The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for the histopathological reporting of carcinomas of the oropharynx and nasopharynx

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Foreword

The cancer datasets published by the Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient.

Each dataset contains core data items (see Appendices C and D) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are those that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 95% of reports on cancer resections should record a full set of core data items. Other, non-core, data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholders were contacted to consult on this document:

- the British Society for Oral and Maxillofacial Pathology (BSOMP)
- the British Association of Head and Neck Oncologists (BAHNO)
- ENT-UK: Secretary
- the British Association of Oral and Maxillofacial Surgeons
- the UK and Ireland Association of Cancer Registries
- the National Cancer Registration and Analysis Service.

No major organisation changes or cost implications have been identified that would hinder the implementation of the dataset.

The information used by the authors to develop this dataset was obtained by undertaking a systematic search of the PubMed database. Key terms searched included 'oropharynx', 'nasopharynx', 'clinical trial', 'prognosis', 'survival', 'surgery', 'chemotherapy' and 'radiotherapy' between January 2011 and July 2026. In addition, abstracts from selected conference proceedings from American Society of Clinical Oncology (ASCO) were screened. The recommendations are in line with those of other national pathology organisations (College of American Pathologists, the Royal College of Pathologists of Australasia) and the ENT-UK Consensus document for the management of patients with head and neck malignancies (www.entuk.org/publications). They incorporate the core data items and commentary from the International Collaboration on Cancer Reporting (ICCR).[1] Published evidence was evaluated using modified SIGN guidance (see Appendix E). Consensus of evidence in the guideline was achieved by expert review. Gaps in the evidence were identified by College members via feedback received during consultation.

The recommendation that primary carcinomas of the oropharynx are investigated for human papillomavirus (HPV) implies that the appropriate analytical facilities should be available and funded and the tests quality assured. Facilities for investigation of the presence of EBV should also be available.

A formal revision cycle for all cancer datasets takes place on a 3-yearly basis. However, each year, the College will ask the author of the dataset, in conjunction with the relevant sub-specialty adviser to the College, to consider whether the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short note of the proposed changes will be placed on the College website for 2 weeks for Fellows' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Professional Guidelines team, Working Group on Cancer Services and Lay Advisory Group and was placed on the College website for consultation with the membership from 4 August to 2 September 2026. All comments received from the Working Group and membership were addressed by the author to the

satisfaction of the Chair of the Working Group and the Clinical Leads for Guideline Adjudication.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Professional Guidelines team and are available on request. The authors have declared no conflicts of interest.

1 Introduction

The dataset has been developed for the reporting of biopsy and resection specimens of the nasopharynx and oropharynx. The protocol applies to all invasive carcinomas of the nasopharynx and oropharynx including the base of tongue, tonsils, soft palate, posterior pharyngeal wall and uvula. Lymphomas and sarcomas are not included. Neck dissections and nodal excisions are dealt with in a separate dataset, and this dataset should be used in conjunction, where applicable.

The primary purpose of this document is twofold:

- to define the set of data necessary for the uniform recording and staging of the core pathological features in cancers of the nasopharynx and oropharynx
- to describe its application in sufficient detail and clarity that reports from different departments will contain equivalent information, allowing comparison of clinical practice and outcomes.

Optimal reporting of specimens from the head and neck area requires a partnership between the pathologist and surgeon/oncologist. The surgeon can help the pathologist to provide the information necessary for patient management by the appropriate handling and labelling of the specimen in the operating theatre. The regular discussion of cases at multidisciplinary team (and other clinicopathological) meetings and correlation with pre-operative imaging studies are important in maintaining and developing this partnership.[2]

The core pathological data are summarised as proformas that may be used as the main reporting format or may be combined with free text as required. The core data differ between nasopharynx and oropharynx, but a common proforma for these primary sites has been employed, in keeping with the ICCR dataset, and the lymph node dataset is common to all sites. Individual centres may wish to expand the detail in some sections, e.g. for sites and subsites, to facilitate the recording of data for particular tumour types.

The guidelines within this dataset should be implemented for the following reasons.

- Certain features of invasive mucosal carcinomas (type, size and grade of the primary carcinoma, the pattern of invasion and proximity of carcinoma to resection margins) have been shown to be related to clinical outcome.[3–11]
  - These features may therefore be important in: deciding on the most appropriate treatment for patients, including the extent of surgery and the use and choice of adjuvant radiotherapy, chemotherapy or targeted therapies;[12] monitoring changing patterns of disease, particularly by cancer registries.
  - These features provide sufficiently accurate pathological information that can be used, together with clinical data, for the patient to be given a prognosis.
- To allow correlation of resection specimens with preoperative imaging.
- To allow the accurate and equitable comparison of surgeons in different surgical units, to identify good surgical and pathological practice, and the selection and comparison of patients in clinical trials.

1.1 Design of this protocol

The RCPath recognises the authority of internationally accepted guidance documents (WHO, AJCC/UICC TNM and ICCR) and, to promote consistent reporting practice, adopts the recommendations of these organisations. This structured reporting protocol has been developed using the framework and data items specified in the ICCR dataset on cancers of the nasopharynx and oropharynx (published in 2024).[1] This protocol includes all the ICCR cancer dataset elements as well as additional information, elements and commentary. Core references have been updated to include relevant new information from 2021 to July 2025.

ICCR dataset elements for these cancers have been included verbatim and are indicated by the blue ICCR logo. ICCR core elements are mandatory, form part of the COSD data and are therefore represented as standards in this document. ICCR (and RCPath) non-core elements are recommended and may be included as guidelines or used routinely according to local practice. In general, non-core elements are those which are agreed should be included in the dataset but are not supported by level III-2 evidence.

Additional non-core data items that have not been included in the ICCR dataset but are recommended by RCPath are involvement of bone (required for TNM staging in some circumstances) and assessment of tumour-infiltrating lymphocytes (TILs).

1.2 Key changes to previous guideline

Key changes made to the previous guideline are outlined in the table below:

Section	Explanation
Whole document	*Change of HPV-negative to HPV-independent to reflect changed terminology*
5 Core data items	*Minor changes in wording and updating of references in all data items to align with ICCR dataset*
5.12 Ancillary studies	*The wording in the RCPath additional comments has been modified, and now clearly states that both p16 IHC and an HPV-specific test are required in all oropharynx SCCs*
6.2 Staging Appendix B	*Change of staging to TNM9*

1.3 Target users and health benefits of this guideline

The dataset is primarily intended for the use of consultant and trainee pathologists when reporting biopsies and resection specimens of mucosal malignancies of the head and neck region and has been developed to aid a consistent approach to the reporting of these cancers.

Surgeons and oncologists may refer to the dataset when interpreting histopathology reports and core data should be available at multidisciplinary meetings to inform discussions on the management of head and neck cancer patients. The core data items are incorporated into the COSD data and are collected for epidemiological analysis by Cancer Registries on behalf of the National Cancer Intelligence Network.

2 Clinical information required for the diagnosis of carcinomas of the nasopharynx and oropharynx

The request form should include patient demographic data, which includes:

- the patient's name
- date of birth
- sex
- hospital and NHS number (where appropriate), or other patient identification number.

Clinical information should include:

- the duration of symptoms
- details of the surgery and whether the intent is curative or palliative
- details of previous pathology reports
- the core clinical data items (see section 5)
- clinical TNM stage (for correlation with pathological findings).
- a history of previous biopsy, resection, radiotherapy or chemotherapy should be included as this may influence the interpretation of the histological changes and should prompt a comment on the extent of any response to treatment.

The request form should provide the opportunity for surgeons to provide annotated diagrams of specimens, either as free-hand drawings or on standard diagrams. Copies of reports that are sent to the Cancer Registries should include the patient's address if possible.

The following should also be recorded:

- the name of the clinician requesting the investigation
- the date and time of the operation
- the date and time at which the specimen was fixed
- the date and time the specimen was received in the laboratory.

