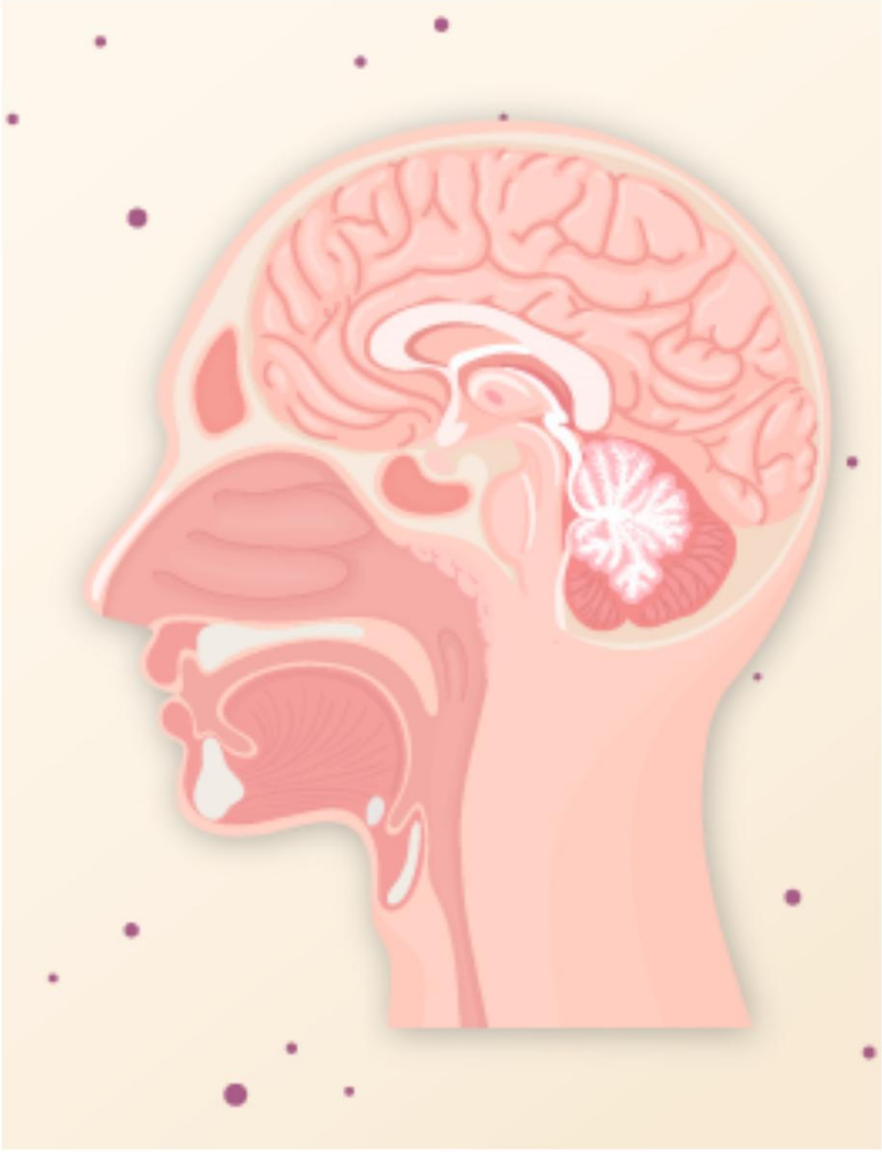
National Cancer Treatment Guideline for Head Neck Cancer 2026



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Disclaimer and Scope of Use

This guideline has been developed by the Ministry of Health, Republic of Maldives, in collaboration with regional healthcare providers and international health authorities. It is intended to serve as a reference framework for clinicians, allied health professionals, and policymakers engaged in the diagnosis, treatment, and management of Head and Neck Cancers, with a specific focus on Oral Cancer within the Maldivian healthcare context.

The recommendations contained herein are based on the best available international evidence, including guidelines from the National Comprehensive Cancer Network (NCCN), the European Society for Medical Oncology (ESMO), and the World Health Organization (WHO), adapted to the resource and infrastructural realities of the Maldives.

> **Note:** *This guideline does not supersede the clinical judgment of qualified healthcare professionals. Treatment decisions should always be individualized, taking into account patient-specific factors, comorbidities, and informed patient preference.*

This document should be reviewed and updated every three years, or sooner if significant new evidence emerges or the national healthcare landscape changes.

Contents

1. Introduction

The Maldives, an archipelagic nation situated in the Indian Ocean, faces distinctive challenges in delivering equitable and effective healthcare, particularly for oncological conditions that demand specialised intervention and sustained long-term management. The dispersed geography of the island nation, limited specialist health infrastructure, shortages of trained oncology professionals, and the widespread prevalence of betel nut (areca nut) and tobacco use among both young and elderly populations significantly compound the challenge of oral cancer prevention, early detection, and treatment.

