Upper Gastrointestinal Cancer – Part 2

Effective Date: X, 2025

SCOPE

Part 2 of this 2-part guideline outlines recommendations for the prevention, screening, diagnosis, management and follow-up of upper gastrointestinal (GI) cancers, including pancreatic cancer, neuroendocrine tumours (NETs) of the pancreas and duodenum, and cancer of the extrahepatic biliary tract. The primary audience for this guideline is family physicians (FPs) and nurse practitioners (NPs) providing first contact or primary health care, as well as general practitioners in oncology (GPOs) and emergency room physicians.

METHODOLOGY

The development of this guideline was sponsored by BC Cancer, Provincial Health Services Organization (PHSA). The recommendations were developed by a working group including family physicians/nurse practitioner (with representation from rural, urban, and Indigenous clinical practice), a general practitioner in oncology, medical oncology, gastroenterology, surgery and radiology.

The development of the recommendations in this guideline was through careful consideration of the clinical evidence, as well as the application of clinical expertise including a peer review process, in order to arrive at consensus for each recommendation. A systematic and reproducible approach to the evidence was used including a rapid review of clinical evidence from 2016 to November/December 2024. The following databases were searched: Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Ovid MEDLINE(R) and Embase. For a detailed list of the research questions applied, search terms used, and the results including a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) table and evidence summary for this rapid review, please contact the Primary Care Program – Family Practice Oncology Network at BC Cancer.

KEY RECOMMENDATIONS

- Screening in the average risk population for upper GI cancers, including extrahepatic biliary and pancreatic cancers is not recommended, but should be considered for certain high-risk groups.[1,2,3] Details on the selection of these patients are included within the guideline (see *Screening*).
- Pancreatic cancer is also associated with some inherited cancer syndromes.[4,5,6]

Consider referral to the BC Cancer Hereditary Cancer Program (HCP) (see *Resources*) for asymptomatic patients with a family history of or suspicious for a germline variant in *LKB1*/*STK11* (Peutz-Jeghers syndrome), *CDKN2A* (familial atypical multiple mole melanoma syndrome), *BRCA1*, *BRCA2*, *ATM*, *PALB2*, *MLH1*, *MSH2*, *MSH6*, *EPCAM*, or *TP53*.

- Painless jaundice should be considered pancreatic or biliary cancer until proven otherwise
- If pancreatic cancer is suspected investigations should be expedited
- A person should be ***referred urgently*** to a specialist if they have obstructive jaundice or an upper abdominal mass
- Offer mainstream genetic testing to all patients with pancreatic cancer or pancreatic neuroendocrine tumours (pNETs)
- If genetic testing is deferred in affected patients, DNA banking should be considered if the disease is rapidly progressing
- There is no evidence that routine imaging or laboratory investigations including Ca 19-9 are useful in detecting recurrent metastatic disease[7]
- Patients facing potentially life-limiting conditions may benefit from advance care planning (see *Resources*)

PREVENTION

The risk of many of these cancers increases with smoking.[8,9,10,11] Diabetes, chronic pancreatitis, and excessive alcohol consumption are associated with pancreatic cancer.[8,10,11] As with many other cancers, preventative measures include reducing alcohol intake, maintaining a healthy weight, exercise and smoking cessation.[12]

SCREENING

The incidence of pancreatic and bile duct cancer is low. The age-standardized incidence rate for pancreatic cancer in British Columbia (B.C.) (15.4 for males and 12.3 for females, per 100,000).[13] There are currently no recommended screening guidelines for pancreatic or bile duct cancer in asymptomatic patients who are not at high risk. Screening with endoscopic ultrasound (EUS) or magnetic resonance imaging (MRI) may be **indicated in patients at high risk** for pancreatic cancer (see *Hereditary and Familial Pancreatic Cancer*.)[1,2,3,4,11,14,15,16]

Background, Risk Factors and Indications for Referral

Pancreatic Cancer

Solid pancreatic cancers are of exocrine or endocrine origin. Exocrine tumors are the most common type of pancreatic cancer, and roughly 92% of these are adenocarcinomas.[17] Neuroendocrine neoplasms amount to approximately 7%.[17]