3 Receipt and preparation of specimens before dissection

Resection specimens should be orientated by the surgeon and may be pinned or sutured to an appropriate mount (e.g. cork board, polystyrene block, foam sponge, KliniTray, if desired. The surgeon should indicate surgically critical margins using metal tags or sutures. Fixation is in neutral buffered formalin for 24–48 hours in a container of adequate size (the volume of fixative should be 10 times that of the tissue). Resection specimens identified as a biohazard risk (e.g. HIV, tuberculosis) should be fixed for at least 48 hours. If tissue is sent fresh from theatres, this should reach the pathology laboratory promptly.

Photography and radiography of the specimen may be used to record the extent of the disease and the sites from which tissue blocks are selected. Surgical margins should be

painted with Indian ink or an appropriate dye to facilitate the later recording of the proximity of carcinoma to the margin.

4 Specimen handling and block selection

4.1 Introduction

The specimen handling and preparation protocol described below is based on contemporary practice and should be regarded as a guide only; it may need to be modified in individual cases. A detailed dissection protocol is beyond the scope of these guidelines, but a summary of dissection methods and block selection is included to facilitate recording of the core data items. More detail can be found in the relevant sections of the *Tissue pathways for head and neck pathology*.[13] It is particularly important to record the macroscopic dimensions of the tumour, the closest margins and any gross invasion of bone.

It is important to identify if the patient has been enrolled in clinical trials before starting to undertake a macroscopic examination of the tumour and the selection of blocks, as the clinical trial protocol may dictate specific requirements in this regard.

4.2 Nasopharynx

Most nasopharyngeal carcinomas are treated non-surgically, so guidance relating to small biopsies is most appropriate for these tumours. Resection specimens of carcinomas from this area typically comprise piecemeal tumour debulking with clearance informed by separate margin biopsies. En-bloc excisions should be carefully orientated by the surgeon so that surgically important resection margins can be appropriately sampled.

4.3 Oropharynx

In general, these specimens may be assessed by slicing the specimen into 3 mm parallel slices, to demonstrate the size of the tumour (T category), the maximum depth of invasion and the tumour proximity to mucosal and deep resection margins.

4.4 Selection and recording of blocks for histology

- At least 1 block per 10 mm diameter of tumour, including 1 selected to demonstrate the maximum depth of invasion; the whole tumour if less than 10 mm. If mega-blocks are used, then the number of blocks will be fewer.

- Blocks of defined mucosal and deep margins.
- Non-neoplastic mucosa (one block).
- A methodical text-based block key, and/or photographic record of blocks taken should be included in the report. This has been included as a non-core dataset item (NC1).

4.5 Trans-oral surgical specimens

The handling of trans-oral laser and trans-oral robotic resection specimens requires particularly close collaboration between surgeon and pathologist.[14] The main tumour resection may be in 1 or more parts, and it is common for separate biopsies from resection margins to be submitted for examination. The specimens should be secured to an appropriate mount (e.g. cork board etc.) so that the anatomical relationships between the pieces are maintained; an annotated diagram should indicate the nature of each piece of tissue. The radial and deep margins should be inked to facilitate assessment of the histological sections. The main tumour should be serially sliced and blocked in its entirety. If possible, biopsies from critical resection margins should be sliced perpendicular to the margin and blocked in their entirety.

Trans-oral robotic surgery is being increasingly used to investigate the head and neck unknown primary tumour. For example, a patient presenting with metastatic HPV-associated squamous cell carcinoma in a lymph node in the neck, with no evidence of a primary tumour following clinical staging may be subject to a tongue base mucosectomy.[15,16] In these circumstances, the tissue should be serially sliced and blocked in its entirety to discover sub-clinical disease. Judicious inking and detailed block annotation is still required, because if microscopic tumour is identified the surgeons and oncologists will need to know the precise tumour location and proximity to the margins to plan further treatment.[14]

[Level of evidence – C. The basis in evidence for block selection is extrapolated from the need to provide microscopic confirmation or evaluation of prognostic and predictive factors.]

5 Core data items

We have set out to use the ICCR dataset in its current form, with appropriate qualifications and clarifications for implementation in UK clinical practice. In addition to the main dataset items, as outlined below, demographic and clinical data should be collected, as per the

ICCR dataset.[1] This includes the patient's name, date of birth, sex, hospital and NHS number (where appropriate), or other patient identification number.

1	Descriptor	Core/Non-core	Responses
ICCR	Clinical Information	Core	Information not provided Information provided
		Non-core	Previous therapy Surgery Chemotherapy Radiotherapy Targeted Therapy Immunotherapy

Neoadjuvant therapy commentary

Treatment with primary chemoradiation is the most common approach for patients with carcinomas of the nasopharynx and oropharynx as a first line therapy. However, for oropharynx cancer patients, primary surgery can be used with or without adjuvant therapy after surgery based on the staging, particularly for small primary tumours and clinically early-stage patients. Neoadjuvant therapy prior to surgery is typically administered in the context of a clinical trial. Patients should be clinically staged based on the features at primary presentation, irrespective of the subsequent treatment undertaken. Salvage surgery may be performed, and prior treatment can have a profound impact on the tumour, including its stage. For this reason, it should be clearly stated if the patient has received prior therapy (definitive or neoadjuvant), whether chemotherapy, targeted therapies, immunotherapies, radiation or multimodality.

Unlike other anatomic sites where pathologic treatment response quantification/characterisation is prognostic and may determine additional treatments, in oropharyngeal carcinomas, this has not been clearly established as clinically significant. However, some data suggests that complete pathologic treatment response may be prognostically favourable, particularly in post-treatment neck dissection specimens.[17]

For nasopharyngeal carcinomas, primary surgical resection is rare. Most patients will receive primary chemotherapy and radiation (usually as concurrent treatment, but as induction chemotherapy for T4 or N2/N3 disease) with post-treatment endoscopy and imaging between 6 to 12 weeks later, with the simple binary presence of viable tumour or not dictating need for additional therapy.[18–20] The degree of treatment response, at least on pathologic grounds, has not been determined to be significant.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

2	Descriptor	Core/Non-core	Responses
ICCR	Operative procedure	Core	Not specified Biopsy Resection Transoral laser resection

			Transoral robotic resection Other Neck dissection Other

Operative procedure commentary

Oropharynx: Many oropharyngeal carcinomas are treated non-surgically so that guidance relating to small biopsies is most appropriate for these tumours.[21] Open surgical resections have become less common. Transoral approaches such as transoral laser microsurgery (TLM) and transoral robotic surgery (TORS) that are less morbid and have shown promising oncologic outcomes and are utilised, particularly for small, early carcinomas, both HPV-associated and independent.[22,23] Resection specimens of carcinomas from this area should be carefully oriented by the surgeon so that surgically important resection margins can be appropriately sampled and reported.

Nasopharynx: Most nasopharyngeal carcinomas are treated non-surgically so that guidance relating to small biopsies is most appropriate for these tumours.[24] The rare primary resection specimens of carcinomas from this area and salvage nasopharyngectomy specimens should be carefully oriented by the surgeon so that surgically important resection margins can be appropriately sampled and reported.

RCPath additional comments

If a neck dissection specimen is submitted, please use the separate neck dissection dataset.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

3 ICCR	**Descriptor**	**Core/Non-core**	**Responses**
	Specimens submitted	Core	Oropharynx (plus subsites) Nasopharynx Neck Other

Specimens submitted commentary

Oropharynx: The oropharynx is the portion of the continuity of the pharynx extending from the plane of the superior surface of the soft palate to the plane of the superior surface of the hyoid bone or floor of the vallecula.[25] The contents of the oropharynx include:

- soft palate
- palatine tonsils
- anterior and posterior tonsillar pillars
- tonsillar fossa
- uvula
- base of tongue (lingual tonsil)
- vallecula

- posterior oropharyngeal wall
- lateral oropharyngeal wall.

Nasopharynx: The nasopharynx is the superior portion of the pharynx and is situated behind the nasal cavity and above the soft palate; it begins anteriorly at the posterior choana and extends along the plane of the airway to the level of the free border of the soft palate.[25] The inferior portion of the soft palate is oropharyngeal and the superior portion nasopharyngeal. Posteriorly, the nasopharynx extends from the level of the free edge of the soft palate to the skull base. The contents of the nasopharynx include:

- nasopharyngeal tonsils (adenoids), which lie along the posterior and lateral aspect of the nasopharynx
- orifices of the Eustachian tubes, which lie along the lateral aspects of the nasopharyngeal wall anterior to the fossa of Rosenmüller
- torus tubarius, which is an elevation of mucosa that separates the Eustachian tube from the fossa of Rosenmüller
- Fossa of Rosenmüller (lateral pharyngeal recess)
- posterior nasopharyngeal wall.

