Upper Gastrointestinal Cancer (Suspected)
Part 1

Effective Date: April 2, 2016

Disclaimer
The Family Practice Oncology Network (FPON) developed this clinical practice guideline following a documented guideline adaptation process. The recommendations in this guideline were adapted with permission from the BC Cancer Agency – Gastrointestinal Cancer Management Guidelines, and unless otherwise stated, are based primarily on evidence sourced and evaluated by the BC Cancer Agency, as well as expert clinical opinion. Additional sources of evidence were evaluated and cited as indicated. Recommendations were finalized following an external peer review. This guideline is intended to give guidance to practitioners on the clinical management of upper gastrointestinal cancer, and is not designed to replace clinical decision-making, or to be considered a standard of care.

SCOPE

Part 1 of this guideline outlines recommendations for the prevention, screening, diagnosis, treatment and follow-up of upper gastrointestinal (GI) disease and cancer in adults, including cancer of the esophagus and stomach. The primary audience for this guideline is community general practitioners providing first contact or primary health care.

KEY RECOMMENDATIONS

- Screening for upper GI cancer (endoscopy, imaging or tumour markers) is not recommended in asymptomatic patients
- Alarm symptoms (i.e. weight loss, dysphagia) and persistence of symptoms despite optimal treatment (4-6 weeks of proton pump inhibitors (PPIs)) should prompt a referral to a surgeon or gastroenterologist for urgent assessment
- Patients presenting with symptoms indicative of upper GI cancer should be referred urgently to a specialist
- Patients facing potentially life-limiting conditions may benefit from advance care planning

PREVENTION

The risk of esophageal cancer drops with reduced use of and exposure to tobacco and cigarette smoke.[1] Preventative measures include reducing alcohol intake, maintaining a healthy weight,

and increasing the consumption of dietary fruits and vegetables.[1,2,3] The risk of stomach cancer is reduced with diets that are low in salt, smoked, or pickled foods.[4,5,6]

Patients with *Helicobacter pylori* (*H. pylori*) should be treated with a combination of antibiotics and antacids.[7,8] After an adequate course of eradication, a follow-up urea breath test is recommended to ensure eradication is successful.

Patients with Barrett's esophagus should be treated to prevent or reduce reflux, and undergo regular surveillance endoscopy.[9,10] Long-term treatment with PPIs should be strongly considered in patients with Barrett's Esophagus.[9,11]

SCREENING

The incidence of esophageal cancer is low (6.51 cases per 100,000 in British Columbia (B.C.).[12] There are currently no recommended screening guidelines for esophageal cancer in asymptomatic patients.[9,13]

Screening for Barrett's esophagus ***is not recommended, but should be considered in patients with persistent reflux,*** or multiple risk factors associated with esophageal adenocarcinoma (*see Risk Factors)*.[9]

As the effectiveness of gastric screening is uncertain in the Western population, screening for gastric cancer is not recommended in asymptomatic patients.[14,15,16] The incidence of gastric cancer is low with 8.16 cases diagnosed in B.C., per 100,000 population.[17] Recent immigrants from high-risk regions (e.g. Korea, Japan, China), especially if there is a family history of gastric cancer in a first-degree relative, should be considered for endoscopy referral.[18,19] Refer patients with a suspected familial syndrome to the Hereditary Cancer Program (see *Resources*) at the BC Cancer Agency, for counseling and genetic testing where feasible.[14]

➢ *Risk Factors*

The incidence of stomach and esophageal cancer increases with increasing age.[20,21] Statistically, men are twice as likely than women to develop stomach cancer, and four times more likely to develop esophageal cancer.[20,21] Exposure to cigarette smoke and consumption of alcohol are additional risk factors.[1]

Risk factors associated with esophageal cancer include:[1,9]

- ≥ 50 years of age
- Chronic gastroesophageal reflux disease
- Smoking
- Alcohol consumption
- Elevated body mass index
- Intra-abdominal distribution of body fat

Risk factors for stomach cancer include:[4,14]

