

# Oral Cavity Cancer

Effective Date: December, 2023



## Background

The incidence of oral cavity cancer is not well documented because it is often grouped with other subsites rather than being described in accord with the anatomical definition. Cancer of the oral cavity comprises nearly 30 percent of all malignant tumours of the head and neck.<sup>1,2</sup> Squamous cell carcinomas (SCCs) represent approximately 90 percent of oral cavity cancer cases. Minor salivary gland cancers, melanomas, lymphomas and sarcomas are less common. Sites of tumour origin of the oral cavity include the buccal mucosa, labial mucosa, floor of mouth, oral tongue, alveolar ridges, retromolar trigone and the hard palate. Lifestyle, habits, demographics, as well as genetic factors influence geographic variations in the incidence of disease. In North America, tobacco smoking and alcohol use are the principal risk factors for developing oral cavity cancer. Oral tobacco use, periodontal disease, radiation and immune deficiency have also been implicated.

Despite improved quality of life for patients with oral cavity cancer over the past 30 years, 5-year overall survival (OS) remains in the range of 50–60 percent.<sup>1,2</sup> Treatment for oral cavity cancer is highly complex because of the variety of tumour subsites and the anatomical constraints of the head and neck. In patients who are successfully treated, they often face significant quality of life issues related to changes in appearance and organ function, such as talking, chewing and swallowing and mental health adverse effects as well.

The literature about oral cavity cancer treatment is composed largely of nonrandomized, retrospective or monocentric studies, hence the importance of treatment being decided on a case-by-case basis by a multidisciplinary team. The ultimate goals of oral cavity cancer treatment are to eliminate the cancer, preserve or restore form and function, minimize treatment complications and to prevent any subsequent new primary cancers. To achieve these goals, current treatment modalities include surgery, radiotherapy (RT), chemotherapy and combined modality treatments. Influencing the choice of treatment are tumour, patient and treatment team factors.<sup>3</sup> Tumour factors that affect the choice of initial treatment of oral cavity cancer are primary site, size and proximity to bone, status of regional cervical lymph nodes, previous treatment and histology. Staging for tumours of the oral cavity are presented in [Appendix A](#). Patient factors include age, general health and tolerance to treatment, occupation, lifestyle and other socioeconomic considerations. Finally, treatment team factors depend on the technical capabilities and support services from various disciplines.

This guideline was developed to outline treatment recommendations for patients with early and advanced stage oral cavity cancer. These guidelines should be applied in the context of the recommendations outlined in Alberta Health Services, Cancer Care Alberta guideline, [The Organization and Delivery of Healthcare Services for Head and Neck Cancer Patients](#).

## Guideline Questions

1. What diagnostic and baseline investigations are recommended for patients with suspected or confirmed oral cavity cancer?
2. What are the recommended treatment options for early-stage oral cavity cancer (T1–2, N0)?

3. What are the recommended treatment options for advanced-stage oral cavity cancer (T3, N0; T4a, Any N; T1–3, N1–3; T4b, any N or unresectable nodal disease or unfit for surgery)?
4. What is the recommended follow-up after treatment for oral cavity cancer?

## Search Strategy

PubMed, MEDLINE and the Cochrane Database of Systematic Reviews were searched to May 6, 2023 for literature on the treatment of oral cavity cancer. The following search terms were used: *mouth floor* (MeSH [Medical Subject Heading]) OR *mouth neoplasm* (MeSH) OR *oral cavity cancer* OR *buccal mucosa cancer* OR *tongue neoplasms* (MeSH) OR *anterior tongue cancer* OR *alveolar ridge cancer* OR *retromolar trigone cancer* OR *hard palate cancer*; results were limited to human subjects (19+ years), published in English. Except in the case of frequent citation, only studies with equal to or greater than 50 patients and who were followed for more than 3 years were considered for the literature review. In addition, studies reporting patient populations with mixed tumour sites were only considered if greater than 50 percent of the patients had oral cavity cancer. Reference lists of included studies were also searched to identify further trials.

The National Guidelines Clearinghouse and SAGE Directory of Cancer Guidelines were also searched from 2008 to 2023 for guidelines on oral cavity cancer.

## Target Population

The recommendations outlined in this guideline are intended for adults over the age of 18 years with oral squamous cell carcinoma.

## Recommendations

The Alberta Provincial Head and Neck Tumour Team reviewed the recommendations of several different guidelines, including those from the Cancer Care Ontario Program in Evidence-based Care,<sup>4</sup> the German Guideline Group<sup>5</sup> and the National Comprehensive Cancer Network (NCCN)<sup>6</sup>. The Alberta Provincial Head and Neck Tumour Team have adopted the recommendations of the NCCN, with modifications to fit the Alberta context.

### 1. Initial Work-up and Supportive Care Evaluations:

The following investigations are recommended at diagnosis for all patients with suspected or confirmed oral cavity cancer:

- Complete head and neck examination
- Biopsy:
  - Please see CPG -008 page 6 for recommendations regarding technique for acquiring oral biopsies. Generally incisional or punch biopsies are preferred to excisional biopsies.

- The specimen needs to be properly oriented (sectioned perpendicularly to the surface to avoid tangential sectioning artifact) by the pathology lab and the report needs to state at the minimum the:
  - diagnosis
  - grade
  - depth of invasion
  - margins (only if shave or excisional biopsy)
  - and optional parameters: worst pattern of invasion, lymphovascular invasion, perineural invasion.
- Nutrition, speech and swallowing evaluation/therapy should be conducted by a registered dietitian and a speech-language/swallowing therapist. This is recommended for patients with poor intake, those with unintentional weight loss, difficulty with speech/swallowing, and/or for patients whose treatment is likely to affect speech/swallowing.
- Computed tomography (CT) with contrast and/or magnetic resonance imaging (MRI) with contrast of primary site and neck, as indicated.
- Positron emission tomography-computed tomography (PET-CT), can be used to determine regional/distant metastases, as required.
- Chest CT scan, if not included with other imaging
- Examination under anesthesia with endoscopy, as required.
- Pre-anesthesia studies
- Dental evaluation including jaw imaging.
- OMFS/Prosthodontist evaluation as indicated.

## 2. Treatment Options for Early-Stage Oral Cavity Cancer (T1–2, N0):

Patient participation in clinical trials is recommended. For standard treatment, all cases should be presented and discussed at a multidisciplinary Tumour Board to decide the best treatment option for each patient.

