lexi-Drugs Online, Hudson, Ohio: UpToDate, Inc; 2013; [cited 27 Apr 2021].

# **Recommended Medications** • Nortriptyline - 10-25 mg qhs. Increase dose by 10-25 mg every 3-4 weeks based on response and Tricyclic tolerability. May require 25-75 mg/day. Often takes 2-3 months for peak effect. (\$20-60/month). antidepressants • Amitriptyline - 10-25 mg ghs. Increase dose by 10-25 mg every 3-4 weeks based on response and (TCAs) cont'd tolerability. May require 25-75 mg/day. Often takes 2-3 months for peak effect. (\$15-20/month). Designamine - 25 mg qhs. Increase based on response and tolerability (~\$25/month). • Evidence: Prokinetic agents may reduce dyspepsia symptoms for some patients, however there is minimal evidence to support use as a first line agent.2 • Mechanism of action: A prokinetic agent increases esophageal peristalsis, increases lower esophageal sphincter pressure, increases gastric motility and peristalsis, thus facilitating gastric emptying.2 • Place in therapy: For patients < 60 who have failed PPI and TCA, a prokinetic agent may be offered.2 • Prior to initiation, ensure patient has: Domperidone Normal QT interval (baseline ECG recommended) o No family history of sudden cardiac death o No current medications that increase the QT interval Withhold treatment if: o QTc is > 470 ms in males o QTc is > 450 ms in females • Starting dose is 5 mg TID AC, titrating up to 10 mg TID AC as a 2-4 week trial.

- Domperidone and/or TCA trials are appropriate within primary care, but not required prior to making a referral. If deemed clinically appropriate, these trials could occur while awaiting specialist consultation.
- There is insufficient data to recommend the routine use of bismuth, antacids, simethicone, misoprostol, anticholinergics, anti-spasmodics, SSRIs, herbal therapies, probiotics, or psychological therapies in dyspepsia. However, these therapies may benefit some patients and, thus, a trial with assessment of response may be reasonable, if clinically appropriate, and could be undertaken while awaiting specialist consultation.

Table 1 – PPI Pricing

PPI	Dosage	Estimated 90-day cost (2021) <sup>4</sup>	Coverage
Rabeprazole	10 mg	\$20	Covered by Blue Cross/non-insured health benefits
Pantoprazole	40 mg	\$35	Covered by Blue Cross/non-insured health benefits
Omeprazole	20 mg	\$35	Covered by Blue Cross/non-insured health benefits
Lansoprazole	30 mg	\$60	Covered by Blue Cross/non-insured health benefits
Dexlansoprazole	30 mg	\$250	Not covered by Blue Cross/non-insured health benefits
Esomeprazole	40 mg	\$210	Not covered by Blue Cross/non-insured health benefits

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

- If alarm features are identified
- If unsatisfactory response to management and/or pharmacological therapy
  - Note: Consider using an advice service before referring

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<sup>&</sup>lt;sup>4</sup> Maximum Allowable Cost (MAC) pricing exists for PPIs paid for by Alberta government sponsored drug programs. The drug plan will only pay the cost of rabeprazole 10 mg for lansoprazole 15 mg, omeprazole 10 mg and rabeprazole 10 mg, or the cost of pantoprazole magnesium 40 mg for all other covered PPIs. The patient will have to pay out of pocket for any difference between that price and the price of the prescribed PPI. See link for details.

• 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.

#### 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>5</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 <a href="Advice Options">Advice Options</a>) to convey your concerns.

### **PRIMERS**

#### Primer on Black Stool

- Possible causes of black stool
  - Upper GI bleeding
  - Slow right-sided colonic bleeding
  - o Epistaxis or hemoptysis with swallowed blood
- Melena is dark/black, sticky, tarry, and has a distinct odour
- · Patient history should include:
  - Any prior GI bleeds or ulcer disease
  - Taking ASA, NSAIDs, anticoagulants, antiplatelets, Pepto Bismol<sup>®</sup>, SSRIs, or iron supplements
  - o Significant consumption of black licorice
  - Significant alcohol history or hepatitis risk factors
  - Any other signs of bleeding (e.g. coffee ground emesis, hematemesis, hematochezia, or bright red blood per rectum)
  - Any dysphagia, abdominal pain, change in bowel movements, constitutional symptoms or signs/symptoms of significant blood loss
- Physical exam should include vitals (including postural if worried about GI bleeding) and a digital rectal exam for direct visualization of the stool to confirm, in addition to the remainder of the exam.
- Initial labs to consider include CBC, BUN (may be elevated with upper GI bleeding), INR.
- If the patient is actively bleeding, suggest calling GI on call and/or the ED for assessment, possible resuscitation, and possible endoscopic procedure.