Pancreatic exocrine carcinomas are associated with poor prognosis, and patients are often asymptomatic until late in the course of the disease. Ampullary cancers have a better prognosis than pancreatic adenocarcinoma. The incidence of pancreatic cancer increases significantly from the age of 60.[13]

Neuroendocrine tumours arise from the diffuse neuroendocrine system of the gut. They are rare and include neuroendocrine tumours of the stomach, duodenum and pancreas. The mean annual incidence rate for pNETs has been reported as 0.25 per 100,000 persons, with the incidence increasing significantly over the past two decades.[17]

Exocrine Pancreatic Cancer

Non-hereditary risk factors include smoking, diabetes mellitus, obesity, and a possible association with *Helicobacter pylori* (*H. pylori*) infection.[11,18,19,20,21]

Endocrine Pancreatic Cancer (Pancreatic Neuroendocrine Tumours (pNETs))

pNETs remain rare and can occur at any age and in both sexes equally.[17]

Hereditary and Familial Pancreatic Cancer

In BC, healthcare providers outside of the BC Cancer HCP can order multi-gene hereditary cancer panel testing through the BC Cancer, Cancer Genetics and Genomics Laboratory, for eligible patients and disclose the results to their patients. This approach, known as "mainstreamed" hereditary cancer testing, significantly shortens time to results, reduces burden and barriers to patients, and increases genetic testing access and targeted treatment options for a more diverse patient population when compared to traditional referrals to the HCP for pre-test genetic counselling and testing (see *Resources)*.

There are hereditary as well as familial pancreatic cancers, and both are eligible for genetic testing. Based on a study of pathogenic gene variants in patients diagnosed with pancreatic ductal adenocarcinoma in the province of British Columbia, we can expect approximately 12% of patients to have actionable cancer susceptibility findings.[5]

Hereditary pancreatic cancer has a genetic component. Familial pancreatic cancer is defined by the presence of at least 1 first-degree relative with pancreatic cancer who also has a first-degree relative with pancreatic cancer (familial pancreatic cancer kindred).

- Patients with the following indications should be screened for pancreatic cancer (see *Resources*):[4]
    - Anyone with a germline *CDKN2A* mutation
    - Anyone with a germline *STK11* mutation (Peutz-Jeghers syndrome)
    - Anyone with a germline mutation in *BRCA1, BRCA2, ATM, PALB2, MLH1, MSH2, MSH6, EPCAM, TP53* **AND** a first-degree (parent, sibling, or child) or second-degree relative who is affected with pancreatic cancer
- Patients with pancreatic cancer (see *Resources*):
    - Offer mainstream hereditary cancer genetic testing to all patients with pancreatic

cancer or pNETs

- If genetic testing is deferred in affected patients or in patients where there is a high degree of suspicion of pancreatic cancer, DNA banking should be considered if disease is rapidly progressing. Refer to the *Resources* section for program information and a referral form

- Unaffected patients with a family history of pancreatic cancer (see *Resources*)
    - HCP referral for testing can be offered to a person with a family history of pancreatic cancer. Refer to the *Resources* section for the HCP guidelines.

Hereditary Pancreatic Neuroendocrine Tumours

Pancreatic neoplasms can occur as part of four hereditary conditions:[22]

- Multiple endocrine neoplasia type 1 (MEN1)
- von Hippel-Lindau disease (VHL)
- Neurofibromatosis type 1 (NF-1; von Recklinghausen disease)
- Tuberous sclerosis complex (TSC)

The most common association of pNETs is with MEN1.[22]

Indications for Referral for Hereditary NETs

Patients with any of the above syndromes should be referred for consultation with the HCP. Patients can also be referred to the mainstream testing referral pathway indicating that the patient is suspected to have one of the four hereditary conditions above, where both positive or uninformative testing will result in an HCP referral.

Cystic Neoplasms of the Pancreas

Pancreatic cysts are common incidental findings on imaging with the majority considered benign. For example, a cystic lesion in a patient with previous pancreatitis will most likely be a pancreatic pseudocyst. These will be stable or decrease in size over time excluding the need for extended follow-up or biopsy.