- Family history of stomach cancer
- Gastric polyps excluding fundic gland and inflammatory/hyperplastic polyps
- Birth in a country where gastric cancer is common (e.g. Japan)
- Previous partial gastrectomy
- *H. pylori*[7,8]
- Intestinal metaplasia[22]

DIAGNOSIS

The gold standard for diagnosis is endoscopy, however, an upper GI series may be considered as an adjunct investigation where endoscopy is not readily available. Patients referred for endoscopy may continue any acid suppression medication, including PPIs or H_2-receptor antagonists. Check with your local endoscopy office with respect to recommendations for other medications including anticoagulation, diabetes medication, etc.

- **Indications for Urgent Referral to a Specialist**
  The presence of the following ***alarm symptoms*** alone or in combination should prompt urgent referral to a specialist:
  - (Progressive) difficulty in swallowing
  - Pain on swallowing
  - Food obstructions
  - Early satiety
  - Persistent vomiting
  - Unexplained weight loss
  - Hematemesis/melena
  - Iron deficiency anemia

- **Consider Referral to a Specialist**
  The presence of the following symptoms should prompt a non-urgent referral to a specialist:
  - Age greater than 55 years with persistent or progression of heartburn (dyspepsia)
  - Persistent or progression of abdominal pain

- **Referral not Recommended**
  For patients less than 55 years of age with dyspepsia and no ***alarm symptoms***, a referral to a specialist is not recommended.

- **Investigations for Diagnosed Esophageal and Stomach Cancer**[9,14]
  Most of these investigations will be arranged by the consulting physician or primary care provider. It is preferable to have these tests ordered at the time of referral, so the results are available at the time of consultation.

CEA, CA 19-9	Baseline tumour markers are recommended at diagnosis.
Computerized tomography (CT) scan	Scan of chest, abdomen, and pelvis is recommended to assess the extent of local involvement and to exclude distant metastases.

STAGING

The TNM classification system is the international standard.[23] Refer to the BC Cancer Agency gastrointestinal guidelines (see *Resources*), for a link to staging diagrams and definitions for T, N, and M descriptors.

TREATMENT

Treatment is as recommended by the surgeon and the oncologist/BC Cancer Agency team.

- *Esophageal Cancer*
  - Early referral to a thoracic surgeon, medical or radiation oncologist is strongly recommended to plan optimal therapy[9]
  - Acid-reducing agents (i.e. PPIs) can reduce symptoms and heal erosive esophagitis; however, their effect on the progression to dysplasia or cancer is unclear[9,11,24]
  - Endoscopic therapy may be considered for patients with Barrett's Esophagus complicated by dysplasia or early esophageal cancer[9]
  - Surgically unresectable or metastatic disease presents an incurable situation and palliative measures are then appropriate

- *Stomach Cancer*
  - As relapse rates remain high, referral to a multidisciplinary team for consideration of perioperative or post-operative treatment is highly recommended
  - In metastatic disease, palliative resection or bypass of the primary tumour is reserved for those with significant bleeding or obstruction (radiation therapy may be considered for bleeding)[14]

- *Gastrointestinal Stromal Tumours*
  - Treatment is dependent on the stage of the tumour, the patient's risk profile, and the presence of metastases
  - The standard treatment is surgical resection
  - Chemotherapy may be prescribed before and may be continued after surgery in patients at risk of recurrent disease[25]
  - Palliative radiotherapy may be of benefit in unresectable disease where bleeding or pain is problematic[25]

- *Gastrointestinal Lymphoma*
  - The GI tract is a frequent site of involvement with lymphoma; it usually involves the stomach, less frequently the small intestine and rarely the colon or esophagus[26]
  - Management is dependent on type, stage and age
  - Resection of GI lymphoma is no longer recommended as earlier diagnosis and current management techniques have reduced the risk of hemorrhage or perforation. Resection is only recommended when it is necessary to establish a definite diagnosis, or to control the complications of hemorrhage or perforation[26]
  - There is a strong association between *H. pylori* and gastric lymphoma (mucosa associated lymphoid tissue type).[27] Antibiotics are recommended to eradicate *H. pylori* in all patients with gastric lymphoma (as primary treatment or after completion of planned chemotherapy and/or radiation) regardless of *H. pylori* testing status[26,27]

Recommend discussing patient preferences, prognosis and quality of life factors with the patient and family prior to endoscopic palliation for malignancy. Treatment on a clinical trial may be considered. Symptom management, best supportive care, and involvement of palliative care services are recommended as indicated by the patient's clinical status.