### Preferred treatment:

- Patients with no contraindication to surgery and who are agreeable should undergo resection of primary site plus/minus ipsilateral or bilateral neck dissection (ND), which should be guided by tumour location and depth of invasion.
- Elective ND is recommended for tumours with a depth  $\geq 4$  mm. For a depth of 2 to 4 mm, clinical judgment should be utilized to determine appropriateness of elective ND.
- If after elective neck dissection, a patient has one pathologically positive node without adverse risk features, RT is optional.
- If a patient has the following adverse pathological risk features, treatment after resection includes:
  - Extranodal extension +/- positive margin: concurrent chemotherapy and radiation.

- Positive margin: if feasible, consider re-resection to achieve negative margins; if re-resection is not possible consider concurrent chemotherapy and radiation.
- Perineural invasion and/or lymphovascular invasion: RT alone; concurrent chemotherapy and radiation may be considered; the decision should be based on clinical judgment and discussion at the multidisciplinary Tumour Board
- If a patient has none of the above adverse risk features, he or she should proceed with follow-up and surveillance.

#### **Alternative treatment:**

- Patients with a contraindication to surgery should undergo definitive RT or concurrent chemotherapy and radiation. Patients who go on to develop recurrent or residual disease should be considered for salvage therapy.
- Please [click here](#) to view the early-stage treatment algorithm.

### **3a. Treatment Options for Advanced-Stage Oral Cavity Cancer (T3,N0; T1–3, N1–3; T4a, any N):**

Inclusion of patients in multimodality clinical trials is recommended. In lieu of a clinical trial, patients should undergo surgery. Patients with N2c neck disease should undergo primary tumour resection and bilateral ND, while all other patients (N0, N1, N2a–b and N3) should undergo primary tumour resection, and ipsilateral or bilateral neck dissection; the decision should be based on clinical judgment and discussion at the multidisciplinary Tumour Board.

If a patient has the following adverse risk features, treatment after resection includes:

- Extranodal extension +/- positive margin: concurrent chemotherapy and radiation or re-resection
- pT3 or pT4, and/or N2 or N3 nodal disease, and/or nodal disease in levels IV or V, and/or perineural invasion, and/or vascular embolism: RT alone; concurrent chemotherapy and radiation may be considered, the decision should be based on clinical judgment and discussion at the multidisciplinary Tumour Board.

Please [click here](#) to view the advanced-stage treatment algorithm.

### **3b. Treatment Options for Very Advanced-Stage Oral Cavity Cancer (T4b, any N or Unresectable Nodal Disease or Unfit for Surgery):**

Patient participation in clinical trials is recommended. In lieu of a clinical trial, patients should undergo therapy dependent on their Eastern Cooperative Oncology Group (ECOG) performance status (PS). ECOG PS levels are presented in [Appendix B](#).

In the instance of residual neck disease and if feasible, conduct ND if the primary tumour site is controlled following the above treatments. For oral cavity cancers, the risk of regional metastases and the need for adjuvant elective ND increases as thickness of the lesion increases.

Please [click here](#) to view the very advanced-stage treatment algorithm.

## Management of metastatic disease<sup>7</sup>:

### First line therapy:

Management of patients with no prior systemic therapy for recurrent or metastatic squamous cell carcinoma of the head and neck is influenced by prior initial treatment for locoregional disease, performance status, comorbidities, tissue programmed death ligand 1 (PD-L1) combined positive score (CPS), and related prognostic factors.

- Patients with no prior systemic therapy for recurrent or metastatic disease, and who have a PD-L1 CPS of <1 or unavailable: platinum-based chemotherapy, with or without immune checkpoint inhibitor, is recommended.
- Patients with no prior systemic therapy for recurrent or metastatic disease who have PD-L1 CPS  $\geq$ 1: immune checkpoint inhibitor therapy with or without chemotherapy is recommended.

## 4. Reconstruction:

The Alberta Provincial Head and Neck Tumour Team agree that patients with oral cavity cancer should be assessed by an experienced Head and Neck Reconstructive Surgeon, as defined in [The Organization and Delivery of Healthcare Services for Head and Neck Cancer Patients](#) guideline, prior to surgical treatment. If reconstruction of surgical defects is required, it should be performed at the discretion of the Head and Neck Reconstructive Surgeon.

## 5. Follow-up and Surveillance:

The following schedule should be taken into account to manage complications related to treatment, to detect disease recurrence and/or the development of new disease:

- Head and neck examination (note that the ranges are based on risk of relapse, second primaries, treatment sequelae, and toxicities):
  - Year 1, every 1 to 3 months
  - Year 2, every 2 to 6 months
  - Year 3–5, every 4 to 8 months
  - After 5 years, annually, as clinically indicated
- Annual thyroid-stimulating hormone (TSH) screening up to 5 years only for those patients that receive post-operative RT to the neck.
- Speech/swallowing assessment at 6 and 12 months post-RT; additional assessment and rehabilitation, as clinically indicated by a speech-language/swallowing therapist.
- Hearing evaluation and rehabilitation, as clinically indicated.
- Follow-up with a registered dietitian to evaluate nutritional status and until the patient achieves a nutritionally stable baseline.

- Recommended dental follow-up occurs in both the hospital and community setting. Typically, patients are referred back to their family dentist for routine dental care at 6 months post-radiation treatment; however, certain patients may choose to continue receiving follow-up care in the hospital clinic. The schedule of Dental follow-up/rehabilitation includes:
  - 6 weeks post treatment
  - 2–3 months post treatment
  - 6 months post treatment
  - 12 months post treatment
  - Yearly after 12 months post treatment
- Physiotherapy is indicated for all patients undergoing major head and neck resection during the first 3–6 months post-operation.

## Discussion

### Diagnosis

Commonly observed signs and symptoms in oral cavity cancer include: non-healing ulcer, pain, bleeding under or around prostheses or ill-fitting dentures. More advanced lesions may present with speech difficulties, dysphasia, otalgia (ear pain), hypersalivation and neck mass(es). A complete head and neck examination is required to begin to diagnose oral cavity cancer. Attention should be paid to tongue mobility, extension to adjacent sites and involvement of the primary echelon nodal drainage levels I and II. In individual cases, endoscopic examination under anesthesia can be used for a more thorough examination, although the actual diagnosis of oral cavity cancer can only be confirmed with a tissue biopsy. Pre-anesthetic studies should precede any invasive procedures requiring general anesthesia in patients who have had previous treatment with surgery, RT or chemotherapy. Imaging studies of the head and neck areas using CT with contrast and/or MRI should be used to assess the extent of local and regional tumour spread, the depth of invasion and lymphadenopathy. Chest imaging, usually CT scan, will identify pulmonary metastasis. Dental/prosthetic evaluation, including jaw imaging is required prior to commencement of treatment in patients at risk of oral complications. Finally, nutrition, speech and swallowing evaluation/therapy are critical to optimize quality of life during and after treatment.