Waldeyer's ring: Waldeyer's ring is formed by a ring or group of extranodal lymphoid tissues at the upper end of the pharynx and consists of the:

- palatine tonsils
- pharyngeal tonsil (adenoids)
- base of tongue/lingual tonsil
- adjacent submucosal lymphatic tissues.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

4 ICCR	Descriptor	Core/Non-core	Responses
	Tumour site	Core	Oropharynx (plus subsites) Nasopharynx (plus subsites) Other Tumour laterality Not specified Left Right Midline

Tumour site commentary

Tumour site is important for understanding the locations within the pharynx in pathology specimens that are involved by tumour and provides information beyond T-classification that may be useful for the management of patients, such as for narrowly targeting radiation therapy and for surgical resection or re-resection.[26,27] Furthermore, most HPV-associated cancers arise in the palatine tonsils or base of tongue. Tumour location may

provide important information about the likelihood of HPV infection, if HPV testing cannot be performed.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

5	Descriptor	Core/Non-core	Responses
ICCR	Tumour maximum dimension	Core	Size (mm)
	Additional dimensions	Non-core	Size (mm)

Tumour dimensions commentary

Tumour dimensions are used for T-classification of oropharyngeal carcinomas, at least for early-stage tumours. In addition, tumour size may be helpful clinically in making decisions about the details of therapy or extent of disease in post-treatment recurrence specimens. At least the greatest tumour dimension should be reported (core); preferably all three dimensions should be evaluated (non-core).

The macroscopic diameter (in millimetres) should be used unless the histological extent measured on the glass slides is greater than what is macroscopically apparent, in which case the microscopic dimension is used. As for other tissues, measurements are made pragmatically, acknowledging distortion of tissues by cautery, processing, and other possible artefacts. For cases where the exact size of the tumour cannot be precisely assessed pathologically, such as transoral resection specimens received fragmented, an estimate should be provided that will allow for provision of one of the T-classifiers that are based on size.[28] Tumour size is also important in salvage nasopharyngectomy specimens as a correlate to prognosis after surgery.[29,30]

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

6	Descriptor	Core/Non-core	Responses
ICCR	Histological tumour type	Core	WHO subtype lists

Histological tumour type commentary

All tumours of the oropharynx and nasopharynx should be classified based on the most recent edition of the WHO Classification of Head and Neck Tumours, 5th edition, 2024.[11]

The latest World Health Organization (WHO) classification of carcinomas of the oropharynx has simplified the nomenclature of oropharyngeal squamous cell carcinoma to HPV-associated (p16 positivity an acceptable surrogate marker) and HPV-independent (p16 negativity an acceptable surrogate marker), removing further histologic typing.[11] This is because for HPV-associated/p16 positive squamous cell carcinomas, histologic subtype (non-keratinising, basaloid, papillary, etc) does not appear to further segregate outcomes in any meaningful or reproducible way. However, even if HPV status is known, the histologic type can still be useful for pathology practice (comparison to possible new primaries, for frozen sections, and for comparison with

possible metastases that may subsequently occur). In this dataset we recommend recording histological type and viral status as separate data items.

For nasopharyngeal carcinomas, the WHO classification still refers to them by histologic type.[11] However, Epstein-Barr Virus (EBV) status should be assessed and reported.

Salivary gland carcinomas are typed based on the 5th Edition WHO classification, and matching the International Collaboration on Cancer Reporting (ICCR) Carcinomas of the major salivary glands dataset.[31] Histologic type essentially defines biologic behaviour among salivary gland carcinomas and thus influences prognosis, patterns of recurrence and thus clinical management.[32,33] Refer to the ICCR Carcinomas of the major salivary glands dataset for more details.[1] The ICCR Carcinomas of the oropharynx and nasopharynx dataset applies only to minor salivary carcinomas arising at these specific sites.

For neuroendocrine carcinomas, there is a paucity of data regarding stage variables and outcome, but histologic typing provides strong and useful information for treatment and prognosis.[34,35] A subset of oropharyngeal NECs are HPV-associated; however, HPV status does not appear to affect prognosis.[36]

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

7 ICCR	**Descriptor**	**Core/Non-core**	**Responses**
	Histological tumour grade	Core	Cannot be assessed Grade 1: Well differentiated Grade 2: Moderately differentiated Grade 3: Poorly differentiated Undifferentiated High grade transformation Other

Histological grade commentary

Only applicable for HPV-negative oropharyngeal SCC and where the HPV status has not been determined. If the tumour is post-treatment, grading is not applicable since there are no studies establishing its significance. The 'other' category should be selected for salivary carcinomas and neuroendocrine neoplasms. Salivary carcinomas should be graded according to grading systems for individual tumour types, when applicable (refer to the ICCR Carcinomas of the major salivary glands dataset for details).[37] Neuroendocrine neoplasms should be graded as per the ICCR Carcinomas of the hypopharynx, larynx and trachea dataset.[38]

For virus-related oropharyngeal and nasopharyngeal squamous cell carcinomas, formal grading is not applicable.[39] HPV-associated oropharyngeal carcinomas and EBV-positive nasopharyngeal carcinomas are prognostically favourable relative to the virus negative ones, yet appear poorly differentiated morphologically due to their lymphoepithelial or non-keratinising morphology.[40,41]

For the virus negative squamous cell carcinomas ('conventional' tumours) in both the oropharynx and nasopharynx, grading is based on the degree of resemblance to the normal epithelium and follows the descriptions in the WHO classification.[11] This is identical to conventional squamous cell carcinomas at other head and neck anatomic subsites. Specific variants of SCC, such as spindle cell, verrucous, basaloid, papillary,

and adenosquamous, have intrinsic biological behaviours and currently do not require grading.

RCPath additional comments

Practically, the most aggressive area (at x10 objective field, or digital equivalent) is graded as well, moderately or poorly differentiated. This system is widely used and prognostically useful even though it suffers from inter-observer variability and sampling issues. While most squamous cell carcinomas will be moderately differentiated, it is important for prognostication to separate well-differentiated and poorly differentiated tumours. Where a tumour has a varied appearance, then the highest grade is recorded. Grading of neuroendocrine neoplasms should follow the principles in the most recent WHO classification.[11]

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

8	Descriptor	Core/Non-core	Responses
ICCR	Extent of invasion	Core	Present (specify) Not identified Cannot be assessed (specify)

Extent of invasion commentary

Extent of tumour invasion is a key parameter used to assign appropriate T category for both oropharyngeal and nasopharyngeal carcinomas.[26,27] T category provides important prognostic information and, therefore, must be documented for resection specimens.[42–47] Because nasopharyngectomies are uncommon and performed as a salvage treatment option, there are limited prognostic data, but pathologic T category appears to correlate with outcomes even in this setting.[48,49] It should be noted that the Tis (carcinoma in situ) category does not apply to either HPV-associated oropharyngeal or EBV-associated nasopharyngeal SCCs. Tumour depth of invasion (DOI) is also not a component of the T category for either nasopharyngeal or oropharyngeal carcinomas regardless of virus status. DOI should not be reported, especially for HPV and EBV-associated SCCs, which often arise from crypt mucosa deep to the surface and the point of origin cannot be determined nor can an accurate depth be measured.

For oropharyngeal carcinomas, a combination of tumour size and extent determine the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC) T category.[26,27] Extension to the lingual surface of the epiglottis warrants classification as pT3 and invasion of the larynx, extrinsic muscle of the tongue, medial pterygoid, hard palate, mandible or beyond is a pT4 tumour. The pT4 category is further subdivided into pT4a and pT4b for HPV-independent tumours only, with invasion of the larynx, extrinsic muscle of the tongue, medial pterygoid, hard palate or mandible defining pT4a tumours and invasion of the lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base or encasement of the carotid artery indicating a pT4b tumour.