Head and Neck Cancers (HNC) represent a heterogeneous group of malignancies arising from the mucosal surfaces of the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, and salivary glands. Among these, Oral Squamous Cell Carcinoma (OSCC) constitutes the most prevalent subtype in the South Asian context and demands focused clinical and public health attention in the Maldives.

The aim of this national guideline is to provide a comprehensive, evidence-based, and standardised framework for the diagnosis, staging, management, and referral of Head and Neck Cancers, with an emphasis on oral cancer, ensuring that patients across all atolls receive consistent and optimal care regardless of geographic location or level of healthcare facility.

The Ministry of Health, in partnership with regional healthcare providers, tertiary centres, and international health agencies, has developed this initiative to:

- Strengthen early detection and reduce diagnostic delays across the referral network.
- Standardise clinical management protocols across primary, secondary, and tertiary care levels.
- Improve cancer care infrastructure and capacity, particularly for underserved atoll communities.
- Increase community and professional awareness of the symptoms and risk factors for oral cancer.
- Define clear, tiered referral pathways that improve patient navigation within the national health system.

2. Literature Review and Epidemiology

Head and neck cancers are among the most common malignancies worldwide, with oral cancer representing a significant and disproportionate burden in South and Southeast Asia. Marked geographic heterogeneity exists in both incidence and mortality, driven by differences in lifestyle risk factor prevalence, access to healthcare, and the availability of early detection programmes.

Global Burden:

Globally, lip and oral cavity cancer ranks as the 16th most common cancer, accounting for approximately 377,713 new cases and 177,757 deaths annually (Global Cancer Observatory, IARC 2020).

The Indian subcontinent accounts for approximately one-third of the global burden of oral cancer. South Asia recorded the highest Age-Standardised Mortality Rate (ASMR) of oral cancer at 6.36 per 100,000 in 2019, followed by Central Europe.

Maldivian Context:

Formal cancer registry data for the Maldives remains limited; however, patterns of tobacco and betel nut use closely mirror those of neighbouring South Asian nations. The use of betel nut (areca nut) mixed with tobacco a known Group 1 carcinogen (IARC) is widespread across all atolls and is a primary driver of OSCC risk in the Maldivian population.

Chewing of betel nut is practised by an estimated 10%-20% of the world's population, with the highest prevalence in South and Southeast Asia and the Pacific. This habit is independently associated with oral submucous fibrosis (a premalignant condition), leukoplakia, and frank invasive OSCC.

Survival and Prognostic Data:

Despite advances in surgical and oncological management, the five-year survival rate for oral cancer in developed countries remains approximately 65%, and is substantially lower in low- and middle-income settings due to late-stage presentation. The prognosis of OSCC is closely linked

to stage at diagnosis with five-year survival exceeding 80% for Stage I disease but falling below 40% for Stage IV disease underscoring the critical importance of early detection and referral.

Socioeconomic Determinants:

Low socioeconomic status is independently associated with increased oral cancer incidence and poorer outcomes, due to higher rates of risk factor exposure, lower health literacy, barriers to care access, and delayed presentation. These factors are particularly relevant in remote atoll communities within the Maldives.

Note: *Evidence consistently shows that stage at diagnosis is the single strongest predictor of survival in oral cancer. Any reduction in diagnostic delay has a proportionate and significant impact on patient outcomes.*

3. Case Definitions and Histological Classification

3.1 Definition

Oral cancer refers to malignant neoplasms arising from the mucosal surfaces of the oral cavity, including the lips, tongue (anterior two-thirds), floor of the mouth, buccal mucosa, upper and lower gingivae, hard palate, and the retromolar trigone. For the purposes of this guideline, Head and Neck Cancer (HNC) encompasses malignancies of the oral cavity, oropharynx, nasopharynx, hypopharynx, larynx, nasal cavity, paranasal sinuses, and major and minor salivary glands.

3.2 Aetiology and Risk Factors

Oral Squamous Cell Carcinoma (OSCC) is primarily a preventable disease driven by environmental exposures. Key established risk factors include:

- Tobacco use (smoked and smokeless forms): dose-dependent relationship with OSCC risk. [1]
- Areca (betel) nut chewing: an independent Group 1 carcinogen (IARC 2004), causing oral submucous fibrosis and OSCC. [2]
- Alcohol consumption: synergistic effect with tobacco combined use multiplies OSCC risk by up to 30-fold. [3]
- Human Papillomavirus (HPV), types 16 and 18: increasingly implicated in oropharyngeal squamous cell carcinoma (OPSCC). [4]
- Chronic sun exposure: predominantly associated with lip cancer (squamous cell carcinoma of the vermilion border). [5]
- Dietary deficiencies and poor oral hygiene: indirect contributory factors. [6]
- Chronic immunosuppression (e.g., post-transplant patients, HIV infection). [7]

3.3 Potentially Malignant Disorders (PMDs)

The World Health Organisation (WHO) introduced the concept of ‘Potentially Malignant Disorders’ (PMDs) in 2005, recognising that the majority of OSCC cases evolve from precursor lesions. Clinicians must be vigilant for the following PMDs:

PMD	Description	Malignant Transformation Rate
Leukoplakia	White patch not rubbed off; cannot be attributed to any other condition	1%-18% (higher for non-homogeneous type)
Erythroplakia	Fiery red patch; cannot be attributed to any other condition	Up to 51%
Oral Submucous Fibrosis (OSMF)	Progressive fibrosis of oral mucosa; closely linked to areca nut use	7%-13%
Erythroleukoplakia	Mixed red and white lesion; high-risk PMD	Up to 28%
Oral Lichen Planus (erosive)	Chronic inflammatory mucosal condition; erosive/atrophic types at higher risk	0.4%-2%

Note: *Any persistent oral mucosal change lasting more than two weeks should be considered a PMD until proven otherwise and must prompt immediate referral for specialist evaluation and biopsy.*

3.4 Histological Subtypes of OSCC

Oral Squamous Cell Carcinoma constitutes over 90% of oral cavity malignancies. Recognised histological subtypes include:

- Verrucous carcinoma (VC) – a low-grade, exophytic variant with a favourable prognosis
- Adenoid/acantholytic/pseudoglandular SCC (AdSCC)
- Spindle cell / sarcomatoid carcinoma (SCSC)
- Adenosquamous carcinoma (ASC)
- Basaloid SCC (BSCC) – aggressive variant with poor prognosis
- Papillary SCC (PSCC)
- Cuniculatum carcinoma
- Mucoepidermoid carcinoma (minor salivary gland origin)

4. Signs and Symptoms

4.1 Potentially Malignant / Early Warning Signs

Clinicians at all levels of the healthcare system should recognise the following early warning features, which warrant urgent evaluation:

- A white or red patch (leukoplakia, erythroplakia) on the mucosa of the mouth, tongue, or gum that does not rub off.
- A non-healing oral ulcer or sore persisting for more than two weeks.
- An unexplained lump, thickening, or hardness in the lip, tongue, cheek, or floor of the mouth.
- Restriction of mouth opening (trismus) or reduced tongue mobility.
- Unexplained numbness or paraesthesia of the lips, tongue, or chin.
- Unexplained bleeding from the oral mucosa without apparent traumatic cause.

4.2 Symptoms of Established Oral Cancer

- Progressively enlarging exophytic or ulcerative oral lesion.
- Pain in the mouth, jaw, or referred ear otalgia (particularly associated with tongue base or tonsillar fossa tumours).
- Difficulty or pain on swallowing (dysphagia / odynophagia).
- Change in voice or hoarseness (laryngeal involvement).
- Unexplained loosening of teeth or poorly fitting dentures.
- Cervical lymphadenopathy – painless, firm, or fixed enlarged lymph node(s) in the neck.
- Unexplained weight loss, fatigue, or anorexia.

4.3 Head and Neck Cancer by Subsite: Key Presenting Features

Subsite	Common Symptoms	Clinical Signs
Oral Cavity	Mouth sore, pain, dysphagia, trismus	Ulcerative/exophytic lesion, induration, cervical LN
Oropharynx	Sore throat, referred otalgia, dysphagia	Tonsil mass, base of tongue lesion, neck node
Nasopharynx	Epistaxis, nasal obstruction, hearing loss, diplopia	Post-nasal mass, cervical LN (often bilateral)
Hypopharynx	Dysphagia, odynophagia, weight loss, hoarseness	Piriform fossa mass, neck node
Larynx	Hoarseness (early), stridor (late), dysphagia	Vocal cord lesion, subglottic spread
Salivary Gland	Painless mass (parotid), facial nerve palsy	Firm parotid/submandibular mass

5. Differential Diagnosis

A number of benign, inflammatory, and infective conditions can mimic the presentation of oral cancer. Clinicians must maintain a high index of suspicion and refer promptly when uncertainty exists.

Category	Condition	Distinguishing Features
Inflammatory / Immune	Recurrent aphthous ulcers (RAS)	Round, shallow, painful; typically <2 cm; heals in 7–14 days
	Oral lichen planus (reticular)	Bilateral white striae (Wickham's striae); confirmed by biopsy
Infective	Oral candidiasis (pseudomembranous)	White plaque; rubs off to reveal erythematous base; responds to antifungals
	Herpetic gingivostomatitis	Acute onset; vesicles → ulcers; associated fever; primary herpes
	Oral hairy leukoplakia	Lateral border of tongue; corrugated white lesion; associated with EBV/HIV
Traumatic	Traumatic ulcer / fibroma	Clear history of trauma; resolves when irritant removed within 2 weeks
Benign Lesions	Geographic tongue / median rhomboid glossitis	Characteristic appearance; changes pattern; asymptomatic
	Necrotising sialometaplasia	Palate; crater-like ulcer mimicking malignancy; self-limiting; biopsy definitive
Systemic	Pemphigus vulgaris / MMP	Desquamative gingivitis; blistering; positive Nikolsky sign; confirmed by biopsy with DIF

Note: *Any oral lesion that persists beyond two weeks without an identifiable benign cause must be biopsied. The clinical appearance alone is insufficient to exclude malignancy.*