### Early-Stage Disease

Approximately 30–40 percent of patients with oral cavity cancer present with stage I and II disease<sup>1</sup>. Surgery is considered the gold standard for treatment because it requires a single intervention and is usually performed with a minimum amount of morbidity. RT is recommended for patients with a contraindication to surgery however the outcomes are typically worse in oral cavity cancer with non-surgical treatments and multiple interventions are required over a period of several weeks and the incidence of long-term sequelae is high (e.g., xerostomia, dysphagia and osteoradionecrosis). Thus,



the choice of treatment (surgery versus RT) should be based on an assessment of the patient's ability to tolerate and accept surgery.

Please see 'Surgical management of the neck' below regarding the surgical management of N0 neck oral cavity cancer patients.

### **Advanced-Stage Disease**

**Surgery:** Patients with advanced-stage oral cavity cancer should be enrolled in multimodality clinical trials, if available, and if the patient is agreeable. The preferred management of advanced, operable head and neck cancers consists of surgical resection followed by adjuvant therapy. Patients treated by surgery and RT are known to experience locoregional recurrence rates of 30 percent, distant metastasis rates of 25 percent and 5-year survival rates of 40 percent<sup>8</sup>. Patients treated in Alberta with post-operative adjuvant RT had a reported 5-year metastasis-free survival rate of 75 percent and this increased to 84 percent with the addition of adjuvant chemotherapy for selected indications<sup>9</sup>.

**Surgical management of the neck:** Lymph node metastasis occurs in approximately 45 percent of patients at presentation of oral cavity SCC<sup>10</sup>. As such, ND has been advocated for the removal and control of metastatic disease in the cervical region<sup>11</sup>. The specific indications for a modified radical versus a selective ND are still under debate. The current literature suggests that modified radical ND, where all five levels of lymphatic tissue are removed, is reserved for extensive disease cases (e.g., N3 disease, extensive extracapsular spread or identifiable disease in levels IV or V)<sup>11</sup>. Selective ND can be used to treat N1 or N2a disease; yielding outcomes similar to those treated with modified radical ND.<sup>9</sup> There is still debate regarding the removal of level IV during selective ND.

Elective ND for patients that do not have clinical or radiologic evidence of cervical metastatic disease can be therapeutic and diagnostic. Supraomohyoid ND for levels I, II and III is the recommended procedure for elective management of the neck<sup>11, 12</sup>. Elective removal of level IV is under debate due to the risk of injury to level IV structures such as the thoracic duct or phrenic nerve. *Spiro et al.* conducted a retrospective review of cN0 floor of mouth and oral tongue SCC patients and found that measurement of tumour thickness is a good way to select those oral cancer patients who are most likely to benefit from elective ND; indicating ND for tongue and floor of mouth tumours, specifically, with a thickness of 2–4 mm depth of invasion<sup>13</sup>. A prospective study of patients with SCC of the tongue found that tumour thickness had prognostic significance for nodal metastasis, local recurrence and survival. The authors found that tumours of up to 3 mm thickness had 10 percent nodal metastasis, 0 percent local recurrence and 100 percent 5-year actuarial DFS; tumour thickness between 3 mm and 9 mm had 50 percent nodal metastasis, 11 percent local recurrence and 77 percent 5-year actuarial DFS; tumours of more than 9 mm thickness had 65 percent nodal metastasis, 26 percent local recurrence and 60 percent 5-year actuarial DFS<sup>14</sup>. *Huang et al.* conducted a meta-analysis of studies examining the relationship between tumour thickness and cervical lymph-node involvement in oral cavity SCC and concluded that the optimal tumour thickness cutoff point for prompting prophylactic neck management is 4 mm<sup>15</sup>.



A systematic review of randomized controlled trials (RCTs) comparing different surgical treatment modalities for oral cavity cancer patients found evidence that elective ND of N0 neck nodes reduces locoregional recurrence<sup>12</sup>. However, the same study found that there is insufficient evidence to conclude that elective ND increases OS or disease-free survival (DFS) compared to therapeutic ND. The authors of the study also concluded that there is no evidence that elective radical ND increases OS compared to elective selective ND.

The application of sentinel lymph node biopsy in the management of oral cavity cancer patients with a clinically negative neck has been reported;<sup>16, 17</sup> however, this procedure is not well-established<sup>11</sup>.

**Chemoradiotherapy:** Data from two trials, phase III Radiotherapy Oncology Group (RTOG) 85-03 and phase II RTOG 88-24 was used to identify characteristics of tumours that predicted locoregional recurrence of disease following surgery and Post-operative RT<sup>18</sup>. The presence of tumors in two or more lymph nodes and/or extranodal extension and/or microscopic-size tumor involvement of the surgical margins of resection were found to impart a high risk of local-regional relapse. Study authors hypothesized that following surgery, the concurrent addition of chemotherapy to RT might increase the likelihood of local-regional control of disease for patients with high-risk characteristics.

In 2004, evidence was established for the use of concurrent postoperative chemotherapy and RT in patients with locally advanced head and neck cancers, with the publication of trials conducted in Europe (European Organization for Research and Treatment of Cancer [EORTC] trial 22931)<sup>19</sup> and the United States RTOG trial 9501<sup>20</sup>. Adjuvant chemotherapy-enhanced RT was shown to be more efficacious than PORT for these tumours in terms of locoregional control and survival. However, additional studies were required to determine which patients were most suitable for such intense treatment<sup>21</sup>.

**Risk levels:** Data from a retrospective subgroup analysis of the selection criteria, clinical and pathologic risk factors, and treatment outcomes from EORTC 22931 and RTOG 9501 showed that microscopically involved resection margins and extranodal extension are the most significant prognostic factors for poor outcome. Adjuvant chemotherapy-enhanced RT improves outcome in patients with one or both of these risk factors who are medically fit to receive chemotherapy<sup>21</sup>. While both EORTC 22931 and RTOG 9501 provided strong evidence on the efficacy of surgery and adjuvant concurrent chemotherapy and RT, they were not specific to the oral cavity site. In a retrospective study to assess survival outcomes of advanced oral cavity SCC treated by differing modalities, authors found that patients receiving postoperative adjuvant chemoRT had improved overall, disease-specific, disease-free and metastatic free survival compared to surgical resection with postoperative adjuvant RT, chemoRT only or RT only ( $p < 0.05$ )<sup>9</sup>. Moreover, patients with extranodal extension and treated with postoperative chemoRT versus postoperative adjuvant RT had 55 percent survival advantage at 5 years ( $p < 0.05$ ).