FOLLOW-UP

Patients who have completed treatment may be returned to the care of their primary care provider who will be asked to manage their follow-up care.

Follow-up care may include:

- Surveillance for recurrent disease or late effects of treatment when indicated
- Monitoring and treating complications and/or side effects
- Providing patient support
- Symptom management, best supportive care, and the involvement of palliative services

Patients with a life-limiting disease or illness may benefit from the development of an advance care plan (ACP) that incorporates the patient's values and personal goals, indicates potential outcomes, and outlines linkages with other health care professionals that would be involved in the care, and their expected roles. The ACP is an opportunity to also identify the patient's alternate substitute decision maker or legal health representative.

Below are general follow-up recommendations. ***Specific recommendations will be provided on the patient's discharge letter.*** At any time the patient and/or primary care provider may consult with the BC Cancer Agency for any follow-up questions or concerns.

- **General Follow-up for Esophageal and Stomach Cancer**[9,14]

Endoscopic surveillance	• Follow-up endoscopy is at the recommendation of the endoscopist
Radiation or surgery	• Patients who develop esophageal strictures as a result of radiation or surgery, may be referred for consideration for dilation or stenting[9]
Routine imaging or laboratory investigations	• There is no evidence that routine imaging or laboratory investigations are useful in detecting recurrences or metastases at a stage where they can be cured[9,14] • Early detection of asymptomatic metastases does not enhance survival[9,14] • Investigations should be performed based on the clinical presentation of a patient who is suspected of having recurrent or metastatic disease[9]
Nutritional	• In patients who have had distal/total gastrectomy, monitoring for B_{12} and iron deficiency is recommended

- **Follow-up for Lymphoma**

After treatment with antibiotics, patients should undergo repeat gastroscopy every six months for two years, then annually for three years.[26] Each time biopsies should be taken to examine for lymphoma and *H. pylori*.[26] If *H. pylori* persists one re-treatment should be tried.[26] If lymphoma persists or recurs more than six months after eradication of *H. pylori*, the patient should be treated with upper abdominal irradiation, or treated for drug-resistant *H. pylori*.[26] Patients should be encouraged to keep their immunizations up to date.[28]

Immunization Recommendations for Patients with Lymphoma[28]

Type of Immunization	When Should it be Given?
Influenza Vaccine	• Every year in autumn
Pneumococcal Vaccine	• At the time of diagnosis, ***if the pneumococcal vaccine can be given at least 2 weeks before initiation of anti-lymphoid cancer treatment.*** If that is not possible, delay until at least 6 months after completion of all lymphoid

	cancer treatment and any other immunosuppressive treatment. Repeat again once 5 years later.
Tetanus/Diphtheria	• Every 10 years.
Meningococcal C Conjugate (MCC) and, 2 weeks later, Meningococcal Quadrivalent Conjugate (A,C,Y,W-135) and Haemophilus Influenzae Type b (HiB) Vaccine	• If the spleen is to be or was removed or treated with radiation, give all 3 at least 2 weeks before splenectomy if possible, or if spleen is already removed, give as soon as possible after splenectomy. Repeat Men-P-ACYW every 5 years. (Note: these vaccines are given free of charge at the local Health Unit Immunization Clinic for patients who have splenectomy).
Polio Vaccine	• Oral polio vaccine should never be taken by patients with lymphoid cancer. It has been replaced by inactivated polio vaccine, which is safe for patients with lymphoid cancer.
Measles (live virus) Mumps (live virus) Rubella (live virus) Yellow Fever (live virus)	• ***Never*** (Exception: see stem cell transplant guidelines, Appendix III - Table 4 of the source document listed below).
Varicella Zoster (chicken pox) Vaccine (Zostavax™ - live attenuated viral)	• At the time of diagnosis, ***if the Zostavax™ can be given at least 2 weeks before initiation of anti-lymphoid cancer treatment***. If that is not possible, delay until at least 6 months after completion of all lymphoid cancer treatment and any other immunosuppressive treatment.