#### **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.

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<sup>&</sup>lt;sup>5</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.

#### 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).
  - $_{\odot}$  However, if the ferritin is > 100  $\mu$ g/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.</li>

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).

#### **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 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 2019, by a multi-disciplinary team led by family physicians and gastroenterologists. For more information, contact the DHSCN at Digestivehealth.SCN@ahs.ca.

#### **Pathway Feedback and 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.



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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.

- Non-urgent gastroenterology electronic advice is available across the province via Alberta Netcare eReferral eConsult (responses are received within five calendar days). Visit the eReferral Learning Centre 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 two (2) hours.
  - In the Edmonton and North Zones by calling 1-844-633-2263 or visiting penconnectmd.com. This service is available from 9 a.m. to 6 p.m. Monday to Thursday and from 9 a.m. to 4 p.m. Friday (excluding stat holidays and Christmas break). Calls are returned within two business days.

#### References

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Moayyedi, P. M., Lacy, B. E., Andrews, C. N., Enns, R. A., Howden, C. W., & Vakil, N. (2017). ACG and CAG clinical guideline: management of dyspepsia. American Journal of Gastroenterology, 112(7), 988-1013. cagacg.org/images/publications/CAG\_CPG\_Dyspepsia\_AJG\_Aug2017.pdf

Dyspepsia resources from the Physician Learning Program for promoting patient education and self-management. albertaplp.ca/our-tools

- Poster #1 albertaplp.ca/our-tools?lightbox=dataItem-knrlhg2h1
- Poster #2 albertaplp.ca/our-tools?lightbox=dataItem-knrlhg2n2
- Gut Health Patient Journal 9c849905-3a37-465a-9612-7db1b9a0a69c.filesusr.com/ugd/7b74c1\_81f1695f08214a66bc339462c52cd011.pdf

Resources for appropriate PPI prescribing. Alberta Health Services - Digestive Health Strategic Clinical Network website.

- PPI guideline ahs.ca/assets/about/scn/ahs-scn-dh-ppi-guideline.pdf
- PPI co-decision making tool ahs.ca/assets/about/scn/ahs-scn-dh-ppi-decision-tool.pdf
- PPI patient poster ahs.ca/assets/about/scn/ahs-scn-dh-ppi-patient-poster.pdf

van Zanten, S. J. V., Flook, N., Chiba, N., Armstrong, D., Barkun, A., Bradette, M., ... & Sinclair, P. (2000). An evidence-based approach to the management of uninvestigated dyspepsia in the era of Helicobacter pylori. Canadian Medical Association Journal, 162(12 suppl), S3-S23. cmaj.ca/content/162/12 suppl/S3

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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			
PPI Depresribing Vignettes	<ul> <li>Predicting Dyspepsia Patient Resources to PPI - youtu.be/XT0MxefpNYQ</li> <li>Clinical Diagnosis of GERD - youtu.be/d_M8_S8lcyl</li> <li>How to Know if PPI is working - youtu.be/tttOBXPLR7U</li> <li>GERD Patients and PPI Doses - youtu.be/u15sPirE4EE</li> <li>How is Dyspepsia Defined? - youtu.be/F0E5rce-NSM</li> <li>Addressing Return of Symptoms - youtu.be/9008u9kyyDU</li> </ul>			

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# **PATIENT RESOURCES**

# Information

Description	Website
General information on dyspepsia (MyHealth.Alberta.ca)	myhealth.alberta.ca/health/pages/conditions.aspx?Hwid=tm6322
General information on dyspepsia (Canadian Digestive Health Foundation)	cdhf.ca/digestive-disorders/dyspepsia/what-is-dyspepsia/
General information on dyspepsia (UpToDate® – Beyond the Basics Patient information)	uptodate.com/contents/search Search: Dyspepsia
Information on domperidone (MyHealth.Alberta.ca)	myhealth.alberta.ca/Health/medications/Pages/conditions.aspx?hwid=fdb6090
Gut Health Patient Journal (Physician Learning Program)	9c849905-3a37-465a-9612- 7db1b9a0a69c.filesusr.com/ugd/7b74c1_81f1695f08214a66bc339462c52cd011.pdf
Dyspepsia Resources (Physician Learning Program)	albertaplp.ca/our-tools

# Services available

Description	Website
Services for patients with 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
Supports to quit smoking (Alberta Quits)	<u>albertaquits.ca</u>
Referral to a Registered Dietitian	<ul> <li>Visit Alberta Referral Directory and search for nutrition counselling.</li> <li>To learn more about programs and services offered in your zone, visit Nutrition Services.</li> <li>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.</li> <li>Patients can also complete the Health Link Dietitian Self-Referral Form.</li> </ul>

# **PATIENT PATHWAY**

• Dyspepsia patient pathway

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