**Reconstruction:** Reconstructive surgery following resection is considered when there is functional and/or aesthetic loss of structures in the oral cavity. Reconstruction of surgical defects should be performed in a manner consistent with head and neck reconstructive principles and should be

performed by a surgeon with expertise in head and neck reconstruction, as defined in the Cancer Care Alberta guideline, [The Organization and Delivery of Healthcare Services for Head and Neck Cancer Patients](#). Mucke and colleagues examined the effect of microvascular free flap reconstruction on survival among 274 patients with oral SCC and found that when they controlled for extent of tumour, only T3 and T4 tumours were significantly associated with survival ( $p < 0.001$ , HR = 0.46, 95% CI, 0.31–0.69)<sup>22</sup>. Small cohort data specific to Alberta has shown that, with appropriate reconstruction and regular attendance at rehabilitation sessions, good functional outcomes can be predicted in patients with early or advanced stage oral cavity cancer<sup>23-28</sup>.

## Site-Specific Treatment

**Anterior 2/3 of tongue:** The incidence of tongue cancer exceeds all other sites in the oral cavity, accounting for almost 30 percent of oral cavity cancer patients<sup>1</sup>. Surgery is recommended for small, anterior and well-lateralized lesions; however, some debate exists regarding the impairment of normal speech and/or swallowing following surgery of large T1 and T2 lesions. A longitudinal study of T2 and T3 patients undergoing surgical resection and radial forearm free flap reconstruction in Alberta found that swallowing and tongue mobility functional problems are not evident 12 months postoperatively<sup>29</sup>. Elective ND is recommended for T2–4 and T1 tumours with a clinically negative neck, especially if the depth of invasion is 4 - 5 mm<sup>6</sup>, because of the high incidence of occult cervical nodal disease<sup>22</sup> and the staging information provided by the ND to help determine the necessity and type of postoperative treatment.

The role of contralateral ND in patients with T1 disease and a clinically negative neck is difficult to define. Lim *et al.* conducted a retrospective comparative study of stage I or II oral tongue SCC patients who had undergone ipsilateral elective ND simultaneously with the primary lesion. The management of the contralateral N0 necks involved observation or elective ND. The 5-year actuarial DFS rates were 82 percent for the observation group and 68 percent for the elective ND group; this difference was not statistically significant ( $p = 0.182$ ). The authors of the study conclude that ipsilateral elective neck management is indicated for stage I and II SCC of the tongue; however, they also suggest that contralateral occult lymph node metastasis is unlikely in early-stage tongue cancer and that elective ND offers no survival benefit in comparison to observation<sup>23</sup>. Conversely, more recent data suggests that early-stage tongue cancer patients have a greater than expected rate of neck failure, with contralateral recurrence accounting for close to 40 percent of recurrences<sup>24</sup>. In this more recent study, neck failure occurred mainly in patients who had primary tumours > 4 mm thick; multivariate analysis indicated that tumour thickness was the only independent predictor of neck failure.<sup>23</sup> Similarly, Bier-Laning *et al.* found that the risk for contralateral metastases was greatest for patients with tumours > 3.75 mm thick and < 9.5 mm thick<sup>25</sup>. A more recent prospective randomized study of N0 neck stage I or II tongue cancer patients found that the 5-year disease-specific survival rate for the observation arm (87 percent) versus the elective ND arm (89 percent) was not significant; however, 37 percent of the patients in the observation arm ultimately required a second surgery, in the form of a ND, and adjuvant RT for recurrent disease<sup>26</sup>.

**Buccal mucosa:** In Southeast Asia, SCC of the buccal mucosa (buccal SCC) is the most common type of oral cavity cancer. In North America and Western Europe it accounts for only approximately 10 percent of all oral cavity cancers<sup>27</sup>. This difference is due mainly to the habit of betel quid chewing in Southeast Asia, which exposes the buccal mucosa to high doses of carcinogens. Literature related to the treatment of buccal SCC is limited to case series, with small patient numbers and variable treatment modalities. In addition, much of the literature originates from Southeast Asia where the treatment approach and disease biology may differ from that in North America. Thus, treatment of these patients has been largely guided by case series from single institutions.

In contrast to large studies from Southeast Asia that involve patients who present at an advanced-stage, most patients documented in studies that originate in Western countries present with early-stage local disease (T1–T2)<sup>28</sup>. In one of the largest North American case series (n=119), *Diaz et al.* reported that 71 percent of buccal SCC patients were treated with surgery exclusively, while 29 percent of patients received preoperative RT or PORT. Patients who received PORT had either extranodal extension or positive margins on final pathological evaluation. The 5-year survival rates for patients with T1, T2, T3 and T4 primary tumours were 79 percent, 65 percent, 56 percent and 69 percent, respectively. Five-year survival rates for patients with N0 and N+ neck disease were 70 percent and 49 percent, respectively. Rates for patients with and without extranodal extension were 24 percent and 69 percent (p=0.0052). Elective treatment of the neck reduced the regional recurrence rate from 25 percent to 10 percent in patients with N0 neck disease, but local recurrence was still about 30 percent irrespective of neck treatment<sup>30</sup>. Similarly, a 10-yr retrospective chart review of Canadian patients treated for buccal SCC at a single institution (n=70) showed surgery (transoral or transmentum cheek flap) was the primary treatment modality for the majority of patients (87 percent)<sup>28</sup>. The general management approach for patients with high-risk pathological features (e.g., extranodal extension, positive margins) was primary surgery with adjuvant RT and chemoRT. Primary RT, with or without chemotherapy, was offered to patients who were medically unfit or refused surgery. At this institution, elective NDs are usually performed in patients with T1 tumours and a depth of invasion greater than 4 or 5 mm and for T2N0 tumours. The overall 5-year survival rate for T1–T2-sized tumours was 73.6 percent and 64.0 percent for T3–T4 tumours. Rates for pN0 patients were 87.3 percent and 50.8 percent for patients with nodal metastases.