Cystic neoplasms of the pancreas, however, exist with the most common being intraductal pancreatic mucinous neoplasm (IPMN). There are 3 subtypes of IPMNs: main duct type (MD-IPMN), branch duct type (BD-IPMN) and mixed (MT-IPMN). All 3 subtypes are considered neoplastic, and MD-IPMN and MT-IPMN are considered high-risk, which require more aggressive intervention.

Indications for Referral for Cystic Neoplasms of the Pancreas

If a cyst is incidentally found on ultrasound, then a dedicated computerized tomography (CT) or

MRI/magnetic resonance cholangiopancreatography (MRCP) of the pancreas is usually recommended to further characterize the lesion. The presence of worrisome or high-risk features will be assessed by the radiologists who will then make appropriate recommendations depending on the findings. In the presence of high-risk features referral to an appropriate specialists will be suggested. In the absence of high-risk features follow up imaging to ensure the benign nature of the cyst will be suggested.

Bile Duct Cancer

Cholangiocarcinoma is a malignancy arising from the biliary ductal epithelium. It can arise in intra-hepatic or extra-hepatic biliary ducts. Extrahepatic lesions may present as obstructive jaundice, while intrahepatic lesions may be mistaken for hepatocellular carcinoma or metastatic disease from an unknown primary site. Over 90% of bile duct carcinomas are adenocarcinomas.[23] The incidence of bile duct cancer peaks in the seventh decade, and occurs slightly more frequently in men than in women.[23] Prevalence is higher in South East Asia, and may be related to chronic parasitic infection of the liver (i.e., liver flukes - *Clonorchis sinensis* and *Opisthorchis viverrini)*.[23]

Risk Factors for Biliary Tract Cancer

Risk factors for bile duct cancer in Western populations include:

- Inflammatory bowel disease[24]
- Primary sclerosing cholangitis[23]
- Congenital choledochal cysts[23]
- Possible exposure to environmental toxins (i.e., dioxins, asbestos, nitrosamines, Thorotrast)[23,25]

The incidence of cholangiocarcinoma in patients with underlying primary sclerosing cholangitis is 8-40%.[23]

Hereditary Biliary Tract Cancer

Of biliary tract cancers, 8-12% are associated with germline pathogenic variants, most commonly ***BRCA1/BRCA2*** (others may include *PALB2, APC, MLH1, MSH2, MSH6, BAP1, ATM, RAD51D*).[26,27,28]

Indications for HCP Referral for Biliary Tract Cancer

The following biliary tract cancer patients should be referred to the HCP:

- Patients with biliary tract cancer (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, gallbladder carcinoma), ***AND*** one or more of the following:

- Diagnosis ≤ age 50
- Personal history of multiple primary cancers (excluding non-melanoma skin cancer (may include sebaceous carcinoma))
- Ashkenazi Jewish ancestry – or provide information on the Jewish BRCA testing program through BRCAinBC (see *Resources).*

DIAGNOSIS

Diagnosis is difficult as many of the symptoms of these cancers are non-specific and can mimic benign or other malignant conditions (e.g., ovarian cancer, gastric cancer, primary peritoneal cancer).

Signs and Symptoms

In pancreatic cancer, the two most common presenting symptoms are abdominal pain and jaundice.[29] Painless jaundice is considered to be pancreatic or biliary cancer until proven otherwise. Persistent abdominal pain and ongoing weight loss should prompt appropriate investigations. Other non-specific symptoms include:

- Fatigue, anorexia, weight loss, dull epigastric pain, early satiety[29]
- Abdominal pain, back pain, or weight loss are usually signs of late-stage disease

NETs present as functional or nonfunctional tumours and are often found incidentally. The majority of tumours are non-functional.

Functional tumours are characterized by excess hormone production resulting in clinical syndromes and are named according to the hypersecreted hormone. Some tumours can cause carcinoid syndrome, which may present as abdominal pain, wheezing, flushing, diarrhea, rapid heartbeat, and facial skin lesions. Insulinomas produce excess insulin and can present as hypoglycemia. Gastrinomas cause hypersecretion of gastrin and can present as peptic ulcer disease.

Non-functional tumours *are not* associated with excess hormone production and present due to tumour bulk. The patient may present with intermittent abdominal discomfort for months or years, often interpreted to be a functional disorder.