6. Diagnostic Workup and Staging

6.1 Clinical Assessment

A systematic approach to clinical assessment is essential at all levels of the referral pathway:

- Complete history: duration of symptoms, risk factor exposure (tobacco, areca nut, alcohol), previous oral lesions, prior cancer treatment, family history.
- Full head and neck examination: bimanual palpation of the oral cavity, examination of all mucosal surfaces, assessment of mouth opening, tongue mobility, dentition, and palate.
- Cervical lymph node examination: systematic palpation of all nodal levels (Level I–VI), noting size, consistency, and fixity.
- Cranial nerve assessment: in particular CN V (trigeminal), CN VII (facial), CN IX, X, XI, XII.
- Fiberoptic nasopharyngoscopy / laryngoscopy: as clinically indicated for oropharyngeal, nasopharyngeal, or laryngeal subsites.

6.2 Diagnostic Investigations

Investigation	Purpose / Indication	Level of Care
Incisional biopsy	Histopathological diagnosis of suspected malignant / premalignant lesion	Secondary / Tertiary
Fine Needle Aspiration Cytology (FNAC)	Evaluation of suspicious cervical lymph nodes	Secondary / Tertiary
Contrast-enhanced CT (CECT) of neck/chest	Nodal staging, assessment of bony involvement, lung metastasis	Tertiary
MRI with and without contrast	Soft tissue characterisation, perineural spread, skull base assessment	Tertiary
Orthopantomogram (OPG) / Dental CT	Assessment of mandibular / maxillary bone involvement; preoperative dental evaluation	Secondary / Tertiary
FDG-PET/CT	Staging of advanced disease, detection of occult primary, assessment of distant metastasis	Tertiary (where available)
Examination Under Anaesthesia (EUA) + Panendoscopy	Assessment of lesion extent, synchronous primaries, mapping for surgery	Tertiary
HPV testing (p16 IHC)	Oropharyngeal SCC – prognostic stratification; guides treatment intensity	Tertiary
Haematology, LFT, RFT, coagulation	Pre-treatment fitness evaluation; assessment for systemic comorbidities	All levels

6.3 TNM Staging System (AJCC 8th Edition)

Staging of oral cavity cancer follows the American Joint Committee on Cancer (AJCC) 8th Edition TNM Classification. Accurate staging is essential for treatment planning and prognostication.

Stage	Numerical Staging	TNM Classification	Description
0	Pre-invasive	Tis N0 M0	Carcinoma in situ; high risk of progression to invasive cancer
I	Early invasive	T1 N0 M0	Tumour ≤2 cm in greatest dimension; no nodal or distant spread
II		T2 N0 M0	Tumour >2 cm but ≤4 cm; no nodal or distant spread
III		T3 N0 M0 / T1–3 N1 M0	Tumour >4 cm OR spread to a single ipsilateral node ≤3 cm
IVA	Advanced locoregional	T4a; N2; any T N2 M0	Moderately advanced local disease or multiple/contralateral nodal involvement
IVB		T4b; any T N3 M0	Very advanced local disease (masticator space, skull base, carotid encasement) or node >6 cm
IVC	Distant metastasis	Any T, Any N, M1	Distant metastases present (lung, liver, bone, brain, distant nodes)

Note: *Depth of Invasion (DOI) is incorporated in AJCC 8th Edition T-staging for oral cavity tumours. DOI >5 mm upstages T1 → T2; DOI >10 mm upstages T2 → T3. This requires careful pathological assessment of the resected specimen.*

7. Oral Cancer Screening

7.1 Rationale for Screening

Despite the fact that the oral cavity is directly accessible for visual inspection, only approximately 30% of oral and pharyngeal cancers are detected at an early stage. Up to 50% are diagnosed at Stage III or IV. This delay significantly worsens prognosis and increases the cost and complexity of treatment.

The principal reason for late diagnosis is multifactorial: patients seeking medical attention too late, diagnostic delays at the primary care level, and the absence of structured screening and referral protocols. In the Maldivian context, geographic barriers to healthcare access add further complexity.

7.2 Recommended Screening Approach

The primary screening tool is a systematic visual and tactile clinical examination of the oral cavity. In accordance with World Health Organization and National Institute of Dental and Craniofacial Research (NIDCR) recommendations, this should include:

- Systematic visual inspection of the face, neck, lips, labial and buccal mucosa, gingivae, floor of the mouth, tongue (dorsal, ventral, and lateral borders), palate, and oropharynx.
- Use of a mouth mirror and adequate lighting to visualise all mucosal surfaces.
- Bimanual palpation of the floor of the mouth, tongue, and regional lymph nodes.
- Documentation of any mucosal abnormality: location, size, colour, texture, and duration.

