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 hypopharynx, larynx and trachea

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Comments	This document will replace the *Dataset for histopathology reporting of mucosal malignancies of the larynx* published in November 2013. In accordance with the College's pre-publications policy, this document was on The Royal College of Pathologists' website for an abridged consultation from 20 April to 18 May 2023. Responses and authors' comments are available to view on final publication. **Dr Brian Rous** **Clinical Lead for Guideline Review**

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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. Pathologists should be able to justify any variation.

Each dataset contains core data items (see Appendices C and D) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD) v9.0 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, with appropriate patient consent, 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
- The British Association of Oral and Maxillofacial Surgeons
- The UK and Ireland Association of Cancer Registries
- National Cancer Registration and Analysis Service.

The information used by the authors to develop this dataset was obtained by undertaking a search of the PubMed database for relevant primary research evidence and systematic reviews on head and neck mucosal malignancies, either specifically in the larynx and hypopharynx or generally in the head and neck where these subsites can be separately identified, from January 2010 to June 2022 (inclusive). Key search terms searched included larynx, hypopharynx, clinical trial, prognosis, survival, surgery, chemotherapy and radiotherapy. 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. They incorporate the core data items and commentary from the International Collaboration on Cancer Reporting (ICCR).[1,2] The level of evidence for the recommendations has been summarised according to modified SIGN guidance (see Appendix E) and the grade of evidence is indicated in the text. No major conflicts in the evidence have been identified and minor discrepancies between studies have been resolved by expert consensus. Gaps in the evidence were identified by College members via feedback received during consultation.

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

A formal revision cycle for all cancer datasets takes place on a three-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 or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required. Major revisions to core data

items, apart from 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 two weeks for members' 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, Lay Network and Working Group on Cancer Services. It was placed on the College website for consultation with the membership from 20 April to 18 May 2023. All comments received from the Working Group and membership have been addressed by the authors to the satisfaction of the Chair of the Working Group and the Clinical Lead for Guideline Review.

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 that they have no conflicts of interest.

1 Introduction

The dataset has been developed for the reporting of biopsy and resection specimens of the larynx and hypopharynx. The protocol applies to all invasive carcinomas of the larynx and hypopharynx including: supraglottis, glottis, subglottis, piriform sinus, lateral and posterior hypopharyngeal wall and post cricoid region extending from the level of the arytenoid cartilage to the inferior border of the cricoid cartilage. This dataset does not apply to the reporting of lymphoma, malignant melanoma and sarcoma and relevant datasets for these tumour groups should be consulted where available. Nodal excisions and neck dissection specimens are dealt with in a separate dataset, *Dataset for the Histopathological Reporting of Nodal Excisions and Neck Dissection Specimens Associated with Head and Neck Carcinomas*, which should be used in conjunction, where applicable.[3]

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 larynx and hypopharynx
- 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 to ultimately improve patient care.

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 (MDT) (and other clinicopathological) meetings and correlation with pre-operative imaging studies are important in maintaining and developing this partnership and improving patient outcomes.

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 does not differ between larynx and hypopharynx and therefore a common proforma for these primary sites, in keeping with the ICCR dataset, has been employed. The lymph node dataset is common to all head and neck 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 anatomical extent of invasion and proximity of carcinoma to resection margins) have been shown to be related to clinical outcome[1,2]
  - these features may therefore be important in: deciding on the most appropriate treatment for particular patients, including the extent of surgery and the use and choice of adjuvant radiotherapy, chemotherapy or targeted therapies;[1,2] 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
- to allow selection and comparison of patients in clinical trials.

1.1 Design of this protocol

RCPath recognises the authority of internationally accepted guidance documents (WHO, American Joint Committee for Cancer [AJCC], Union for Cancer Control [UICC] TNM and ICCR)[1,2,4–6] and promotes consistent reporting practice while adopting 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 larynx, hypopharynx & trachea (published in 2018).[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 2018 to October 2021.

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.