Investigations

While the incidence of these cancers is low, it is important to maintain a high index of suspicion in patients with persistent symptoms. If cancer is suspected imaging investigations should be expedited. Patients presenting with **painless jaundice** should have **urgent imaging** within 1 week.

- Initial cancer investigations should include abdominal imaging:
    - multi-phasic pancreatic computed tomography (CT) abdomen/pelvis may be considered as the initial imaging modality

    - ultrasound of the abdomen may be considered when CT is unavailable
- Initial laboratory investigations should include CBC, creatinine, and liver function tests, with the timing dependent on the level of clinical suspicion
- If there is a high degree of suspicion (e.g., painless jaundice), CA 19-9 serum antigen could be ordered.[7]CA 19-9 is not specific for these pancreatic cancer, and therefore there could be other causes.[7]

Urgent Referral to a Specialist

A person should be ***referred urgently*** to a specialist if they have:

- obstructive jaundice
- an upper abdominal mass

Equity and Access

Consider regional limitations in accessing services and individual patient barriers to care. Consider the applicability of a trauma-informed approach for patients who may require additional support in order to feel safe, or to develop trusting relationships with healthcare services or providers.[30] A trauma-informed approach may enable practitioners to work in partnership with patients and to empower them to make choices about their health and wellbeing.[30]

Provincial Language Services (PHSA) provides language services to health authorities, family practice practitioners, specialist offices, and other allied health professionals in B.C. Interpreting services are intended to reduce or eliminate language barriers wherever possible and are designed to enable two-way communication that optimizes the delivery of safe and equitable care. Services are provided in more than 200 languages and are available 24/7 at no charge to patients and/or their families. Sign language interpreting, intervenor and Communication Access Realtime Translation (CART) services are available for deaf, deaf-blind and hard-of-hearing patients when accessing most healthcare services in B.C. (see *Resources*).

Indigenous Patient Navigators

Indigenous patient navigators (IPNs) are available at PHSA to support culturally safe experiences for Indigenous Peoples. IPNs collaborate with Indigenous Peoples and their families to ensure access to high-quality care that is trauma-informed, culturally safe and free of racism and discrimination. For more information about IPNs or for information on how patients can self-refer for their services, refer to the *Resources* section.

STAGING

The TNM (tumour-node-metastasis) classification system is the international standard.[31] Refer to BC Cancer for a link to staging diagrams and definitions for T, N, and M descriptors (see *Resources*).

TREATMENT

Treatment will be recommended by the surgeon and the oncologist/BC Cancer team.

- ***Pancreatic Cancer***

Surgical treatment offers the only potential cure for resectable carcinoma of the pancreas. Neoadjuvant or adjuvant therapy may be offered. Surgery, chemotherapy, or radiation therapy may be indicated for palliation. Early integration of a palliative approach to care with a referral to the pain and symptom management/palliative care team could be considered as evidence indicates that patients live longer with this approach, have a better quality of life and less depressive symptoms.[32,33]

- ***Neuroendocrine Tumours***

A multidisciplinary approach to the treatment of NETs is recommended. Patients with resectable NETs can expect a good intermediate term prognosis. Resectable NETs are managed by endoscopic or surgical resection. A variety of systemic therapies are also available and will be determined by the multidisciplinary team. Unresectable metastatic disease may benefit from debulking for palliation. For gastrin-producing NETs, proton pump inhibitors (PPIs) should be used to control acid-related symptoms.

- ***Biliary Tract Cancer***

Surgery of resectable tumours is the only potentially curative treatment available. Adjuvant chemotherapy is considered in these patients and should be referred to medical oncology for assessment. Patients with advanced disease may achieve a prolonged period of palliation through surgical, endoscopic and radiological drainage procedures. In a palliative setting, systemic therapy and/or radiation therapy may provide a benefit.

FOLLOW-UP

At the discretion and direction of the oncologist, the patient may be discharged to the primary care provider.

Follow-up care may include the following:

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

- Consideration for referral to supportive care services as appropriate (see *Resources)*

There is currently no evidence that routine imaging or laboratory investigations – including Ca 19-9 – are useful in detecting recurrent metastatic disease, and early detection of asymptomatic metastases does not enhance survival. Investigations should be performed based on the clinical presentation of a patient who is suspected of having recurrent or metastatic disease.