7.3 Adjunctive Screening Tools

While conventional visual examination remains the standard, the following adjunctive tools may be considered as supplementary aids (not as replacements) in resource-appropriate settings:

- Toluidine Blue (Tolonium Chloride) vital staining: enhances identification of high-risk lesions; may increase sensitivity but has limited specificity.
- VELscope / Vizilite (fluorescence-based devices): may assist in identifying abnormal tissue, but evidence remains insufficient to recommend routine use as a standalone screening tool.

- Oral brush biopsy (OralCDx): useful as an adjunct when incisional biopsy is not immediately feasible.

7.4 High-Risk Groups for Targeted Screening

The following populations should be prioritised for systematic opportunistic oral cancer screening at primary and secondary care encounters:

- Adults aged ≥40 years with a history of tobacco use (smoked or smokeless).
- Regular betel nut / areca nut chewers (with or without tobacco).
- Heavy alcohol consumers.
- Individuals with previously identified oral premalignant lesions.
- Immunocompromised individuals (post-transplant, HIV-positive).
- Individuals with a previous head and neck cancer diagnosis.

Note: *Any mucosal abnormality that persists beyond two weeks in a high-risk patient should be assumed to be potentially malignant until histopathological assessment proves otherwise. Immediate referral to secondary or tertiary care is mandatory.*

8. Pathway of Patient Referrals

A clearly defined, tiered referral pathway is essential to ensure timely and appropriate management of oral cancer in the Maldives. The following framework delineates responsibilities and referral criteria at each level of the national healthcare system.

8.1 Overview of the Three-Tier Referral System

Level	Facility	Responsible Clinician	Role in Referral Pathway
Primary Care	Island Health Centres; Atoll Hospitals	General Practitioners; Primary Care Physicians; Community Health Workers	Screening; initial assessment; risk factor counselling; referral upward
Secondary Care	Regional Hospitals (e.g., IGMH regional facilities)	General Dentists; ENT Specialists; General Surgeons; Radiologists	Clinical assessment; imaging; FNAC; incisional biopsy; referral for oncology
Tertiary Care	Tertiary Hospitals in Malé (e.g., IGMH, ADK, Hulhumale Hospital)	Oncosurgeons; Medical Oncologists; Radiation Oncologists; Oral & Maxillofacial Surgeons; MDT Team	Definitive staging; MDT discussion; surgery; chemotherapy; radiotherapy; palliative care

8.2 Detailed Referral Pathway by Clinical Scenario

Scenario A – Patient Presenting with Suspected Oral Lesion at Primary Care Level

Primary care clinician identifies a suspicious oral mucosal lesion or relevant symptom:

Step 1 – Initial Assessment at Island Health Centre / Atoll Hospital:

- Conduct a thorough oral cavity and head and neck examination.
- Document the lesion: site, size, colour, surface, and duration.
- Assess risk factors: tobacco, betel nut, alcohol, prior lesions.
- Provide basic risk factor counselling and smoking cessation advice.
- If the lesion has been present for less than two weeks and an identifiable cause exists (e.g., trauma), treat and review at two weeks.

- If the lesion persists beyond two weeks, has no identifiable benign cause, or exhibits high-risk features (induration, fixity, bleeding, cervical lymphadenopathy): IMMEDIATE REFERRAL to secondary care.

Step 2 – Assessment at Regional Hospital (Secondary Care):

- Specialist assessment by General Dentist, Oral Surgeon, or ENT Surgeon.
- Obtain imaging as indicated: OPG (orthopantomogram) for bony involvement; chest X-ray for baseline.
- Perform FNAC of any suspicious cervical lymph node.
- Incisional biopsy of suspicious oral mucosal lesion.
- Refer promptly to tertiary care if histopathology confirms dysplasia, premalignancy, or malignancy.

Step 3 – Tertiary Care Management (MDT):

- Complete clinical, radiological, and pathological staging (CECT, MRI, FDG-PET/CT as indicated).
- Multidisciplinary Team (MDT) meeting: oncosurgery, medical oncology, radiation oncology, radiology, pathology, dental, nutrition, speech and swallowing therapy.
- Pre-treatment dental assessment and oral rehabilitation.
- Nutritional assessment and dietitian involvement.
- Speech and swallowing evaluation.
- Fertility and reproductive counselling where applicable.
- Hepatitis B screening (prior to chemotherapy).
- Definitive treatment: surgery, radiation, chemotherapy, targeted therapy, or combination (per Section 9).

Scenario B – Patient Presenting with Cervical Lymphadenopathy as Primary Complaint

- Primary care: exclude infective/inflammatory cause; if lymphadenopathy persists >3–4 weeks or is associated with weight loss, night sweats, or other systemic symptoms – REFER to secondary care.
- Secondary care: FNAC of lymph node; baseline imaging (neck ultrasound, chest X-ray); ENT or oral examination to identify primary site; refer to tertiary care.
- Tertiary care: staging workup including CECT neck and chest, MRI, FDG-PET/CT; direct laryngoscopy/nasopharyngoscopy to identify occult primary; MDT review and definitive management.