For nasopharyngeal carcinomas, tumour extent alone determines UICC and AJCC T category.[26,27] Tumour confined to the nasopharynx with or without extension to the oropharynx and/or nasal cavity is a pT1 tumour. pT2 tumours extend into the parapharyngeal space and/or adjacent soft tissue (medial or lateral pterygoids or prevertebral muscle). pT3 tumours involve bony structures at the skull base, cervical vertebrae, pterygoids and/or paranasal sinuses. pT4 tumours have intracranial

extension, involvement of cranial nerves, hypopharynx, orbit, parotid gland and/or extensive soft tissue involvement beyond the lateral surface of the lateral pterygoid muscle.

[Level of evidence – C/D. The basis in evidence for inclusion is case-control or cohort studies.]

9	Descriptor	Core/Non-core	Responses
ICCR	Perineural invasion*	Core	Not identified Present Indeterminate

Perineural invasion commentary

Traditionally, the presence of perineural invasion (neurotropism) is an important predictor of poor prognosis in head and neck cancer of virtually all sites.[50,51] This refers to standard haematoxylin and eosin (H&E) stained material showing the presence of tumour growing in the perineural plane/space and not to tumour simply surrounding or near to nerves. The relationship between perineural invasion and prognosis appears to be largely independent of nerve diameter.[52] The few studies (mostly surgical resection-related) looking at perineural invasion exclusively in oropharyngeal squamous cell carcinomas show either borderline significance or none, when controlling for HPV status, etc.[8–10] Perineural invasion is uncommon in HPV-associated tumours and, thus, its significance may be difficult to establish. Although its impact in oropharyngeal tumours may not be equivalent to other anatomic subsites in the head and neck, it is still an important data element and may impact decisions on therapy. If it is the only risk factor present, then by American Society for Radiation Oncology (ASTRO) guidelines it may be used to administer post-operative radiation after informed patient discussion.[53,54]

There are no data on perineural invasion for nasopharyngeal carcinomas, so it is considered ‘not applicable’ for these tumours.

[Level of evidence – C/D. The basis in evidence for inclusion is case-control or cohort studies.]

10	Descriptor	Core/Non-core	Responses
ICCR	Lymphovascular invasion	Core	Not identified Present Indeterminate

Lymphovascular invasion commentary

The presence or absence of lymphovascular invasion should be mentioned if carcinoma is clearly identified within endothelial-lined spaces. This must be carefully distinguished from retraction artefacts. It is not necessary to distinguish between small lymphatics and venous channels. While the presence of nodal metastases indicates that lymphatic invasion must be present, this element should only be reported as positive when lymphovascular invasion is identified microscopically in the primary tumour specimen. Otherwise, it should be listed as ‘not identified’. Several retrospective studies on surgically treated oropharyngeal squamous cell carcinoma show a statistically significant decrease in prognosis for patients with lymphovascular space invasion, independent of

other clinical and pathologic features.[8–10,51,55] The presence of lymphovascular invasion may impact decisions on therapy. If it is the only risk factor present, then by ASTRO guidelines it may be used to advise post-operative radiation after informed patient discussion.[25]

Cases that are still equivocal after taking additional steps may be reported as 'indeterminate' for lymphovascular invasion, but this designation should be sparingly used and it is useful to provide the reason in a comment in the report.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

*Not applicable for nasopharynx

11 ICCR	Descriptor	Core/Non-core	Responses
	Margin status – invasive carcinoma	Core	Involved (specify margin) Not involved (distance) Cannot be assessed
	Margin status – in situ carcinoma	Core	Not applicable Involved (specify margin) Not involved (distance) Cannot be assessed

Margin status commentary:

Positive resection margins are a consistently adverse prognostic feature in patients with oropharyngeal squamous cell carcinoma, when tightly defined, although this impact might be less in the HPV-associated patient.[8–10,51,55] The definition of a positive margin is controversial.[56,57] However, several studies support the definition of a positive margin to be invasive carcinoma or carcinoma in situ/high-grade dysplasia present at margins (microscopic cut-through of tumour).[56] The reporting of surgical margins should also include information regarding the distance of invasive carcinoma or severe dysplasia/carcinoma in situ from the surgical margin. Tumours with 'close' margins also carry an increased risk for local recurrence,[56,58,59] but the definition of a 'close' margin is not standardised as the effective cut-off varies between studies and between anatomic subsites and the risk of a close margin may be lower in HPV-associated tumours. Thus, distance of tumour from the nearest margin should be recorded when it can be measured. Distance may not be feasible to report if separate margin specimens are submitted in addition to the main specimen. In this instance, state that margins are negative, but do not provide a distance. Margin evaluation may not be possible in TLM specimens, if the tumour is excised in pieces and the true margins are not designated by the surgeon. It may be possible to refine the margin status following discussion with the surgical team.

Because of the uncertainty and difficulty (if not impossibility) of telling in situ from invasive ('metastasis-capable') SCC in crypt-derived (usually viral-associated) tumours of the oropharynx and nasopharynx, the reporting is simplified here just as 'distance of closest carcinoma' to the margin, without reference to invasive or in situ. Reporting of surgical margins for non-squamous carcinomas should follow those used for such tumours at all head and neck subsites.

RCPath additional comments

An alternative method for recording the margin status is to use the UICC Residual Tumour (R) Classification:[60]

- RX Presence of residual tumour cannot be assessed
- R0 No residual tumour
- R1 Microscopic residual tumour
- R2 Macroscopic residual tumour.

Whichever system is used, it should be by local agreement, with the surgical and pathology teams clear as to interpretation.

On occasion, additional descriptive comments on the margins will be required, for example where the tumour is 0 mm from the margin in the main specimen, but additional margin biopsies are clear.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

12 ICCR	Descriptor	Core/Non-core	Responses
	Ancillary studies	Core*	Viral/tumour markers Not performed Performed p16 immunohistochemistry High risk HPV EBV (EBER) ISH

Ancillary studies (including viral testing) commentary

In resource-limited practices (or when only extremely limited biopsy samples are available that preclude further testing etc.) where p16/HPV (oropharynx) or EBV (nasopharynx) testing cannot be performed, staging and treatment of patients will be inherently different.[61] The American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) recommend that oropharyngeal squamous cell carcinomas that cannot be tested for p16/HPV be regarded and treated as HPV-negative.[26,27] This guidance should be followed for completing the ICCR Carcinomas of the oropharynx and nasopharynx dataset.

Given that most HPV-associated oropharyngeal squamous cell carcinomas are non-keratinising morphologically, arise deep in the tonsillar parenchyma, have cystic nodal metastases, and may have particular clinical features such as arising in non-smokers who are younger than typical head and neck squamous cell carcinoma patients, certain patients can be strongly suspected as having HPV-associated tumours. Non-keratinising histologic morphology, present in 50–60% of oropharyngeal squamous cell carcinoma, correlates very well with positive HPV status.[62] However, prediction of HPV status by such surrogate marker and clinical grounds is less reliable than direct p16/HPV testing.[63] Thus, when determining optimal treatment for patients, local practices must carefully exercise their own judgment and decide on what grounds they can classify patients as (likely) HPV-associated in their populations.

It is now well established that HPV plays a pathogenic role in a large subset of oropharyngeal squamous cell carcinomas.[64,65] A smaller subset of nasopharyngeal carcinomas is related to transcriptionally active high-risk HPV,[66] but the prognostic

significance is less certain than in the oropharynx. HPV-associated oropharyngeal carcinoma represents a unique squamous cell carcinoma type with proven more favourable prognosis than for HPV-independent tumours.[67] Staging of these patients is now different from that for HPV-independent tumours and treatment differences are being evaluated in clinical trials.

There are many methods for testing HPV status with p16 immunohistochemistry emerging as a simple, thoroughly validated prognostic marker in oropharyngeal SCC.[68] The most used criterion for positivity as a surrogate marker is moderate to intense, block-like, nuclear and cytoplasmic staining in ≥70% of the tumour cells, with the caveat that the correlation with HPV status is not 100%.[39,69,70] The combination of p16 immunohistochemistry with non-keratinising morphology is very strongly associated with transcriptionally active high-risk HPV in the oropharynx.[62] Even so, a small minority of patients will be misclassified.[71–73] Emerging evidence indicates that p16/HPV discordant tumours are associated with reduced survival compared to double positive tumours.[72–75] Furthermore, the p16/HPV discordant population may be significantly larger in low HPV prevalence geographic regions. HPV specific tests include in situ hybridisation for DNA, PCR for HPV-DNA, RT-PCR for HPV-mRNA, and in situ hybridisation for mRNA. There is no consensus on the best methodology for HPV testing but the WHO, AJCC, UICC, and a College of American Pathologists Expert Panel have all recommended p16 immunohistochemistry. Thus, p16 is considered 'core' in oropharyngeal SCCs.

