

PATHWAY PRIMER

"Head and neck cancers are a heterogeneous group of tumors, consisting predominantly of squamous cell cancers of the lip, mouth, pharynx, larynx and cervical esophagus, adenocarcinomas of the major and minor salivary glands and thyroid and occasional tumours of connective tissue origin." (bccancer.bc.ca,2023) [21]

Head and neck squamous cell carcinomas (HNSCC's) develop from the mucosal epithelium in the oral cavity, pharynx, and larynx, and are the most common malignancies of the head and neck. HNSCC is the sixth most common cancer worldwide, with 890,000 new cases and 450,000 deaths in 2018. The incidence of HNSCC continues to rise and is anticipated to increase by 30% (1.08 million new cases annually) by 2030. (GLOBOCAN 2023) [9, 22]

The main risk factors for HNSCC are the use of tobacco products, excessive alcohol consumption and HPV infections.

Oropharyngeal HNSCC's are comprised of two distinct clinical entities: HPV-positive and HPV-negative HNSCC.

- HPV-negative HNSCCs of the oral cavity, hypopharynx, larynx, and some oropharyngeal are primarily associated with tobacco and alcohol use. [1]
- HPV-positive HPV-positive HNSCC's typically arise from the tonsil, base of tongue, palate, or pharyngeal walls (oropharyngeal).
 - They are associated with a younger age at diagnosis, lesser (or no) smoking history, and a better overall prognosis compared with HPV-negative HNSCC.
 - HPV-positive HNSCC commonly presents with painless neck adenopathy in the absence of other symptoms related to the oropharyngeal primary.
 - The incidence of HPV- positive HNSCC, primarily oropharyngeal squamous cell carcinoma (OPSCC), is rising. [1]

There is no screening tool for HNSCC. Physical examination is the primary approach for early detection. **Most** patients present with advanced-stage HNSCC.

- Earlier presentations or pre-malignant lesions present as leukoplakia (white patches) or erythroplakia (red patches) in the oral cavity. HPV-positive HNSCC commonly presents with a persistently enlarging, painless neck mass.
- Adults with a persistent, enlarging neck mass in the absence of other head and neck symptoms should be considered high-risk for HPV-associated oropharyngeal cancer, and should be urgently referred to ENT/ Otolaryngology -Head and Neck Surgery. [1,3]

EXPANDED DETAILS

1. History: Risk Factors

Age (over 40 years)

- Median age of diagnosis for non-virally associated (HPV-negative and EBV-negative) HNSCC is 66 years. [9]
- Median age of diagnosis for HPV-associated oropharyngeal cancer and EBV-associated nasopharyngeal cancer is ~53 years and ~50 years, respectively. [9]

Tobacco

- The risk of HNSCC in smokers is approximately ten times higher than that of never-smokers. [12]
- 70–80% of new HNSCC diagnoses are associated with tobacco and alcohol use.
- Cessation does lower the risk of developing HNSCC, but it is not certain to what degree. There is data to suggest that the risk returns to that of a never smoker after about 20 years of stopping. [12]

Alcohol consumption

- Moderate to heavy alcohol consumption is associated with higher risks of certain head and neck cancers.
 - Moderate alcohol drinking is defined as limiting consumption to 2 drinks or less in a day for men and 1 drink or less in a day for women.
 - Heavy alcohol drinking is defined as having 4 or more drinks on any day or 8 or more drinks per week for women and 5 or more drinks on any day or 15 or more drinks per week for men). [19]
- Moderate drinkers have 1.8-fold higher risk of oral cavity and pharynx cancers and 1.4-fold higher risk of larynx cancers than non-drinkers.
- Heavy drinkers have 5-fold higher risks of oral cavity and pharynx cancers. 2.6-fold higher risks of larynx cancers. [12]
- The risks of these cancers are substantially higher among persons who consume this amount of alcohol AND use tobacco. [12]

Betel nut, paan, pituri

- Betel quid (paan) chewing is common in many parts of Asia and in migrant Asian populations around the world, with an estimated global usage of 600 million to 1.2 billion people. [4]
- It has a psychostimulatory effect. [4]
- Betel quid consists of a mixture of areca nut (which alone is carcinogenic), slaked lime, and betel leaf, that can may be combined with tobacco, sweeteners, and/or spices. [4]
- Regional variations include mawa, naswar, khaini, and zarda. There are many betel quid substitutes (e.g., gutka, pan masala) that are widely available. [4]