Scenario C – Emergency / Urgent Referral Criteria

The following features mandate URGENT (same-day or next-day) referral to tertiary care, bypassing secondary care where appropriate:

- Rapidly enlarging neck mass.
- Stridor or respiratory compromise due to laryngeal/hypopharyngeal tumour.
- Severe dysphagia with nutritional compromise or aspiration risk.
- Active haemorrhage from an oral/pharyngeal tumour.
- Facial nerve palsy of suspected malignant aetiology.
- Trismus with suspected deep space involvement.

8.3 Referral Pathway Summary Diagram

The following flow diagram summarises the stepwise referral pathway for suspected Head and Neck / Oral Cancer:

STEP 1 – PRIMARY CARE LEVEL
Island Health Centres / Atoll Hospitals

- Screening and initial clinical assessment
- Risk factor identification and counselling
- Lesion <2 weeks + identifiable cause → Treat and REVIEW at 2 weeks
- **Lesion >2 weeks / high-risk features → REFER to Secondary Care**

▼ **REFER** ▼

STEP 2 – SECONDARY CARE LEVEL
Regional Hospitals

- Specialist clinical assessment (Dentist / ENT / Oral Surgeon)
- Imaging: OPG, chest X-ray, neck ultrasound
- FNAC of suspicious cervical lymph node
- Incisional biopsy of oral lesion
- **Histopathology confirms dysplasia / malignancy → URGENT REFER to Tertiary Care**

▼ **REFER** ▼

STEP 3 – TERTIARY CARE LEVEL (MDT)
Tertiary Hospitals in Malé – Oncosurgery / Medical Oncology / Radiation Oncology

- Complete radiological staging: CECT, MRI, FDG-PET/CT
- EUA + panendoscopy where indicated
- MDT meeting: oncosurgery, medical oncology, radiation oncology, radiology, pathology, dental, dietitian, speech therapy
- Pre-treatment dental assessment, nutritional optimisation, fertility counselling
- **Definitive treatment: surgery ± adjuvant radiotherapy ± chemotherapy / systemic therapy**

▼ **POST-TREATMENT** ▼

FOLLOW-UP – Shared Care (Tertiary + Secondary + Primary)

- Structured follow-up at tertiary centre; shared care with regional hospital as clinically indicated
- Surveillance imaging, dental review, nutritional and speech therapy follow-up
- **Recurrence: re-refer immediately to tertiary care for MDT review**

9. Treatment

9.1 Principles of Treatment

Treatment of Head and Neck Cancer, particularly oral cancer, is multimodal and must be individualised based on tumour subsite, clinical and pathological stage, histological features, patient performance status, patient preferences, and the available multidisciplinary expertise. All treatment decisions must be made within a Multidisciplinary Team (MDT) framework.

9.2 Treatment by Stage

Stage	Disease Extent	Recommended Treatment Approach
Stage 0 (CIS)	Carcinoma in situ	Surgical excision with clear margins; close surveillance
Stage I-II	T1-T2, N0, M0	Single modality: surgery (preferred) or definitive radiotherapy. Elective neck dissection considered for DOI >4 mm.
Stage III-IVA	T3-T4a or N+, M0	Surgery (primary resection + neck dissection) + adjuvant radiotherapy ± concurrent cisplatin-based chemotherapy (if adverse features present).
Stage IVB	Unresectable locoregional disease	Definitive concurrent chemoradiotherapy (cisplatin + radiotherapy) OR cetuximab + radiotherapy for cisplatin-ineligible patients.
Stage IVC	Distant metastatic disease	Systemic therapy (platinum-based doublet ± cetuximab; pembrolizumab for PD-L1 CPS ≥20). Palliative radiotherapy for symptom control. Best supportive care.

9.3 Surgery

Surgery remains the cornerstone of treatment for resectable oral cavity cancer. Key surgical principles include:

- Wide local excision with minimum 1 cm clear histological margins.
- Neck dissection (selective or comprehensive) based on nodal status and primary tumour characteristics.
- Reconstruction: primary closure for small defects; local/regional flaps (pedicled pectoralis major, submental, nasolabial flaps) or free microvascular flaps (radial forearm, anterolateral thigh, fibula osteocutaneous) for complex defects. [8]

- Mandibulectomy (marginal or segmental) when mandibular periosteum or bone is involved.
- Maxillectomy (infrastructure, total, or radical) for maxillary tumours.

Adverse Pathological Features Mandating Adjuvant Therapy:

- Positive or close surgical margins (<1 mm).
- Extranodal extension (ENE) of nodal disease.
- Multiple positive lymph nodes.
- Perineural invasion (PNI) or lymphovascular invasion (LVI).
- T3 or T4 primary tumour stage.

9.4 Radiotherapy

Radiotherapy is an integral component of Head and Neck Cancer management, used in the following settings:

- Definitive radiotherapy: for early-stage laryngeal / oropharyngeal cancers where organ preservation is achievable; or for patients unfit for surgery.
- Adjuvant (post-operative) radiotherapy: for adverse pathological features following surgical resection, delivered to the primary site and bilateral neck.
- Palliative radiotherapy: for symptom control in unresectable or metastatic disease.