Source: BC Cancer Agency – Cancer Management Guidelines – Lymphoma, Chronic Leukemia, Myeloma – Appendices – Appendix III – Immunizations for Patients with Lymphoma, Hodgkin Lymphoma, Myeloma and Leukemia, available at http://www.bccancer.bc.ca/health-professionals/professional-resources/cancer-management-guidelines/lymphoma-chronic-leukemia-myeloma/appendices

For Travel to Developing Countries: Less than 4 weeks: No immunization; Greater than 4 weeks: Hepatitis A; Inactivated typhoid injectable vaccine (Note: oral typhoid vaccine is a live bacteria and should not be given); Hepatitis B.

RESOURCES

➢ REFERENCES

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➢ PHYSICIAN AND PATIENT RESOURCES

- **BC Cancer Agency**, www.bccancer.bc.ca
  - Gastrointestinal Clinical Practice Guidelines www.bccancer.bc.ca/HPI/CancerManagementGuidelines/Gastrointestinal/default.htm
  - Hereditary Cancer Program, for referrals: 604-877-6000 (ext. 672198), www.screeningbc.ca/Hereditary/ForHealthProfessionals/ReferralProcess.htm
  - *Carcinoma of the Esophagus/Cardia (Esophagogastric Junction) Staging Diagram,* is available at www.bccancer.bc.ca/health-professionals/professional-resources/cancer-management-guidelines/gastrointestinal/esophageal-esophagogastric-junction - Staging
- **BC Guidelines**, BCGuidelines.ca
  - *Dyspepsia with or without Helicobacter pylori Infection – Clinical Approach in Adults – December 2009*
  - *Gastroesophageal Reflux Disease – Clinical Approach in Adults – January 2009*
- **British Columbia Ministry of Health**
  - *My Voice – Expressing my Wishes for Future Health Care Treatment – Advance Care Planning Guide,* available at www.health.gov.bc.ca/library/publications/year/2013/MyVoice-AdvanceCarePlanningGuide.pdf
  - Provincial advance care planning resources are available at www.gov.bc.ca/advancecare
- **HealthLink BC**, www.healthlinkbc.ca , 8-1-1 (toll free in B.C.), 7-1-1 TTY (Deaf and hearing-impaired)
- **ImmunizeBC,** www.immunizebc.ca
  - Public Health Unit Immunization Clinics, www.immunizebc.ca/finder

➢ ABBREVIATIONS

ACP – advance care plan
CA 19-9 – cancer antigen 19-9
CBC – complete blood count
CEA – carcinoembryonic antigen
CT – computerized tomography
GI – gastrointestinal
HiB – Haemophilus Influenzae Type b
LDH – lactate dehydrogenase
MCC - Meningococcal C Conjugate
Men-P-ACYW - Meningococcal Quadrivalent Conjugate (A,C,Y,W-135)
PPIs – proton pump inhibitors
TSH – thyroid stimulating hormone

➢ ASSOCIATED DOCUMENTS

The following documents accompany this guideline:

- Family Practice Oncology Network – Upper Gastrointestinal Cancer (Suspected) – Part 2 (available at www.bccancer.bc.ca/health-professionals/networks/family-practice-oncology-network/guidelines-protocols).

➢ **RENEWAL DATE**

This guideline will be reviewed 3-5 years following the effective date, unless changes in clinical evidence warrant an earlier revision.