EBV is associated with the non-keratinising types of nasopharyngeal carcinomas in most patients. The most reliable detection method for EBV is in situ hybridisation for EBV encoded early RNA (EBER) present in cells latently infected by EBV, and is recommended because it is a modestly strong favourable prognostic marker.[40] A subset of patients with nasopharyngeal carcinoma are related to transcriptionally-active high-risk HPV.[71,76,77] Most of these tumours are described as non-keratinising differentiated using the WHO terminology. They are EBV (EBER) negative and p16 positive. HPV is not clearly prognostic in nasopharyngeal carcinomas. Testing for HPV/p16 in EBV negative non-keratinising carcinomas, however, is at the discretion of the local practice. It may be indicated in routine clinical practice to help alert the clinician that this may be an oropharyngeal primary tumour that is secondarily involving the nasopharynx and not because the HPV is of proven prognostic benefit in such tumours.[71,76,77]

RCPath additional comments

Given that both the ICCR and WHO guidance pragmatically advocates the use of p16 expression alone to infer HPV status for disease classification, there is a body of literature from case control studies which demonstrates the shortcomings of such an approach.[78,79] In particular, the identification of a p16 positive, HPV-negative population, with poor prognosis, demonstrates the usefulness of the addition of an HPV specific test as part of diagnostic workup.[80] Furthermore, in cases where p16 immunostaining is equivocal (50–70% staining or when staining is extensive but weak), HPV-specific tests can be used to resolve uncertainty. For this reason, and particularly where HPV status is used for prognosis or prediction, HPV specific testing must be undertaken in addition to the assessment of p16 expression in all oropharynx SCCs.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies]

6 Non-core data items

NC1	Descriptor	Core/Non-core	Responses
	Block Identification Key	Non-core	
The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks in some cases. Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies and/or clinical trials. This should also include representative blocks for ancillary studies, specifying those blocks best representing tumour and/or normal tissue for further study.			

NC2	Descriptor	Core/Non-core	Responses
	Tumour infiltrating lymphocytes (TIL)	Non-core	3-group scoring system • High TIL – prominent TIL infiltrate in >80% of tumour • Moderate TIL – patchy TIL infiltrate in 20–80% of tumour • Low TIL – absent/low TIL infiltrate in <20% tumour
There is accumulating evidence that assessment of tumour-infiltrating lymphocytes (TIL) has prognostic and potentially predictive significance, particularly in the context of immunotherapy. Immunophenotyping studies have examined the prognostic significance of lymphocyte subsets (e.g. CD8+ T-cells, CD4+ T-cells, FoxP3+ regulatory T-cells, B-cells) in head and neck squamous cell carcinoma (HNSCC),[72,81–83] but simple semi-quantitative TIL assessment on H&E sections has consistently shown clinical validity as a prognostic marker in both HPV-independent and HPV-associated disease.[57,72–74] There is some anatomical subsite variation in the degree of immune infiltration; oropharyngeal tumours, which arise in lymphoid-rich tissues, have higher number of TILs,[75] and most HPV+ cancers contain high or moderate TIL levels.[73] There is some debate as to whether pre-existing lymphoid stroma in tumours (tonsillar tissue) should be excluded from assessment; in practice, it is not possible to determine whether this stroma is ‘active’ or ‘passive’; however, RNA sequencing studies have shown broadly activated T-cells in HPV+ and HPV- oropharyngeal tumours suggesting that local lymphoid tissue is involved in an anti-tumour response.[84] There is no consensus for a common TIL scoring system across different cancers, and infiltration patterns vary between tumour types. Most issues pertain to the relative importance of stromal TIL (sTIL) or intratumoral TIL (iTIL) or delineating different regions of the tumour, tumour margin and core. Recent guidelines by the International Immuno-oncology Biomarker Working Group recommended quantifying sTIL and iTIL in the tumour core and margin as a continuous variable percentage.[85] However, this scoring			

system has not been tested in HNSCC. Several large HNSCC studies have shown the prognostic utility of a 3-group semi-quantitative scoring system, scoring tumours as TILhigh (TIL infiltrate in >80% of tumour), TILmoderate (TIL infiltrate in 20–80% of tumour) and TILlow (TIL infiltrate in <20% of tumour).[57,72,73] Assessment is made under low-power magnification, ideally from a full-face H&E section (small biopsies may not account for infiltrate heterogeneity) and considering the body of the tumour and the invasive front to provide a single score. Combining TILhigh and TILmoderate groups to generate a 2-group scoring system retains prognostic significance,[73,74] although, given the possibility that immunotherapy may be more effective in TILhigh patients, it is probably better to retain a 3-group scoring system at present. In practice, most of the lymphocytes assessed in this way sit within tumour stroma; assessment of TIL at the tumour/host interface as 3-groups (continuous/patchy/absent) has similarly been shown to be prognostic.

It is not yet established whether H&E-based assessment can accurately predict therapy response, and in future, analysis of immune cell subsets or functional status (activation/exhaustion markers) may be required, particularly in the context of immunotherapy drug selection; combining TIL assessment with, for example, PD1/PDL1 or other therapeutic markers, may have utility. The advent of digital pathology technologies will also enable rapid quantitative assessment of lymphocyte numbers, subsets and tissue distribution, which may play a future role in for tumour immune characterisation.

[Level of evidence – C/D. The basis in evidence for inclusion is case-control or cohort studies]

NC3	**Descriptor**	**Core/Non-core**	**Responses**
	Bone invasion	Non-core	Present Absent

The involvement of maxillary or mandibular bone may be by erosion of the cortex, or infiltration of medullary cavity. Cortical erosion is not classified as bone invasion per se. In the mandible, invasion of the inferior alveolar neurovascular bundle should be noted.[60] The presence or absence of carcinoma at the bone margins should be recorded.

[Level of evidence – B. The presence of bone involvement is important for accurate staging of oropharyngeal and nasopharyngeal malignancies.]

NC4 ICCR	**Descriptor**	**Core/Non-core**	**Responses**
	Co-existent pathology	Non-core*	None identified Present (specify)

Coexistent pathology commentary

Some coexistent pathologic findings can be significant for the index cancer, the most obvious of which is areas of extensive or discontinuous surface squamous dysplasia, but coexistent diseases or other malignancies (such as lymphoma) could be clinically relevant. Judgment of the reporting pathologist will dictate the information provided in this section.

[Level of evidence – D. The basis in evidence for inclusion is expert opinion.]

7 Diagnostic coding and staging

7.1 General comments

For carcinomas of the oropharynx, there is no allowance for a single tumour that is 'multifocal'. Although multiple synchronous and metachronous primary oropharyngeal squamous cell carcinomas are uncommon and are usually of the same high risk HPV type, there is no data to suggest that they are not simply separate primary tumours.[86] Thus, for oropharyngeal carcinomas, each distinct focus should be considered a separate primary tumour and should receive its own separate dataset.

For nasopharyngeal tumours, even if the tumour appears to be multifocal clinically and pathologically, these are regarded and treated as a single primary.[87–89]

7.2 Staging

13 ICCR	Descriptor	Core/Non-core	Responses
	Pathological staging (UICC TNM8/TNM9)	Core	See Appendix B

Pathological staging commentary

This protocol recommends the T-classification schemes published for the pharynx by the UICC and the 8th edition of the AJCC.[25,60] It is quite noteworthy that the oropharyngeal carcinomas staging has been modified significantly from past systems, as the identification of HPV-associated oropharyngeal SCC as a specific subgroup means that the older versions ineffectively stratify outcomes.[90] In essence, a separate TNM classification was introduced for the first time in the 8th edition to address the need for HPV-associated oropharyngeal cancers.