At the time of patient discharge, the BC Cancer team provides specific recommendations for the primary care provider for ongoing patient care. Refer to the ***patient's discharge letter*** for guidance on ongoing care. The patient and/or primary care provider may consult with BC Cancer for any follow-up questions or concerns.

Patients with a life-limiting disease or illness may benefit from the development of an advance care plan (ACP) (see *Resources*) that incorporates the patient's values and personal goals, indicates potential outcomes, and outlines linkages with other healthcare 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.

RESOURCES

➢ REFERENCES

Placeholder

➢ HEALTHCARE PROVIDER AND PATIENT RESOURCES

- **BC Cancer**
    - Hereditary Cancer Program, referrals, Vancouver: 604-877-6000 (ext. 672198), Abbotsford: 604-851-4710 local 645174
        - Fraser Health Authority, **(F) 604.851.4720**, (T) 604.851.4710 local 645174
        - All other BC/Yukon, **(F) 604.707.5931**, (T) 604.877.6000 local 672198
    - HCP referral form, available at www.bccancer.bc.ca/coping-and-support-site/Documents/Hereditary%20Cancer%20Program/HCP_Form-ReferralForm.pdf
    - HCP Mainstream Genetic Testing: information and requisition, available at https://cancergeneticslab.ca/genes/hereditary-cancer-panel/
    - Pancreatic Cancer Screening in BC For Individuals at Increased Risk: FAQ, available at http://www.bccancer.bc.ca/coping-and-support-site/Documents/Hereditary%20Cancer%20Program/HCP_GuidelinesManuals_FamilialPancreaticCancer.pdf
    - **Gastrointestinal Tumour Group Clinical Pathways**, http://www.bccancer.bc.ca/health-professionals/professional-resources/clinical-care-pathways/tumour-specific-pathways
- **BC Centre for Disease Control**
    - Guidelines for the immunization of individuals at high risk for vaccine-preventable diseases, available at www.bccdc.ca/health-professionals/clinical-resources/communicable-

disease-control-manual/immunization/immunization-of-special-populations

- **Canadian Cancer Society**
  - Supportive care (physical, practical, emotional and spiritual) resources:
    - Supportive care for pancreatic cancer, available at https://cancer.ca/en/cancer-information/cancer-types/pancreatic/supportive-care
    - Supportive care for biliary tract cancers, available at https://cancer.ca/en/cancer-information/cancer-types/biliary-tract/supportive-care
    - Supportive care for neuroendocrine tumours (NETs), available at https://cancer.ca/en/cancer-information/cancer-types/neuroendocrine-tumours/supportive-care
- **Canadian Cholangiocarcinoma Collaborative**, www.cholangio.ca
- **Cholangio-Hepatocellular Carcinoma Canada**, www.mychcc.ca
- **Trauma-Informed Care Resources**
  - Trauma-Informed Practice (TIP) – Resources, available at www2.gov.bc.ca/gov/content/health/managing-your-health/mental-health-substance-use/child-teen-mental-health/trauma-informed-practice-resources
  - *Trauma-Informed Approaches in the Context of Cancer Care in Canada and the United States: A Scoping Review*, available at https://pmc.ncbi.nlm.nih.gov/articles/PMC10594848/
- **British Columbia Ministry of Health**
  - *My Voice–Expressing My Wishes for Future Health Care Treatment–Advance Care Planning Guide*, available at www2.gov.bc.ca/assets/gov/people/seniors/health-safety/pdf/myvoice-advancecareplanningguide.pdf
  - Provincial advance care planning resources, available at www.gov.bc.ca/advancecare
- **HealthLink BC**, www.healthlinkbc.ca, 8-1-1 (toll free in B.C.), 7-1-1 (deaf and hearing-impaired)
  - Recommended vaccines for adults, including patients with immunocompromising conditions, available at www.healthlinkbc.ca/health-library/immunizations/schedules/recommended-vaccines-adults
  - Find health care near you, access virtual health services, learn about primary care in British Columbia, or register for a family doctor or nurse practitioner, www.healthlinkbc.ca/find-care
- **Indigenous Cancer Control**, Improving Cancer Control for Indigenous People, www.bccancer.bc.ca/our-services/services/indigenous-cancer-control
  - Indigenous patient navigators (IPNs) by PHSA site – information is available at www.phsa.ca/our-services/programs-services/indigenous-health#Programs--&--services
  - IPNs at BC Cancer – information is available at www.bccancer.bc.ca/our-services/services/indigenous-cancer-control#Indigenous--Patient--Navigators
- **Pancreas Centre BC**, https://pancreascentrebc.ca/home
  - Familial Pancreatic Cancer Program (FPCP), https://pancreascentrebc.ca/research#panel-5