1.2 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 MDT 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 larynx and hypopharynx

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

- name
- date of birth

- sex
- hospital and NHS number (where appropriate) or other patient identification number.

Clinical information should include:

- duration of symptoms
- details of surgery and whether the intent is curative or palliative
- details of previous pathology reports
- core clinical data items (see section 5)
- Clinical TNM stage (for correlation with pathological findings).
- history of previous biopsy, resection, radiotherapy or chemotherapy as this may influence the interpretation of 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 freehand 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:

- name of the clinician requesting the investigation
- date and time of the operation
- date and time of fixation
- date and time of specimen receipt by 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™). The surgeon may send annotated photographs of the resection specimen to aid the pathologist with orientation. The surgeon should indicate surgically critical margins using metal tags, sutures or ink. The surgeon should state clearly on the request form if ink has been used as this may fade during the fixation process. Fixation is in neutral buffered formalin for 24–48 hours in a container of adequate size. Resection specimens identified as a biohazard risk should be fixed for at least 48 hours (e.g. HIV, tuberculosis). If tissue is sent fresh from theatres, this should reach the pathology laboratory promptly. Refer to the COVID-19 Resources Hub for the latest COVID-19 related guidance.

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. Identifying laterality (left and right) with two different coloured inks is advised, particularly if mega blocks are to be employed.

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 brief 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 RCPath document *Tissue Pathways for Head and Neck Pathology*.[7] It is particularly important to record the macroscopic dimensions of the tumour, the closest margins and any gross invasion of laryngeal cartilage.[8,9]

It is important to identify if the patient has been enrolled in clinical trials prior to engaging in a trimming procedure as the clinical trial protocol may dictate specific requirements with regards to sampling.

The following commentary is intended to assist pathologists to understand the complex anatomy of the larynx and related structures.[1]

The supraglottis includes the epiglottis, aryepiglottic fold (laryngeal aspect), arytenoid, ventricular bands (false cords) and laryngeal ventricles.

The glottis extends from the ventricle to approximately 1 cm below the free level of the true vocal cord and includes the vocal cords, anterior commissure and posterior commissure.

The subglottis extends from approximately 1 cm below the level of the true vocal cord to the inferior rim of the cricoid cartilage.

Note that transglottic carcinomas cross the ventricles in a vertical direction arising in either the glottis and/or supraglottic larynx.

The hypopharynx is the part of the pharynx extending from the plane of the superior border of the hyoid bone (or floor of the vallecula) to the plane corresponding to the lower border of the cricoid cartilage. The contents of the hypopharynx include left and right piriform sinuses which expand bilaterally and forward around the sides of the larynx and lie between the larynx and the thyroid cartilage; the lateral and posterior hypopharyngeal walls and postcricoid region extend from the level of the arytenoid cartilages to the inferior border of the cricoid cartilage.

The paraglottic space is a fat-containing space antero-lateral and deep to the ventricles and saccules and filled with adipose tissue and connective tissue (see Figure 1); it is bounded by the conus elasticus inferiorly, the thyroid cartilage laterally, the quadrangular membrane medially and the piriform sinus posteriorly.

The pre-epiglottic space is anterior to the base of the epiglottis and is filled with adipose tissue and connective tissue (see Figure 2); it is triangular and is bounded by the thyroid cartilage and thyrohyoid membrane anteriorly, the epiglottis and thyroepiglottic ligament posteriorly and the hyoepiglottic ligament at its base.