By UICC/AJCC convention, the designation 'T' refers to a primary tumour that has not been previously treated. The symbol 'p' refers to the pathologic classification of the stage, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumour adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. There is no pathologic M0 category as this designation requires clinical evaluation and imaging. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathological staging is usually performed after surgical resection of the primary tumour and depends on documentation of the anatomic extent of disease, whether the primary tumour has been completely removed. If a biopsied tumour is not resected for any reason (e.g. when technically unfeasible) and if the highest T and N categories or the M1

category of the tumour can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer, and thus this information should be provided.

For identification of special cases of TNM or pTNM classifications, ‘y’ and ‘r’ prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis. The ‘y’ prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e. neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a ‘y’ prefix. The ycTNM or ypTNM categorises the extent of tumour present at the time of that examination. The ‘y’ categorisation is not an estimate of tumour prior to multimodality therapy (i.e. before initiation of neoadjuvant therapy). The ‘r’ prefix indicates a recurrent tumour when staged after a documented disease-free interval and is identified by the ‘r’ prefix: rTNM.

Reporting of pathological staging categories (pT, pN, pM) is based on the evidence available to the pathologist at the time of reporting. As indicated in UICC TNM8 and AJCC TNM8,[26,27] the final stage grouping of a patient's tumour is based on a combination of pathological staging and other clinical and imaging information.

Pathological staging should not be reported if the submitted specimen is insufficient for definitive staging, especially with biopsy samples (core needle, incisional or excisional). Staging is based on the submitted resection, and even if there is gross residual disease or is tumour at the margin, pT staging should only be reported on findings in the resection specimen and/or at operation.[26,27]

RCPath additional comments

In keeping with RCPath guidance, UICC TNM9 should be implemented from 1 January 2026. Pathologists may wish to include both UICC TNM8 and UICC TNM9 in their reports in the interim if this may result in different management and should clearly indicate which staging system has been used.

[Level of evidence – C. The basis in evidence for inclusion is well-conducted case-control or cohort studies.]

8 Reporting of small biopsy specimens

When assessing a biopsy specimen, only elements specific to the biopsy should be reported and the remaining items that are applicable to surgically resected tumours should be omitted. The data that can be obtained from small biopsy specimens will be determined, in part, by their size. The type of carcinoma and its grade (where applicable) are the minimum data, as these may determine treatment. It is recognised that, in large tumours, the grade in superficial biopsy material may not be representative of the most aggressive part of the invasive front. If severe dysplasia is present, this should be recorded as it may influence the siting of excision margins. It is not realistic to assess reliably the tumour thickness or presence of vascular invasion in small biopsies.

9 Frozen section diagnosis

The initial diagnosis of carcinoma will usually be made before definitive surgery is performed. On occasions, intra-operative frozen section diagnosis of the nature of a neoplasm will be required. While it will usually be possible to identify the presence of neoplastic tissue, the nature of a poorly differentiated neoplasm may be impossible to determine on frozen sections.

The assessment of the presence or absence of carcinoma at surgical resection margins is the most common indication for intra-operative frozen section diagnosis. The surgeon should select the tissue for frozen section diagnosis with care, bearing in mind that it is not usually possible to section material more than 10 mm in diameter. There is evidence from a recent meta-analysis that frozen sections reduce the risk of positive margins during transoral surgery for oropharyngeal carcinomas.[91]

The report on the frozen section specimen(s) should normally form part of, or accompany, the final diagnostic report on the case.

10 Support of research and clinical trials

It is important to be aware of local protocols for tissue banking and engagement with national initiatives for the further classification of tumours, (such as was implemented in the 100,000 Genomes project). Other features, such as assessment of the effects of biological therapy/immunotherapy, may be important but are currently beyond the remit of this dataset.

11 Specific aspects of individual tumours not covered elsewhere

Immunohistochemical assessment for PD-L1 expression can predict response to anti-PD-L1 immunotherapy, although this is variable and has certain limitations.[92,93] However, several different anti-PD-L1 clones are available from different manufacturers, and the published clinical trials have examined specific clones linked to the activity of specific anti-PD-L1 immunotherapy agents. Moreover, these tests use different algorithms and cut-offs to identify which patients are more likely to benefit from each immunotherapeutic agent.[92]

Since PD-L1 testing is required only for some patients with advanced head and neck cancer and each immunotherapeutic agent needs a different PD-L1 test; reflex testing of all specimens is not recommended at present. However, individual departments should set up a process to enable prompt PD-L1 testing by a trained pathologist in an accredited laboratory for any patient requiring this test. Participation in relevant immunohistochemistry EQA is mandatory for laboratories involved in PD-L1 assessment. The results of such testing should be incorporated into the pathology report (including the antibody used) when it is available; such testing should not delay the primary report.

12 Criteria for audit

As recommended by the RCPath key assurance indicators (www.rcpath.org/resourceLibrary/g181-key-assurance-indicators-for-pathology-services.html) and those in other relevant standards (e.g. ISO15189), a structured program of audit and service evaluation is recommended to cover all aspects of the reporting of these specimens. The standards to be employed were previously stated in the RCPath KPI documentation (2013) and, while this document has been replaced, many of the standards therein are useful benchmarks for a quality service. These should only be taken as a guide and should be all standards audited should be subject to local agreement of quality parameters.

- Cancer resections should be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPath cancer datasets.
  - Standard: 95% of reports must contain structured data
  - Standard: 80% of resection specimens will include 100% data items presented in a structured format.

The RCPath KPI document requires a statement of agreement between the laboratory and users of the laboratory services regarding turnaround times for specific patient pathways. Suggested turnaround times for biopsies and resection specimens are presented below, come from a combination of the RCPath KPI document and updated to reflect current practice, but these should be subject to local agreement:

- standard: 80% diagnostic biopsies will be reported within 7 calendar days of the biopsy being taken

- standard: 80% of all histopathology specimens (excluding those requiring decalcification) will be reported within 10 calendar days of the specimen being taken.

The inclusion of SNOMED or SNOMED-CT codes:

- standard: 95% reports should have T, M and P codes.

The availability of pathology reports and data at MDT meetings:

- standard: 90% of cases discussed at MDT meetings where biopsies or resections have been taken should have pathology reports/core data available for discussion
- standard: 90% of cases where pathology has been reviewed for the MDT meeting should have the process of review recorded.

Utilisation of ancillary tests:

- standard: 90% of oropharyngeal squamous cell carcinoma are tested using p16 immunohistochemistry and are reported as p16/HPV positive or negative according to the recommended cut offs.

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Appendix A SNOMED coding

SNOMED topography should be recorded for the site of the tumour. SNOMED morphology codes should be recorded for the diagnosis/tumour morphology.

Versions of SNOMED prior to SNOMED CT ceased to be licenced by the International Health Terminology Standards Development Organisation from 26 April 2017. It is recognised that versions of SNOMED 2, SNOMED 3/RT and SNOMED CT are in use in the UK.

SNOMED Procedure codes (P codes in SNOMED 2/3/RT) should be recorded for the procedure. P codes vary according to the SNOMED system in use in different organisations, therefore local P codes should be recorded and used for audit purposes.

A list of applicable SNOMED morphology and topography codes should be provided.

Morphological item	**SNOMED code**	**SNOMED CT terminology**	**SNOMED CT code**
Squamous cell carcinoma in situ	M-80702	Squamous cell carcinoma in situ, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	1162893000
Squamous cell carcinoma	M-80703	Squamous cell carcinoma, no International Classification of Diseases for Oncology subtype (morphologic abnormality) Squamous cell carcinoma of pharynx (disorder)	1162767002 408649007
Microinvasive squamous carcinoma	M-80705	Squamous cell carcinoma, microinvasive (morphologic abnormality)	12478003
Keratinising squamous carcinoma	M-80713	Squamous cell carcinoma, keratinising (morphologic abnormality) Keratinising squamous cell carcinoma of nasopharynx (disorder)	18048008 698011002
Non-keratinising squamous carcinoma	M-80723	Squamous cell carcinoma, large cell, non-keratinising (morphologic abnormality)	45490001

Spindle cell squamous carcinoma	M-80743	Squamous cell carcinoma, spindle cell (morphologic abnormality)	10288008
Adenoid squamous carcinoma	M-80753	Adenoid squamous cell carcinoma (morphologic abnormality)	85956000
Adenosquamous carcinoma	M-85603	Adenosquamous carcinoma (morphologic abnormality)	59367005
N/A		Human papillomavirus positive squamous cell carcinoma (morphologic abnormality)	783212001

Note: This is not a comprehensive list of all malignancies and other codes should be used as necessary.