**Floor of mouth:** Floor of mouth SCCs are aggressive oral cavity neoplasms that can quickly metastasize to cervical nodes due to the lack of any substantial fascial barriers. Patients with floor of mouth cancer typically present with painful infiltrative ulcerative lesions that may bleed<sup>1</sup>. The preferred treatment approach in operable patients is usually surgery because of the risk of radiation-induced bone necrosis. Surgical treatment outcomes vary directly with tumour size and the status of the surgical margins; negative margins can be technically difficult to achieve without rim mandibulectomy due to the proximity of and/or occult invasion into the mandible<sup>1</sup>. PORT with or without concomitant chemotherapy is indicated for patients who have positive margins, mandibular bone erosion or pathologically positive lymph nodes after elective ND.

Rodgers *et al.* conducted a retrospective analysis of 194 patients managed with curative intent for previously untreated floor of mouth SCC. 117 patients received RT alone, 36 patients received surgery alone and 41 patients received surgery and RT together (10 patients were treated preoperatively and 31 patients were treated postoperatively). The authors of the study found that initial and ultimate control rates for RT alone or surgery alone for early-stage lesions did not differ significantly. On the other hand, combined therapy for T3 and T4 lesions was clearly associated with a significant improvement in local control rates compared to single modality therapy. However, 5-year cause-specific survival was not significantly different for advanced-stage lesions between combination (63–25 percent) and single modality groups (67–25 percent for surgery alone and 67–20 percent for RT alone), due to the effect of distant metastases. In conclusion, the authors recommend surgery for early-stage floor of mouth cancer and combination therapy for advanced-stages<sup>31</sup>.

Floor of mouth cancers have a high incidence of occult nodal disease and therefore, prophylactic ND is recommended in most cases. The Alberta Provincial Head and Neck Tumour Team members agree with the recommendations of the National Comprehensive Cancer Network, which state that for SCC, the depth of invasion is currently the best predictor of occult metastatic disease<sup>6</sup>. The NCCN recommends that for tumours with a depth greater than or equal to 4 mm, elective ND should be strongly considered if RT is not already planned; conversely, for a depth less than 2 mm, elective ND is only indicated in highly selective situations<sup>6</sup>. Clinical judgment should be used to determine the appropriateness of dissection for tumours with a depth between 2 to 4 mm.

**Retromolar trigone:** The retromolar trigone is the firm area just behind the back molars in the lower jaw. SCC of the retromolar trigone is relatively uncommon; patients usually have a long history of tobacco abuse and heavy alcohol consumption<sup>32</sup>. The presenting symptom is typically pain that is exacerbated by chewing. In comparison to other sites in the oral cavity, local recurrence rate is higher with these tumours due to microscopic extension to the mandible and maxilla; therefore, it is important to determine the true invasive margin. For tumours involving the retromolar trigone, the optimal extent of surgery is controversial<sup>32</sup>; a resection margin of at least 1 cm in all directions is recommended<sup>11</sup>.

Treatment options for retromolar trigone cancer include surgery and RT. Patients with early-stage lesions are usually treated with single modality surgical management, whereas patients with advanced-stage disease are frequently treated with primary surgery and adjuvant RT or chemoRT. Mendenhall *et al.* compared treatment outcomes for retromolar trigone SCC patients treated with RT alone or RT combined with surgery. The 5-year cause-specific survival rates after definitive RT compared with surgery and RT were as follows: stages I–III, 56 percent and 83 percent; stage IV, 50 percent and 61 percent; and overall, 52 percent and 69 percent, respectively. Multivariate analyses found that the likelihood of cure was better with combined treatments in comparison to RT alone. The authors of the study conclude that the optimal treatment for patients with SCC of the retromolar trigone is surgery, particularly in comparison to RT alone, which has a high probability of severe complications such as osteoradionecrosis. That being said, the authors do recommend that PORT be employed for those with a significant risk of residual disease, particularly patients with positive

margins and/or extracapsular extensions. High-risk patients should also be considered for adjuvant chemotherapy to be administered concomitantly with PORT<sup>32</sup>.

As with other oral cavity cancers, early lesions of the retromolar trigone are characterized by early invasion of the mandible and high rates of regional metastases. As such, elective ND in levels I–III is recommended.

**Hard palate and alveolar ridge:** Malignant neoplasms of the hard palate and upper alveolar ridge comprise approximately 5 percent of oral cavity malignancies<sup>1</sup>. Unlike other areas of the oral cavity where SCC makes up the majority of pathology, the palate is rich in minor salivary gland carcinomas and other rare malignancies<sup>1</sup>. Few studies report the treatment of hard palate cancer due to the relatively rare incidence of disease; studies that do report outcomes are small (n=<50); thus, no strong evidence exists suggesting that any specific treatment is more effective than the other.

The alveolar ridges are the bony ridges of the mandible and maxilla that encase the sockets of the teeth. Early lesions of the alveolar ridges are often initially evaluated during a visit to the dentist for gingival bleeding. Like, hard palate SCC, the peer-reviewed literature specifically pertaining to the outcomes of therapy for alveolar ridge SCC is limited by small sample size and failure to separately analyze outcomes by site and treatment modality<sup>33</sup>.

Generally speaking, most lesions of the hard palate and alveolar ridge are treated with primary surgery. Combined modality therapy provides better locoregional disease control than single modality therapy<sup>2</sup>. PORT with or without concomitant chemotherapy is indicated for patients with positive resection margins, bone erosion or pathologically positive lymph nodes after elective ND<sup>2</sup>.

Tumours of the hard palate rarely metastasize to the neck because the periosteum serves as an early barrier to spread<sup>2</sup>; therefore, a ND is rarely warranted in the absence of demonstrable regional disease. If disease extends beyond the hard palate, however, elective treatment of the neck is indicated even in N0 neck patients.

## Follow-up

There are no RCTs which have compared pre-defined follow-up strategies with no follow-up. Thus, there is no definitive evidence suggesting that any specific programme is better or more efficient at detecting recurrences or improving survival and quality of life. Oral cavity cancer behaves differently in each person and follow-up plans should take into consideration the individual's situation. The Canadian Cancer Society suggests that the following symptoms should be reported to a doctor without waiting for the next scheduled appointment<sup>34</sup>:

- Pain
- Discharge from the wound
- Trismus (difficulty opening the jaw)
- Weight loss
- Changes in vision, hearing or taste
- Difficulty in chewing, speech or swallowing

- Any new lump or swelling in the oral cavity or neck

Patients should be educated about symptomology and the need for additional visits if any of the above symptoms arise. The chance of oral cavity cancer recurring is greatest within the first three years, so close follow-up is needed during this time<sup>35</sup>.