- **Patient Resources**
  - BC Cancer – Supportive Care, available at www.bccancer.bc.ca/our-services/services/supportive-care
    - Nutrition Services, www.bccancer.bc.ca/our-services/services/supportive-care/nutrition
  - BRCAinBC – BRCA genetic testing program for any adult of Jewish ancestry living in British Columbia and the Yukon, available at https://brcainbc.ca/free-jewish-brca-testing-program
  - Canadian Association of Gastroenterology – Other GI Organizations
    - Canadian Nutrition Society/la Société canadienne de nutrition (CNS/SCN), available at https://cns-scn.ca
  - Inspire Health – Supportive Cancer Care, available at https://inspirehealth.ca
  - My Gut Feeling – Stomach Cancer Foundation of Canada, available at www.mygutfeeling.ca
- **Pathways™**
  - Medical Care Directory, available at https://pathwaysmedicalcare.ca
  - Community Service Directory, available at https://pathwaysbc.ca/community
- **Primary Care Networks**, information is available at https://fpscbc.ca/what-we-do/system-change/primarycare-networks
- **Provincial Health Services Authority**
  - Indigenous Health, Patient Navigators, information available at www.phsa.ca/our-services/programs-services/indigenous-health
  - Provincial Language Service, (T) 604-297-8400, 1-877-BC Talks (228-2557) (toll free in B.C.), (F) 604-297-9304, available at www.phsa.ca/health-professionals/professional-resources/language-services
- **University of British Columbia, Continuing Professional Development (UBC-CPD)**
  - *Management of Helicobacter pylori in 2023: who should be tested, treated, and how*, available at https://thischangedmypractice.com/management-of-helicobacter-pylori/

➢ ABBREVIATIONS

ACP – advance care plan
B.C. – British Columbia
BD-IPMN – branch duct type - intraductal pancreatic mucinous neoplasm
CART – Communication Access Realtime Translation
CBC – complete blood count
CT – computerized tomography
EUS – endoscopic ultrasound
FAQ – frequently asked questions
FPs – family physicians

GI – gastrointestinal
GPOs – general practitioners in oncology
H. pylori – *Helicobacter pylori*
HCP – Hereditary Cancer Program
HNPCC – hereditary nonpolyposis colorectal cancer
IPMN – intraductal pancreatic mucinous neoplasm
IPNs – Indigenous patient navigators
MALT – mucosa-associated lymphoid tissue type
MEN1 – Multiple endocrine neoplasia type 1
MRCP – magnetic resonance cholangiopancreatography
MRI – magnetic resonance imaging
MD-IPMN – main duct type - intraductal pancreatic mucinous neoplasm
MT-IPMN – mixed duct type - intraductal pancreatic mucinous neoplasm
NF-1 – Neurofibromatosis type 1
NPs – nurse practitioners
PHSA – Provincial Health Services Authority
PPIs – proton pump inhibitors
PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
TIP – trauma-informed practice
TNM – tumour-node-metastasis
TSC – Tuberous sclerosis complex
UBC-CPD – University of British Columbia, Continuing Professional Development
VHL – von Hippel-Lindau disease
XR – x-ray

➢ ASSOCIATED DOCUMENTS

The following document accompanies this guideline:

- Upper Gastrointestinal Cancer – Part 1, available at www.bccancer.bc.ca/health-professionals/networks/family-practice-oncology-network#Guidelines--and--Resources

DISCLAIMER

This guideline is intended to provide guidance to primary healthcare providers in B.C. on the clinical management of upper gastrointestinal cancer. This guideline is not designed to replace professional judgment of a healthcare professional and is not to be considered a standard of care.

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