Topography item	**SNOMED code**	**SNOMED CT terminology**	**SNOMED CT code**
Oropharynx	T-60200	Oropharyngeal structure (body structure)	31389004
Anterior wall (glosso-epiglottic area)	T-53122	Structure of junctional region of epiglottis with oropharynx (body structure)	113280004
Base of tongue	T-53130	Mucosa of base of tongue (body structure)	245832000
Vallecula	T-60230	Structure of vallecula of epiglottis (body structure)	42275007
Lateral wall	T-61100	Structure of lateral wall of oropharynx (body structure)	19120004
Tonsil	T-60220	Tonsillar structure (palatine) (body structure)	75573002
Tonsillar fossa and pillars	T-61240	Tonsillar fossa structure (body structure)	32163006
Tonsillar pillars	T-61150	Palatine arch structure (body structure)	21294006
Posterior wall	T-60210	Structure of posterior wall of oropharynx (body structure)	12999009
Inferior surface of soft palate	T-51120	Inferior surface of soft palate (body structure)	303339004
Uvula	T-51130	Uvula palatina structure (body structure)	26140008
Nasopharynx	T-23000	Entire nasopharynx (body structure)	181200003

Postero-superior wall	T-23001	Entire posterior wall of nasopharynx (body structure) Entire superior wall of nasopharynx (body structure)	361936002 179268001
Lateral wall (includes fossa of Rosenmüller)	T-23002	Entire lateral wall of nasopharynx (body structure)	361937006
Inferior wall (superior surface of soft palate)	T-51122	Entire superior surface of soft palate (body structure)	362081003

Procedure codes (P)

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure. Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

Appendix B TNM classification

This provides updated information on staging using UICC TNM 9, which should be used for all tumours diagnosed after 1 January 2026.[1]

Primary tumour (T)

HPV-associated oropharynx

T0 No evidence of primary tumour, but p16-positive (HPV-associated) cervical node(s) metastasis present.

T1 Tumour 2 cm or less in greatest dimension.*

T2 Tumour more than 2 cm but not more than 4 cm in greatest dimension.

T3 Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis.

T4 Tumour invades any of the following: larynx,** deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), medial or lateral pterygoid muscle, hard palate, mandible, pterygoid plates (medial and/or lateral), nasopharynx, skull base; or encases carotid artery.

* The anatomical structure of the tonsil crypts and lingual tonsil means that the basement membrane is incomplete and no carcinoma in situ is recognised.

** Mucosal extension to lingual surface of the epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of the larynx.

HPV-independent oropharynx

T1 Tumour 2 cm or less in greatest dimension.

T2 Tumour more than 2 cm but not more than 4 cm in greatest dimension.

T3 Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis.

T4a Tumour invades any of the following: larynx,* deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), medial pterygoid, hard palate, or mandible.

T4b Tumour invades any of the following: lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base; or encases carotid artery.

*Mucosal extension to lingual surface of the epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of the larynx.

Nasopharynx

TX Primary tumour cannot be assessed.

T0 No evidence of primary tumour, but EBV-positive (EBV-associated) cervical node metastases present.

T1 Tumour confined to the nasopharynx, or extends to oropharynx and/or nasal cavity without para-pharyngeal involvement.

T2 Tumour with extension to para-pharyngeal space or infiltration of the medial pterygoid, lateral pterygoid and/or prevertebral muscles.

T3 Tumour invades bony structures of skull base, cervical vertebra, pterygoid structures and/or paranasal sinuses.

T4 Tumour with any of the following: intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, parotid gland, and/or infiltration beyond the lateral surface of the lateral pterygoid muscle.

Residual tumour (R)

An R classification can be used to record the presence/absence of tumour remaining after curative therapy.

RX Presence of residual tumour cannot be assessed.

R0 No residual tumour.

R1 Microscopic residual tumour.

R2 Macroscopic residual tumour.

Reference

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Appendix C Reporting proforma for carcinomas of the oropharynx and nasopharynx

Surname…… Forenames…….… Date of birth…… Sex.....

Hospital……..…….…… Hospital no……..... NHS/CHI no……

Date of receipt…….…… Date of reporting…… Report no……

Pathologist……... Surgeon……..……

Clinical information (Core/non-core)

Information not provided □ Information provided □

Specify type: Surgery □ Chemotherapy □ Radiotherapy □

Targeted therapy □ specify if available …….

Immunotherapy □ specify if available …….

Operative procedure (Core) (select all that apply)

Not specified ☐

Biopsy □ Resection ☐ Transoral laser microsurgical resection ☐ Transoral robotic surgical resection ☐

Neck dissection □ Other, specify ☐ …….

Specimens submitted (Core) (select all that apply)

Not specified ☐

Oropharynx ☐

Palatine tonsil ☐ Base of tongue/lingual tonsil ☐ Soft palate ☐ Uvula ☐

Vallecula □ Tonsillar pillars □ Pharyngeal wall (posterior) ☐ Pharyngeal wall (lateral) ☐

Other, specify ☐……

Nasopharynx ☐, specify if necessary ……

Neck dissection □

Other □, specify ……..

Tumour site (Core) (select all that apply)

Cannot be assessed □

Oropharynx □ Left □ Right □ Midline □ Laterality not specified □

Palatine tonsil □ Base of tongue/lingual tonsil □ Soft palate □ Uvula □

Vallecula □ Tonsil pillars □ Pharyngeal wall (posterior) □ Pharyngeal wall (lateral) □

Other □, specify ……..……

Nasopharynx □ Left □ Right □ Midline □ Laterality not specified □

Nasopharyngeal tonsils (adenoids) □ Fossa of Rosenmüller □ Lateral wall □

Other □, specify ……..

Tumour dimensions (Core/Non-core)

Maximum tumour dimension (largest tumour) …….mm

Additional dimensions (largest tumour) ……..mm x ……..mm

Cannot be assessed, specify ……

Histological tumour type (Core)

Salivary gland carcinoma, specify type □ ……

Neuroendocrine carcinoma, specify type □ ……..

Other, specify type □ …….

Carcinomas of the oropharynx

HPV-associated squamous cell carcinoma □

HPV-independent squamous cell carcinoma □

Other □, please state ……..

Carcinomas of the nasopharynx

Non-keratinising squamous cell carcinoma □

Differentiated □ Undifferentiated □

Keratinising squamous cell carcinoma □ Basaloid squamous cell carcinoma □ Nasopharyngeal papillary adenocarcinoma □

Cannot be assessed, specify □ ……..…….

Histological tumour grade (Core)

Not applicable □ GX: Cannot be assessed □ G1: Well differentiated □ G2: Moderately differentiated □

G3: Poorly differentiated □ Undifferentiated □ High grade transformation □ Other, specify □……

Extent of invasion (Core)

Specify ……. Not applicable □ Cannot be assessed, specify □ ……

Perineural invasion (Core) (Not applicable for nasopharynx)

Not identified □ Present □ Indeterminate, specify □ ……..

Lymphovascular invasion (Core) (Not applicable for nasopharynx)

Not identified □ Present □ Indeterminate, specify □ ……..

Bone invasion (Non-core)

Not identified □ Present □ Not applicable □ Cannot be assessed, specify □ ……

Margin status (Core)

Invasive carcinoma[i]

Involved □ specify margin(s) if possible …….

Not Involved □ Distance of tumour from closest margin …… mm □ Cannot be assessed □

Specify the closest margin if possible …….

[i] There is no clear morphologic distinction between invasive and in situ carcinoma for HPV-positive oropharyngeal and EBV-positive nasopharyngeal carcinomas, so all carcinoma at margin should be included in evaluation simply as ‘involved by carcinoma’.

Carcinoma in situ[ii]

Involved □ specify margin(s) if possible …….