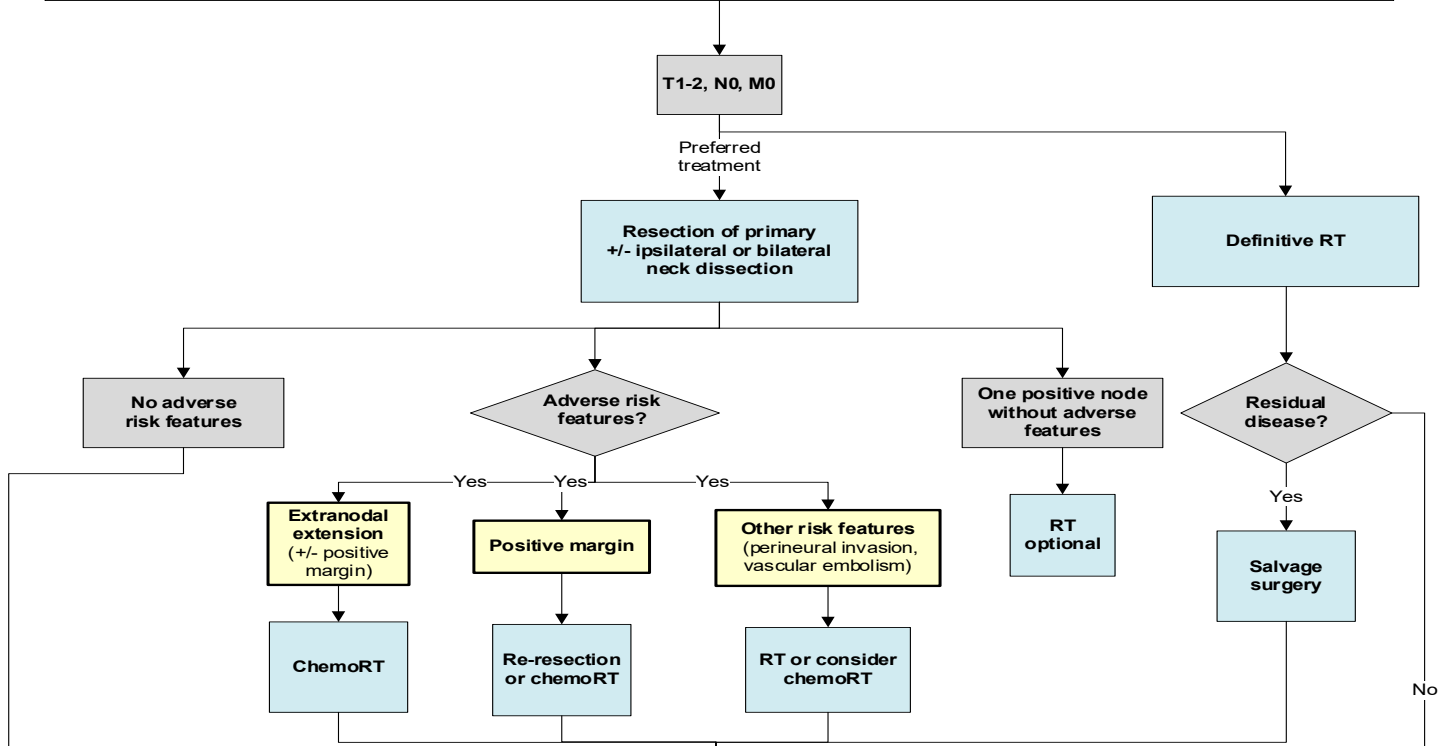
Treatment for oral cavity cancer, in general, is highly complex and can result in substantial side effects experienced by the patient, such as self-esteem and body image issues, dry mouth, difficulty chewing, speech and swallowing problems, taste changes and dental problems, to name a few<sup>36</sup>. Supportive care plans should be incorporated into follow-up strategies to help cope with these side effects.

# Treatment Algorithms

## Early-Stage Oral Cavity Cancer (T1-2, N0)

The Head and Neck Tumour Team encourages patient participation in clinical trials. In addition, all patient cases should be presented & discussed at a multidisciplinary Tumour Board.

- Workup**
- Complete head and neck examination
  - Biopsy
  - Chest imaging
  - Nutrition, speech and swallowing evaluation/therapy should be conducted by a registered dietician and a speech-language/swallowing therapist and is recommended for patients who have significant weight loss (>10% ideal body weight), and/or difficulty with speech/swallowing, and/or for patients whose treatment is likely to affect speech/swallowing
  - Computed tomography (CT) with contrast and/or magnetic resonance imaging (MRI) with contrast of primary site and neck, as indicated
  - Positron emission tomography-computed tomography (PET-CT), as indicated
  - Chest CT scan, if not included with other imaging
  - Examination under anesthesia with endoscopy, as indicated
  - Preanesthesia studies
  - Dental/prosthetic evaluation, including jaw imaging, as indicated



- Follow-up and Surveillance**
- Head and neck examination (note that the ranges are based on risk of relapse, second primaries, treatment sequelae, and toxicities):
    - Year 1, every 1 to 3 months
    - Year 2, every 2 to 6 months
    - Year 3–5, every 4 to 8 months
    - After 5 years, annually, as clinically indicated
  - Annual thyroid-stimulating hormone (TSH) screening up to 5 years only for those patients that receive post-operative RT to the neck
  - Speech/swallowing assessment at 6 and 12 months post-RT; additional assessment and rehabilitation, as clinically indicated by a speech-language/swallowing therapist
  - Hearing evaluation and rehabilitation, as clinically indicated
  - Follow-up with a registered dietician to evaluate nutritional status and until the patient achieves a nutritionally stable baseline
  - Routine dental follow-up/rehabilitation and evaluation up to 3 years, specifically:
    - Half-way through treatment
    - At the end of treatment
    - 6 weeks post treatment
    - 2–3 months post treatment
    - 6 months post treatment
    - 12 months post treatment
    - Yearly for the next 2 years
  - Physiotherapy is indicated for all patients undergoing major head and neck resection during the first 3–6 months post-operation