Geography (i.e., Southeast Asia)

- In East and southeast Asia, EBV-associated nasopharyngeal carcinoma is endemic. [9]
- An adult, who lived in Southeast or East Asia, presenting with a new neck mass should receive a complete head and neck evaluation with close attention to the nasopharynx.
- Note if there is history of Betel quid/ pituri use.[4]

Sex (assigned male)

- The assigned male to assigned female ratio for HPV-positive HNSCC incidence ranges from **three to six** times, due to higher rates of persistent oropharyngeal HPV infection in assigned males despite similar prevalence of anogenital HPV infection. [10,17]
- The time to oral infection clearance is longer in assigned males than in assigned females, and smoking may increase oral HPV persistence in assigned males.[10,17]
- A higher immune response is present after infection in assigned females than assigned males, which could contribute to the assigned male predominance of oral HPV infection. [10,17]

UV / sunlight for mucosa (red part) of lip

• Excessive exposure of UV light to lips increases risk of developing cancer which (considered an oral cancer). Tobacco uses in any form increases this risk. [20]

Immunosuppression

There are risks associated with immunosuppression that may make a patient more susceptible to head and neck cancers.

- Increased susceptibility to oncogenic viruses such as EBV and HPV or immunodeficiency diseases such as HIV.
- Propensity of immunosuppressive drugs have been shown to encourage metastatic disease. These drugs include but not limited to:
 - Cyclosporin, Tacrolimus, Azathioprine, Mycophenolate mofetil (as well as other drugs used for conditions like autoimmune disease and inflammatory conditions.
 - When used in combination, the cancer risk increases. The risk of cancer also increases with duration
 of use and when combined with other risk factors such as UV light exposure and smoking. [14,15,16]

Sexual History [HPV exposure (orogenital)

- Sexual behavior is a risk factor for HNSCCs, mainly oropharyngeal cancers.
- Greater risk with **>5 oral** sexual partners. [<u>18</u>]
- HPV infection prevalence in oral region is generally lower than in genital region and is more frequent in assigned males than in assigned females. [18]
- Increased risk of oral infection per sexual partner is greater for assigned males than for assigned females. [10,17]
- Higher rates of transmission occur from assigned females to assigned males than from assigned males to assigned females. [10,17]
- Increased risk of Oropharyngeal HNSCC in assigned male spouses of assigned females with cervical cancer and in situ cancer. [11]

HPV

HPV infection is associated with most oropharyngeal cancers (>70%) and a small minority of other cancer sites in the head and neck. A recent U.S. study showed that the incidence of oropharyngeal cancer sites that are most commonly associated with HPV infection (e.g., tonsil, oropharynx) increased by 2% per year between 2007-2017, while the incidence of oropharyngeal cancers sites that are not associated with HPV infection (e.g., lip, hypopharynx) decreased by -0.4% per year [25]. A Canadian study found a similar trend between 1992 and 2012 [26]. This suggests that, over time, we can expect to see a higher proportion of oropharyngeal cancer patients with HPV-associated HNSCC.

Patients diagnosed with HPV-positive oropharyngeal HNSCC:

- are often younger and can lack tobacco and alcohol exposure when compared to those patients with HPV-negative HNSCC.[9]
- can have cervical neck metastases that may be cystic and can often be mistaken for branchial cleft cysts, contributing to delay in diagnosis. [1]
- may present as a symptomatic mass of the tonsil or base of tongue, with or without accompanying lymphadenopathy OR
- as an asymptomatic neck mass without a symptomatic primary site. Most of these cancers arise from deep crypts in the palatine and lingual tonsils.[1]

Notes regarding presentation:

- Presentation in people 40 to 59 years of age. [26]
- Patients with oropharyngeal HNSCC **may not** have histories of significant tobacco or alcohol use; however, these patients should still be assessed for these risk factors as it may affect prognosis when coexisting with HPV-positive disease. [8]
- Oropharyngeal HNSCC that is caused primarily by HPV type 16 is increasing among younger people in North America and northern Europe. It has a latency period of 10 to 30 years after oral sex exposure.[9]

Risk Factors for HPV-positive Oropharyngeal Squamous Cell Carcinoma:

The incidence of HPV-positive HNSCC continues to rise, especially in populations that are not vaccinated against HPV prior to HPV exposure.