Not Involved □ Distance of tumour from closest margin …… mm □

Specify closest margin ……..

Not applicable[iii] □ Cannot be assessed, specify □ …….

ii Applicable for oropharyngeal surface mucosal disease only; not for tonsillar crypt epithelium.

iii Only applicable for HPV-negative oropharyngeal and EBV-negative nasopharyngeal tumours and for tonsillar surface disease. High-grade dysplasia is synonymous with moderate/severe dysplasia.

Coexistent pathology (Non-core)

None identified □

Present □ specify …….

Ancillary studies

Viral testing/viral tumour markers – Oropharynx

Not performed/unknown □ Performed □ (select all that apply)

p16 Immunohistochemistry □ Positive □ Negative □ Criteria used to determine results, specify …….

High risk HPV specific testing □

DNA PCR □ Not identified □ Present □

DNA in situ hybridisation □ Not identified □ Present □

E6/E7 mRNA in situ hybridisation □ Not identified □ Present □

E6/E7 mRNA RT-PCR □ Not identified □ Present □

Viral testing/viral tumour markers – Nasopharynx

Not performed/unknown □ Performed □

EBV (EBER) in situ hybridisation – Positive □ Negative □

Pathological staging (Core)

UICC TNM 9th edition

TNM Descriptors □ (only if applicable) specify: (select all that apply)

M – multiple primary tumours □ r – recurrent □ y – post-therapy

Primary tumour (pT) (Core) □ Specify …….

Appendix D Reporting proforma for carcinomas of the nasopharynx and oropharynx in list format

Core/ Non-core	Element name	Values	Implementation notes
Core/ Non-core	**Clinical Information**	**Core:** Single selection value list: • Information not provided • Information provided **Non-core:** Multi selection value list (select all that apply): • Surgery • Chemotherapy • Radiotherapy • Targeted therapy, specify if available • Immunotherapy, specify if available	
Core	**Operative procedure**	Core: Multi selection value list (select all that apply): • Not specified OR • Biopsy (excisional, incisional), specify Resection, specify – Transoral laser microsurgical resection – Transoral robotic surgical resection – Other, specify • Neck (lymph node) dissection,* specify • Other, specify	*If a neck dissection is submitted, then a separate dataset is used to record the information.
Core	**Specimens submitted**	Core: Multi selection value list (select all that apply): • Not specified OR • Oropharynx – Palatine tonsil	

Core/ Non-core	Element name	Values	Implementation notes
		– Tonsil pillar – Base of tongue/lingual tonsil – Soft palate – Uvula – Vallecula – Pharyngeal wall (posterior) – Pharyngeal wall (lateral) – Other, specify • Nasopharynx, specify if necessary • Other, specify	
Core	**Tumour site**	Core: Multi selection value list (select all that apply): • Cannot be assessed OR • Oropharynx Left Right Midline Laterality not specified – Palatine tonsil – Tonsil pillar – Base of tongue/lingual tonsil – Soft palate – Uvula – Vallecula – Pharyngeal wall (posterior) – Pharyngeal wall (lateral) – Other, specify • Nasopharynx Left Right Midline	

Core/ Non-core	Element name	Values	Implementation notes
		Laterality not specified – Nasopharyngeal tonsils (adenoids) – Fossa of Rosenmüller – Lateral wall – Other, specify • Other, specify including laterality	
Core/ Non-core	**Tumour dimensions**	**Core:** Maximum tumour dimension (largest tumour) ___ mm Cannot be assessed, specify Non-core: Additional dimensions (largest tumour) ___ mm x ___ mm	
Core	**Histological tumour type**	Core: Multi selection value list (select all that apply): • Salivary gland carcinoma, specify type • Neuroendocrine carcinoma, specify type • Other, specify type **Carcinomas of the oropharynx** • HPV-associated squamous cell carcinoma • HPV-independent squamous cell carcinoma **Carcinomas of the nasopharynx** • Non-keratinising squamous cell carcinoma	Value list from the WHO Classification of Head and Neck Tumours (2024). Note that permission to publish the WHO classification of tumours may be needed in your implementation. It is advisable to check with the International Agency on Cancer research (IARC).

Core/ Non-core	Element name	Values	Implementation notes
		Single selection value list: – Differentiated – Undifferentiated (lymphoepithelial) • Keratinising squamous cell carcinoma • Basaloid squamous cell carcinoma • Nasopharyngeal papillary adenocarcinoma • Cannot be assessed, specify	
Core	**Histological tumour grade**	Core: Single selection value list: • Not applicable • GX: Cannot be assessed • G1: Well differentiated • G2: Moderately differentiated • G3: Poorly differentiated • Undifferentiated • High grade transformation • Other, specify • Cannot be assessed, specify	
Core	**Extent of invasion**	**Non-core:** Single selection value list: • Present Specify …….. • Not identified • Cannot be assessed, specify	
Core	**Perineural invasion**	Core: Single selection value list: • Not identified • Present • Indeterminate, specify	Not applicable for nasopharynx.

Core/ Non-core	Element name	Values	Implementation notes
Core	**Lymphovascular invasion**	Core: Single selection value list: • Not identified • Present • Indeterminate, specify	Not applicable for nasopharynx.
Non-core	**Bone invasion**	Core: Single selection value list: • Absent • Present • Cannot be assessed, specify	
Core	**Margin status**	Core: Single selection value list/text/numeric: **Invasive carcinoma**** • Involved – Specify margin(s), if possible • Not involved – Distance of tumour from closest margin ___ mm – Distance not assessable – Specify closest margin, if possible **Carcinoma in situ***** • Involved – Specify margin(s), if possible • Not involved – Distance of tumour from closest margin ___ mm – Distance not assessable – Specify closest margin, if possible • Not applicable *** OR	** There is no clear morphologic distinction between invasive and in situ carcinoma for HPV-positive oropharyngeal and EBV-positive nasopharyngeal carcinomas, so all carcinoma at margin should be included in evaluation simply as 'involved by carcinoma'. *** Only applicable for HPV-negative oropharyngeal and EBV-negative nasopharyngeal tumours and for tonsillar surface disease. High-grade dysplasia is synonymous with moderate/severe dysplasia.

Core/ Non-core	Element name	Values	Implementation notes
		• Cannot be assessed, specify	
Non-core	**Coexistent pathology**	**Non-core:** Multi selection value list (select all that apply): • None identified OR • Present, specify	
Core/ Non-core	**Ancillary studies**	Core: Single selection value list: **Viral testing/viral tumour markers** Not performed/unknown **Oropharynx** • Performed (select all that apply) p16 immunohistochemistry – Positive – Negative – Criteria used to determine results, specify • High risk HPV specific testing Single selection value list: – DNA PCR – Not identified – Present – DNA in situ hybridisation – Not identified – Present – E6/E7 mRNA in situ hybridisation – Not identified – Present – E6/E7 mRNA RTPCR – Not identified	

Core/ Non-core	Element name	Values	Implementation notes
		– Present **Core: Viral testing/viral tumour markers** **Nasopharynx** • Performed – EBV (EBER) in situ hybridisation – Positive – EBV (EBER) in situ hybridisation – Negative	
Core	**Pathological staging** (UICC TNM 9th edition) TNM descriptors	Core: Choose if applicable: • m – multiple primary tumours • r – recurrent • y – post-therapy	
Core	**Primary tumour (pT)**	Core: Free text **HPV-positive oropharynx** **HPV-independent oropharynx** **Nasopharynx**	

Appendix E Summary table – explanation of grades of evidence

(modified from Palmer K et al. BMJ 2008;3371832)

Grade (level) of evidence	Nature of evidence
Grade A	At least 1 high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal, and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high- quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal, and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix F AGREE II guideline monitoring sheet

The cancer datasets of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Introduction
2 The health question(s) covered by the guideline is (are) specifically described	Introduction
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	Introduction
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword and Introduction
12 There is an explicit link between the recommendations and the supporting evidence	2–11
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	2–11
16 The different options for management of the condition or health issue are clearly presented	2–11

17 Key recommendations are easily identifiable	2–11, Appendices C, D
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices A–D
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	Section 12
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interest of guideline development group members have been recorded and addressed	Foreword