Standard radiotherapy doses:

- Definitive: 66–70 Gy in 33–35 fractions over 6–7 weeks (conventional fractionation) or 60–66 Gy with altered fractionation.
- Adjuvant: 60 Gy to the surgical bed; 66 Gy to high-risk areas (positive margins, ENE).
- Palliative: 20 Gy in 5 fractions or 30 Gy in 10 fractions (standard palliative regimens).

Intensity-Modulated Radiotherapy (IMRT) is the current standard of care, minimising dose to critical structures including the parotid glands (reducing xerostomia), spinal cord, and mandible.

9.5 Systemic Therapy

Concurrent Chemotherapy

High-dose cisplatin (100 mg/m² every 3 weeks) concurrent with radiotherapy is the standard regimen for locoregionally advanced disease. It is used in:

- Definitive chemoradiotherapy for unresectable disease.
- Adjuvant concurrent chemoradiotherapy for positive margins or extranodal extension.

Cisplatin contraindications (renal impairment, hearing loss, peripheral neuropathy, poor performance status): consider weekly cisplatin (40 mg/m²) or cetuximab as alternatives.

Induction Chemotherapy

Induction (neoadjuvant) chemotherapy with TPF (docetaxel, cisplatin, and 5-fluorouracil) may be considered in selected cases of unresectable or borderline resectable locoregionally advanced disease, as part of an organ preservation strategy or to downstage prior to definitive local therapy.

Targeted Therapy

Cetuximab (an anti-EGFR monoclonal antibody) is used in combination with radiotherapy as an alternative to cisplatin-based chemoradiotherapy in patients with locoregionally advanced disease who are ineligible for platinum-based chemotherapy, and in the recurrent/metastatic setting as part of the EXTREME regimen.

Immunotherapy

Pembrolizumab (anti-PD-1 checkpoint inhibitor) is approved by the FDA and EMA for recurrent/metastatic HNSCC as:

- First-line monotherapy for PD-L1 CPS ≥20 tumours (or combination with chemotherapy for all comers). [9]
- Second-line therapy after platinum-containing chemotherapy failure. [10]

9.6 Pre-Treatment Assessment Checklist

The following must be completed prior to initiation of any treatment modality:

- Full haematological and biochemical evaluation (FBC, LFT, RFT, coagulation, LDH).
- Hepatitis B surface antigen and core antibody (particularly prior to immunotherapy or chemotherapy).
- Dental assessment and oral rehabilitation (extraction of non-restorable teeth; prophylactic fluoride trays).
- Nutritional assessment with dietitian input; consideration of prophylactic percutaneous endoscopic gastrostomy (PEG) tube placement for patients at high risk of dysphagia.
- Speech and swallowing evaluation with speech-language therapist (pre- and post-treatment baseline).
- Smoking cessation counselling: active smokers have significantly worse treatment outcomes and higher complication rates; structured cessation support should be offered.
- Fertility and reproductive counselling for patients of reproductive age prior to chemotherapy or pelvic radiotherapy.
- Psychosocial assessment and supportive care planning.

10. Supportive Care and Multidisciplinary Approach

Optimal outcomes in Head and Neck Cancer require a comprehensive, patient-centred, multidisciplinary team (MDT) approach that extends beyond oncological treatment to address functional, nutritional, psychological, and social needs.

MDT Discipline	Role and Responsibilities
Oncosurgery	Primary resection, reconstruction, neck dissection, operative planning
Medical Oncology	Systemic therapy planning (chemotherapy, targeted therapy, immunotherapy); toxicity management
Radiation Oncology	Radiotherapy planning (IMRT/VMAT), simulation, dosimetry, acute and late toxicity management
Dental / Oral Medicine	Pre-treatment dental assessment, fluoride application, prosthetic rehabilitation, osteoradionecrosis prevention
Dietitian / Nutritionist	Pre-treatment nutritional optimisation, enteral nutrition support (NG/PEG), monitoring during treatment
Speech & Swallowing Therapist	Pre- and post-treatment assessment; dysphagia rehabilitation; voice rehabilitation post-laryngectomy
Palliative Care Team	Pain management, symptom control, end-of-life planning, advance care directives
Psycho-oncology / Social Work	Psychological support, depression/anxiety management, social support and financial counselling
Radiology	Imaging reporting, image-guided biopsy, interventional radiology
Pathology	Histopathology, cytopathology, IHC, molecular biomarker analysis (HPV, PD-L1)

11. Follow-Up and Surveillance

Structured post-treatment follow-up is essential for the early detection of locoregional recurrence, distant metastasis, second primary tumours, and management of treatment-related late effects.