HPV infection that leads to HNSCC is transmitted by oral sex.[9] Specific sexual behaviors related to number of sexual partners:

- >5 oral sexual partners [18]
- Increased risk of oropharyngeal HNSCC in assigned male spouses of assigned females with cervical cancer and in situ cancer. [11]
- The ubiquity of HPV infection is important, as up to 85% of adults may have an HPV infection at some point from any of the over 120 subtypes. However, only a small percentage develops malignancy, these are mostly related to the HPV-16 subtype. [9]
- The effectiveness of prophylactic HPV vaccination is less well defined for oropharyngeal cancer than for anogenital and cervical cancers. Nevertheless, a decreased incidence is expected but may not be clear until after 2060. [5]

The prognosis is generally better for patients with HPV-positive oropharyngeal cancer as they tend to have a better response to cancer treatment. [6]

How to Prevent Head and Neck Cancer- YouTube video

1. History: Symptoms

Symptom	Inclusion criteria	Exclusion criteria	Action
Neck and Face Lump or Mass Defined: neck masses are any mass below the mandible, above the clavicle, and deep to the skin, although it may involve the overlying skin secondarily	 Lacks infectious history Mass has been present for ≥ 3 weeks *** If ultrasound has previously been performed (prior to use of this pathway) and an incidental finding of mass or architecturally abnormal (i.e., cystic) lymph node has been found, referral should be made urgently 	 Obvious infectious source If patient presents with any of the following, refer to Lymph Node Assessment Primary Care Pathway: Lymphadenopathy above AND below the clavicle Drenching night sweats Unexplained fever Unexplained fever Unexplained weight loss < 40 years of age 	Send a high priority/ urgent referral to Otolaryngology – Head and Neck Surgery Referrals must include: - Detailed symptom list - Risk assessment - State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY"
Non-healing Oral Lesion or Mass / Oropharynx Lesion or Mass PHOTO REFERENCE: Oral Cancer Images – Oral Cancer Foundation] Information and Resources about Oral Head and Neck Cancer	 Persistent ulceration of the oral mucosa White or red mucosal change in the oral cavity (leukoplakia or erythroplakia) Exophytic or endophytic mass in the oral cavity or oropharynx Asymmetrically enlarged tonsil in the absence of infectious symptoms 	 Acute traumatic ulcers Viral stomatitis Allergic stomatitis Chemotherapy- induced stomatitis Bacterial stomatitis 	Send a high priority/ urgent referral to Oral Maxillofacial Surgery OR Otolaryngology- Head and Neck Surgery Referrals must include: - Detailed symptom list - Risk assessment - State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY"
Acute onset hoarseness with or without risk factors OR Change in voice OR Persistent sore throat	 A significant history of smoking and drinking alcoholic beverages who has unremitting (symptoms persistent for greater than 3 weeks), and Worsening hoarseness accompanied by throat pain should be considered to have laryngeal cancer until it is proven otherwise. 	 Infectious symptoms suggestive of viral or bacterial laryngitis. OR Symptoms attributable to: A sentinel event such as surgery or ingestion of a foreign body. Hypothyroidism Rheumatoid arthritis, gout, and systemic lupus erythematosus 	Send a high priority/ urgent referral to Otolaryngology - Head and Neck Surgery Referrals must include: - Detailed symptom list - Risk assessment - State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY"

		 Inflammatory disorders (such as amyloidosis, sarcoidosis, and GPA (granulomatosis with polyangiitis Neurodegenerative disorders, (such as myasthenia gravis) Gastroesophageal or laryngopharyngeal reflux Voice abuse/overuse 	
Dysphagia for Solids Dysphagia requires assessment to identify functional, neurologic, inflammatory, or malignant cause	- Presence of odynophagia and mass with risk factors of head and neck cancer (as above).		- A dynamic imaging study i.e., swallowing study can help to identify cause and presence of mass in the absence of other risk factors.
Persistent Oral Bleeding from unknown source	-Oral or pharyngeal ulceration or mass	 Bleeding attributable to periodontal disease Bleeding diathesis 	Send a high priority/ urgent referral to Oral Maxillofacial Surgeon OR Otolaryngology – Head and Neck Surgery Referrals must include: - Detailed symptom list - Risk assessment - State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY"
Unilateral Epistaxis	 Associated with nasal mass, neck mass, sinonasal swelling or cranial nerve pathology Acute onset with persistent or recurrent episodes 	 Chronic condition Bleeding attributable to dryness, trauma, foreign body, rhinitis, or sinusitis 	Send a high priority/ urgent referral to Otolaryngology – Head and Neck Surgery Referrals must include: - Detailed symptom list - Risk assessment - State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY"