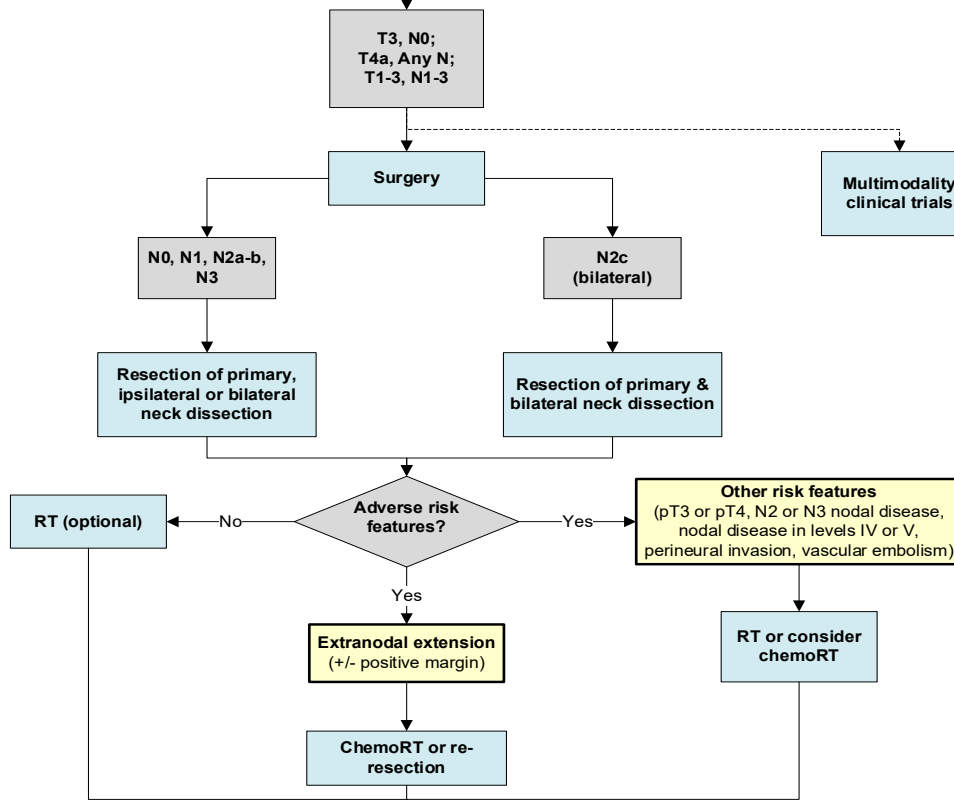


## Advanced-Stage Oral Cavity Cancer (T3,N0; T4a, any N; T1-3,N1-3)

The Head and Neck Tumour Team encourages patient participation in clinical trials.  
In addition, all patient cases should be presented & discussed at a multidisciplinary Tumour Board.

### Workup

- Complete head and neck examination
- Biopsy
- Chest imaging
- Nutrition, speech and swallowing evaluation/therapy should be conducted by a registered dietician and a speech-language/swallowing therapist and is recommended for patients who have significant weight loss (>10% ideal body weight), and/or difficulty with speech/swallowing, and/or for patients whose treatment is likely to affect speech/swallowing
- Computed tomography (CT) with contrast and/or magnetic resonance imaging (MRI) with contrast of primary site and neck, as indicated
- Positron emission tomography-computed tomography (PET-CT), as indicated
- Chest CT scan, if not included with other imaging
- Examination under anesthesia with endoscopy, as indicated
- Preanesthesia studies
- Dental/prosthetic evaluation, including jaw imaging, as indicated



### Follow-up and Surveillance

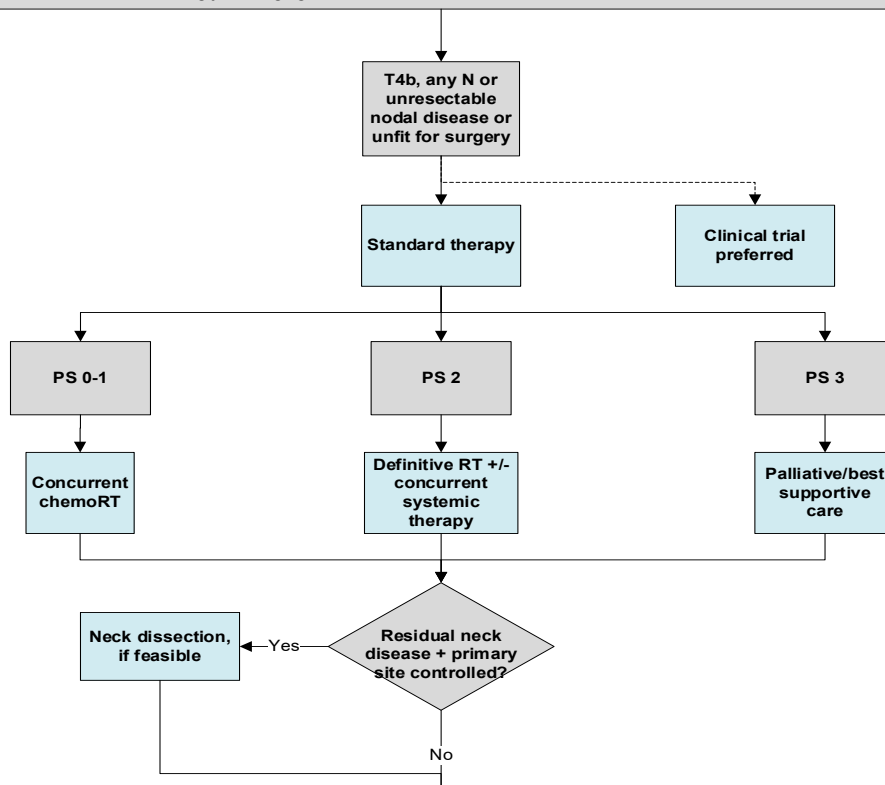
- Head and neck examination (note that the ranges are based on risk of relapse, second primaries, treatment sequelae, and toxicities):
  - Year 1, every 1 to 3 months
  - Year 2, every 2 to 6 months
  - Year 3–5, every 4 to 8 months
  - After 5 years, annually, as clinically indicated
- Annual thyroid-stimulating hormone (TSH) screening up to 5 years only for those patients that receive post-operative RT to the neck
- Speech/swallowing assessment at 6 and 12 months post-RT; additional assessment and rehabilitation, as clinically indicated by a speech-language/swallowing therapist
- Hearing evaluation and rehabilitation, as clinically indicated
- Follow-up with a registered dietician to evaluate nutritional status and until the patient achieves a nutritionally stable baseline
- Routine dental follow-up/rehabilitation and evaluation up to 3 years, specifically:
  - Half-way through treatment
  - At the end of treatment
  - 6 weeks post treatment
  - 2–3 months post treatment
  - 6 months post treatment
  - 12 months post treatment
  - Yearly for the next 2 years
- Physiotherapy is indicated for all patients undergoing major head and neck resection during the first 3–6 months post-operation

## Very Advanced-Stage Oral Cavity Cancer (T4b, any N or Unresectable Nodal Disease or Unfit for Surgery)

The Head and Neck Tumour Team encourages patient participation in clinical trials.  
In addition, all patient cases should be presented & discussed at a multidisciplinary Tumour Board.