Follow-Up Period	Frequency of Review	Key Assessments
Year 1 (post-treatment)	Every 1-3 months	Clinical exam, symptoms review, CECT neck ± chest at 3 months post-treatment
Year 2	Every 2-4 months	Clinical exam, imaging as indicated by symptoms or findings
Years 3-5	Every 4-6 months	Clinical exam; annual imaging if high-risk features
Beyond Year 5	Annual review	Screening for second primary tumours; late effects review

11.1 Additional Follow-Up Monitoring

- Thyroid function tests (TFT): every 6-12 months for patients who received neck irradiation (radiation-induced hypothyroidism risk).
- Dental review: every 6 months for patients who received radiotherapy to the oral cavity or oropharynx (osteoradionecrosis prevention).
- Annual chest CT or chest X-ray for patients with a smoking history or prior lung/distant metastasis.
- Speech and swallowing therapy: continued rehabilitation as clinically indicated.
- Nutritional monitoring and support: particularly for patients with post-treatment dysphagia or trismus.

12. Palliative Care

Palliative care should be integrated into the management of all patients with Head and Neck Cancer from the time of diagnosis, not reserved for the end-of-life phase. Early integration of palliative care is associated with improved quality of life, better symptom control, and, in some studies, improved survival.

12.1 Indications for Palliative-Intent Treatment

- Stage IVC (distant metastatic) disease.
- Locoregionally advanced disease not amenable to curative-intent surgery or radiotherapy.
- Disease recurrence after prior curative treatment, where re-treatment with curative intent is not feasible.
- Poor performance status (ECOG ≥3) precluding aggressive oncological treatment.

12.2 Palliative Interventions

- Palliative radiotherapy: for pain, bleeding, or obstructive symptoms.
- Systemic therapy: single-agent or doublet platinum-based chemotherapy; pembrolizumab monotherapy for eligible patients.
- Nutritional support: nasogastric or PEG tube feeding to maintain hydration and caloric intake.
- Tracheostomy: for airway compromise secondary to tumour obstruction.
- Opioid analgesia and adjuvant analgesics (tricyclics, gabapentinoids for neuropathic pain).
- Anxiolytics and antidepressants for psychological distress.
- Advance care planning and documentation of patient wishes; family communication.

Note: *Palliative care referral should not be delayed until curative options are exhausted. Concurrent oncology and palliative care management improves patient comfort, autonomy, and outcomes throughout the disease trajectory.*

13. References

The following references have been cited in the preparation of this guideline. All clinical recommendations are grounded in the best available international evidence and adapted to the Maldivian healthcare context.

1. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncology. 2009;45(4-5):309–316. doi:10.1016/j.oraloncology.2008.06.002
2. International Agency for Research on Cancer (IARC). Betel-quid and Areca-nut Chewing and Some Areca-nut Derived Nitrosamines. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Vol 85. Lyon: IARC Press; 2004.
3. Hashibe M, Brennan P, Chuang SC, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. Cancer Epidemiology, Biomarkers & Prevention. 2009;18(2):541–550.
4. Gillison ML, Koch WM, Capone RB, et al. Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. JNCI: Journal of the National Cancer Institute. 2000;92(9):709–720.
5. Marx RE, Stern D. Oral and Maxillofacial Pathology: A Rationale for Diagnosis and Treatment. 2nd ed. Chicago: Quintessence Publishing; 2012.
6. Conway DI, Petticrew M, Marlborough H, Berthiller J, Hashibe M, Macpherson LMD. Socioeconomic inequalities and oral cancer risk: A systematic review and meta-analysis of case-control studies. International Journal of Cancer. 2008;122(12):2811–2819.
7. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. Lancet. 2007;370(9581):59–67.
8. Urken ML, Cheung K, Marboe CC, et al. Analysis of 213 free flaps for head and neck reconstruction: indications and outcomes. Head & Neck. 2012;34(5):629–634.
9. Burtness B, Harrington KJ, Greil R, et al. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. Lancet. 2019;394(10212):1915–1928.
10. Ferris RL, Blumenschein G Jr, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. New England Journal of Medicine. 2016;375(19):1856–1867.

11. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 2.2024. Fort Washington, PA: NCCN; 2024. Available at: www.nccn.org
12. European Society for Medical Oncology (ESMO). ESMO Clinical Practice Guidelines: Squamous Cell Carcinoma of the Head and Neck. Annals of Oncology. 2020;31(11):1462–1475. Available at: www.esmo.org
13. World Health Organization. International Agency for Research on Cancer (IARC). Global Cancer Observatory – Cancer Today. Geneva: WHO; 2020. Available at: https://gco.iarc.fr
14. Ministry of Health, Republic of Maldives. National Cancer Control Strategy. Malé: Ministry of Health; 2022.
15. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians. 2021;71(3):209–249.
16. Amin MB, Edge SB, Greene FL, et al., eds. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017.
17. Rettig EM, D'Souza G. Epidemiology of head and neck cancer. Surgical Oncology Clinics of North America. 2015;24(3):379–396.
18. Lorch JH, Goloubeva O, Haddad RI, et al. Induction chemotherapy with cisplatin and fluorouracil alone or in combination with docetaxel in locally advanced squamous-cell cancer of the head and neck: long-term results of the TAX 324 randomised phase 3 trial. Lancet Oncology. 2011;12(2):153–159.