Unilateral Otalgia and Hearing Loss	ring Loss tonsil or oropharyngeal mass or ipsilateral neck mass - Associated with mass or ulceration in the externa	Send a high priority/ urgent referral to Otolaryngology – Head and Neck Surgery. Referrals must include:
auditory canal on otoscopy - Persistent not intermittent	 Detailed symptom list Risk assessment State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY" 	

2. Assessment/ Physical Exam (should include the following):

Performing a Screening Exam: Head & Neck Cancer Screening - YouTube [24]

- Inspection of the oral cavity and oropharynx for ulceration of mucosa, swelling, and red or white patches.
 Use of florescence visualization is recommended if available.
- Inspection of the anterior nasal cavities and otoscopy
- Inspection of the facia, scalp skin
- Palpation of the neck for lymphadenopathy

Images of Oral Cancers - <u>Oral Cancer Images – Oral Cancer Foundation | Information and</u> Resources about Oral Head and Neck Cancer [23]

If the patient presents with:

- Lymphadenopathy above and below the clavicle
- Drenching night sweats
- Unexplained fever
- Unexplained weight loss
- < 40 years of age

REFER TO LYMPHOMA PATHWAY

Lymph Node Assessment Primary Care Pathway (albertahealthservices.ca)



3. Referral to Specialty Care

When to Refer

- The patient has physical exam finding(s) or symptom(s) that have persisted longer than 3 weeks despite management.
- The patient has prior imaging- If ultrasound has previously been performed (beyond this pathway) and an incidental finding of mass or architecturally abnormal-i.e., cystic lymph node has been found- referral should be made via this HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY.

Send a high priority/ urgent referral to:

Otolaryngology -Head and Neck Surgery for ALL PATHWAY RELATED CONCERNS OR

Oral Maxillofacial Surgery (OMFS for ORAL LESIONS ONLY

* (Some services provided by OMFS may not be covered through public coverage).

Referrals MUST Include:

- 1. Detailed symptom list
- 2. Risk assessment
- 3. State "As per HEAD & NECK CANCER DIAGNOSIS & REFERRAL PATHWAY"

STANDARD RISK SYMPTOMS - Seen by specialist care: as triaged by Otolaryngology - Head and Neck Surgery

- Send referral as above.
- If the pt has more than one symptom the triaging physician will assess the risk and pt will be seen sooner as required.
- All DI will be arranged by Specialty Care

HIGH RISK SYMPTOMS - Seen by specialist care: goal within 4 weeks

- Order CT Neck with contrast (include the Chest if pt has enlarged neck lymph nodes). The requisition requires: a detailed symptom list and risk assessment AND must state:
- "URGENT High risk symptoms for head and neck malignancy as per H&N Cancer Diagnosis Pathway"
- Serum creatinine is required within 90 days prior to CT scans with contrast

FOR ALL PATIENTS

- ULTRASOUND and Cone Beam Computed Tomography (CBCT) ARE NOT recommended.
- Any required biopsies will be arranged by the surgeon.
- Referral to specialty care should not be delayed for any testing.

Referral Process

Referral pathways are guidelines to help referring providers know what information, labs and diagnostic imaging are required with their referral to a specialty. These pathways are co-designed with Primary and Specialty Care, AHS Operations, and patients to ensure the right amount of information is included throughout the referral process to triage the patient as quickly as possible. To ensure referring providers have referral information at their fingertips, referral pathways may link to clinical pathways when available. AHS manages referral pathways and extensive work is ongoing as part of the <u>Alberta Surgical Initiative</u>. If you have questions or want to know more about the referral pathway development process, please email <u>access.ereferral@ahs.ca</u>.

Continued on next page.

Referral to Otolaryngology - Head and Neck Surgery

- Urgent Referral Call surgeon on call via RAAPID or call 911.
- Follow the Provincial Adult Otolaryngology Referral Pathway.
- <u>Alberta Referral Directory</u> is also a helpful resource for all referral information. Search "Head and neck".

Referral to Oral Maxillofacial Surgery

- Urgent Referral Call surgeon on call via RAAPID or call 911.
- Follow the Provincial Adult Oral and Maxillofacial Surgery Referral Pathway.
- <u>Alberta Referral Directory</u> is also a helpful resource for all referral information. Search "Oral maxillofacial".

Currently there are Oral Maxillofacial Surgeons practicing in Calgary, Edmonton, Grand Prairie, Lethbridge, and Red Deer.