### Workup

- Complete head and neck examination
- Biopsy
- Chest imaging
- Nutrition, speech and swallowing evaluation/therapy should be conducted by a registered dietician and a speech-language/swallowing therapist and is recommended for patients who have significant weight loss (>10% ideal body weight), and/or difficulty with speech/swallowing, and/or for patients whose treatment is likely to affect speech/swallowing
- Computed tomography (CT) with contrast and/or magnetic resonance imaging (MRI) with contrast of primary site and neck, as indicated
- Positron emission tomography-computed tomography (PET-CT), as indicated
- Chest CT scan, if not included with other imaging
- Examination under anesthesia with endoscopy, as indicated
- Preanesthesia studies
- Dental/prosthetic evaluation, including jaw imaging, as indicated



### Follow-up and Surveillance

- Head and neck examination (note that the ranges are based on risk of relapse, second primaries, treatment sequelae, and toxicities):
  - Year 1, every 1 to 3 months
  - Year 2, every 2 to 6 months
  - Year 3–5, every 4 to 8 months
  - After 5 years, annually, as clinically indicated
- Annual thyroid-stimulating hormone (TSH) screening up to 5 years only for those patients that receive post-operative RT to the neck
- Speech/swallowing assessment at 6 and 12 months post-RT; additional assessment and rehabilitation, as clinically indicated by a speech-language/swallowing therapist
- Hearing evaluation and rehabilitation, as clinically indicated
- Follow-up with a registered dietician to evaluate nutritional status and until the patient achieves a nutritionally stable baseline
- Routine dental follow-up/rehabilitation and evaluation up to 3 years, specifically:
  - Half-way through treatment
  - At the end of treatment
  - 6 weeks post treatment
  - 2–3 months post treatment
  - 6 months post treatment
  - 12 months post treatment
  - Yearly for the next 2 years
- Physiotherapy is indicated for all patients undergoing major head and neck resection during the first 3–6 months post-operation

The Head and Neck Tumour Team encourages patient participation in clinical trials.  
In addition, all patient cases should be presented & discussed at a multidisciplinary Tumour Board.

- Restage to assess recurrent or persistent disease – consider PET scan
- Biopsy of recurrent lesion(s), as clinically indicated

- Treatment should be individualized based on patient performance status and extent of disease

**Local disease**

*See algorithm for Early-Stage Oral Cavity Cancer*

**Regional disease**

*See algorithm for Advanced-Stage Oral Cavity Cancer*

**Distant disease**

*See algorithm for Advanced-Stage Oral Cavity Cancer*

**Unresectable nodal disease or unfit for surgery**

*See algorithm for Very Advanced-Stage Oral Cavity Cancer*

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## Appendix A: TNM Classification<sup>37</sup>

Primary tumour (T)	
TX	Primary tumour cannot be evaluated
Tis	Carcinoma <i>in situ</i>
T1	Tumour ≤ 2 cm or less at its greatest dimension
T2	Tumour > 2 cm but depth of invasion is ≤ 5 mm in greatest dimension
T3	Tumour > 4 cm in dimension
T4a	Moderately advanced local disease
	Tumour invades adjacent structures only (e.g. the bones of the jaw or face, deep muscle of the tongue, skin of the face, or the maxillary sinus)
T4b	Very advanced local disease
	Tumour invades masticular space, pterygoid plates or skull bases and/or encases internal carotid artery
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, ≤ 3 cm in greatest dimension
N2	Metastasis in a single ipsilateral lymph node, > 3 cm but ≤ 6 cm in greatest dimension
	Metastases in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension
	Metastases in bilateral or contralateral lymph nodes, none > 6 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node > 3 cm but ≤ 6 cm in greatest dimension
N2b	Metastases in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension
N2c	Metastases in bilateral or contralateral lymph nodes, none > 6 cm in greatest dimension
N3	Metastasis in a lymph node > 6 cm in greatest dimension
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
Stage grouping	
0	Tis N0 M0
I	T1 N0 M0
II	T2 N0 M0
III	T3 N0 M0
	T1 N1 M0
	T2 N1 M0
	T3 N1 M0
IVA	T4a N0 M0
	T4a N1 M0
	T1 N2 M0
	T2 N2 M0
	T3 N2 M0
	T4a N2 M0
IVB	Any T N3 M0
	T4b Any N M0
IVC	Any T Any N M1

## Appendix B: ECOG Performance Status<sup>38</sup>

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead



## Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial Head/Neck Tumour Team. Members include otolaryngology – head and neck surgeons, radiation oncologists, medical oncologists, dentists, nurses, pathologists, and patient advisors. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Head/Neck Tumour Team, external participants identified by the Working Group Lead, and a methodologist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Resource Unit Handbook](#).

This guideline was originally developed in 2014 and updated in 2023.

## Levels of Evidence

<b>I</b>	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
<b>II</b>	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
<b>III</b>	Prospective cohort studies
<b>IV</b>	Retrospective cohort studies or case-control studies
<b>V</b>	Studies without control group, case reports, expert opinion

## Strength of Recommendations

<b>A</b>	Strong evidence for efficacy with a substantial clinical benefit; strongly recommended
<b>B</b>	Strong or moderate evidence for efficacy but with a limited clinical benefit; generally recommended
<b>C</b>	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.); optional
<b>D</b>	Moderate evidence against efficacy or for adverse outcome; generally not recommended
<b>E</b>	Strong evidence against efficacy or for adverse outcome; never recommended

## Maintenance

A formal review of the guideline will be conducted in 2026. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

## Abbreviations

ChemoRT, chemoradiotherapy; CT, computed tomography; DFS, disease-free survival; ECOG, Eastern Cooperative Oncology Group; EORTC, European Organization for Research and Treatment of Cancer; MRI, magnetic resonance imaging; MeSH, medical subject heading; NCCN, National Comprehensive Cancer Network; ND, neck dissection; OS, overall survival; PS, performance status; PET-CT, positron emission tomography-computed tomography; PORT, postoperative radiotherapy; RCT, randomized controlled trial;

RT, radiotherapy; RTOG, Radiotherapy Oncology Group; SCC, squamous cell carcinoma; TNM, tumour/node/metastasis; TSH, thyroid-stimulating hormone

## Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Head/Neck Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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## Conflict of Interest Statements

**Dr. Robyn Banerjee** has nothing to disclose.

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