*Some services provided by OMFS may not be covered through public coverage. Refer to Otolaryngology if cost concerns.

CONSIDERATIONS:

A. If the patient presents with:

- Lymphadenopathy above and below the clavicle
- Drenching night sweats
- Unexplained fever
- Unexplained weight loss
- < 40 years of age

REFER TO LYMPHOMA PATHWAY

Lymph Node Assessment Primary Care Pathway (albertahealthservices.ca)

B. Mental Health

The mental health and wellbeing of Head and Neck Cancer survivors is a concern. The literature notes the **second highest rate of suicide** (63.4 cases per 100,000 individuals) after those with pancreatic cancer (86.4 cases per 100,000 individuals), when compared with survivors of other cancers (23.6 cases per 100,000 individuals). Psychological distress and compromised quality of life are likely factors for suicide." [9]

Patients can call 811 for mental health support 24/7 from anywhere in Alberta.



PROVIDER RESOURCES

Cancer work up in Alberta	Diagnostic Workup and Staging of Head and Neck Cancer (albertahealthservices.ca)
Cancer Care Information	The Organization and Delivery of Healthcare Services for Head and Neck Cancer Patients (albertahealthservices.ca)
Cancer Care Information	Oral & Dental Care Management in Head & Neck Cancer (albertahealthservices.ca)
Cancer Care Information	Cancer Care Alberta Home Alberta Health Services
HPV Vaccine eligibility and schedule	07.241 Human Papillomavirus Vaccine Biological Page (albertahealthservices.ca)

PATIENT RESOURCES

Head and Neck Cancer Information for Patients	Head and Neck Cancer: Information and Resources for Patients and Families (albertahealthservices.ca)
Head and Neck Cancer Surgery for Patients	Surgery for Head and Neck Cancer: Information and Resources for Patients and Families (albertahealthservices.ca)
Living well with cancer supports and resources	www.wellspring.ca
Cancer Care Information	Cancer Care Alberta Home Alberta Health Services
Head and Neck Cancer Information for Patients	Head and Neck Cancer Alliance (headandneck.org)
Cancer Information for the Public	Canadian Cancer Society Canadian Cancer Society
Head and Neck Cancer support for patients	Head and Neck Cancer Support Society By the patients, for the patients (head-way.org)

BACKGROUND

About this Pathway

- The creation of the Head & Neck Cancer Diagnosis & Referral Pathway builds on the success of earlier pathways
 including lung, breast, and prostate cancer. Building out multiple cancer diagnosis pathways has begun to create
 end-to-end pathways for cancer patients in Alberta on a provincial scale with the goals of expedited cancer
 diagnosis and providing better support to patients through that process.
- Initial work on this pathway was started in May 2022 and is being implemented over two years. Patients, providers, and administrators from relevant areas were brought together to gather information on current experiences with head and neck cancer diagnosis, collect data on how the system is performing and review best practice evidence. Provincial principles of care, strategic areas for improvement in Alberta and a provincial measurement and reporting framework were defined.
- Primary Care providers were engaged to co-design pathways with patients and representatives from oncology, head and neck surgery, otolaryngology, pathology, diagnostic imaging, and dental practice.
- Local implementation teams will be engaged in work around planning and pathway roll-out, determination of barriers and facilitators, and shared learnings with other sites. Performance dashboard reports will be developed and disseminated to provide feedback to clinical teams on pathway performance and outcomes. Sustainability planning will be initiated early with implementation teams to ensure successful transition of pathways to operations at the end of the initiative.

Authors & conflict of interest declaration

This pathway was reviewed and revised under the auspices of the Cancer Strategic Clinical Network (CSCN) in 2022, by a multi-disciplinary team led by family physicians, oncologists and head and neck surgeons. Names of participating reviewers and their conflict of interest declarations are available on request. For more information contact the CSCN at <u>Cancerdiagnosispathways@albertahealthservices.ca</u>.

Pathway review process, timelines

• Specialty access 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 June 2024. However, we welcome feedback at any time. Please email comments to <u>Cancerdiagnosispathways@albertahealthservices.ca</u> and/ or <u>AlbertaPathways@ahs.ca</u>.

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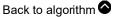
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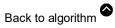
DISCLAIMER

This pathway represents evidence-based best practice but does not override the individual responsibility of healthcare 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 healthcare professional. It is expected that all users will seek advice of other appropriately qualified and regulated healthcare providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.



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