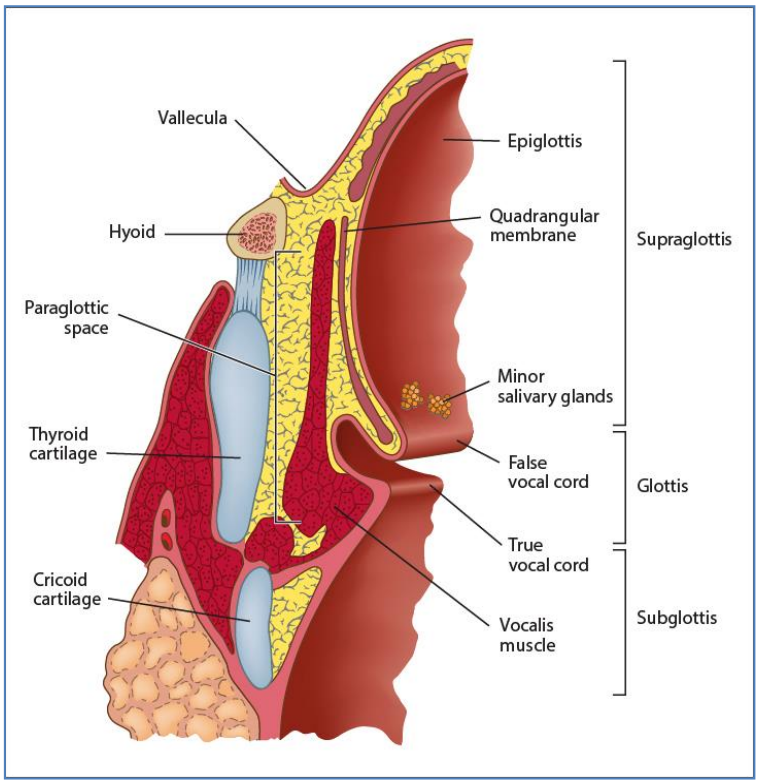

Figure 1. Coronal section through the larynx to show the main structures and paraglottic space. © 2023 International Collaboration on Cancer Reporting Limited (ICCR).

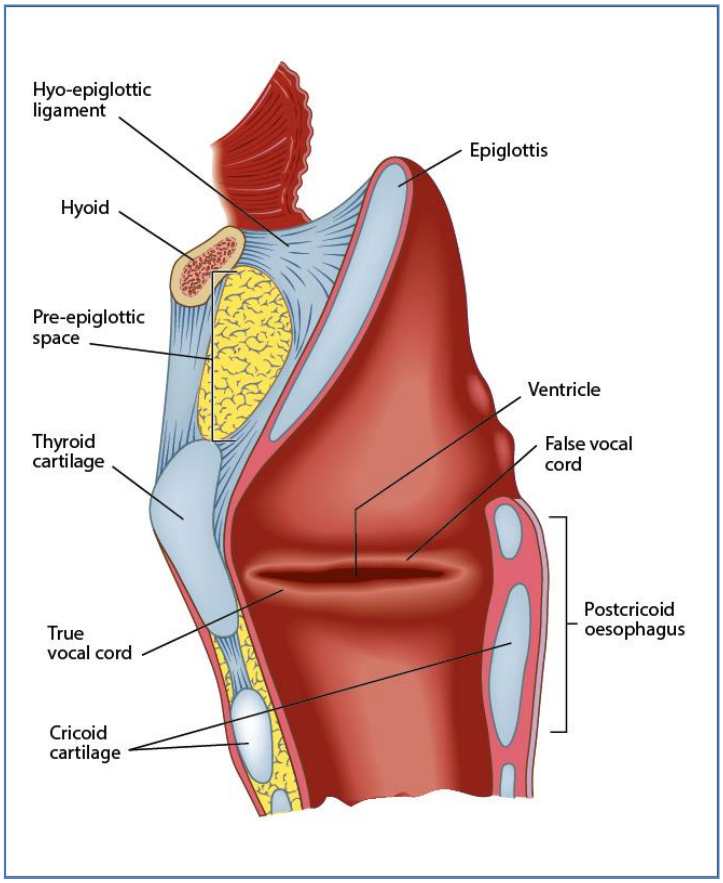

Figure 2. Sagittal section through the larynx to show main structures and the pre-epiglottic space. © 2023 International Collaboration on Cancer Reporting Limited (ICCR).

4.2 Laryngectomy and pharyngolaryngectomy specimens

Horizontal slices 3–5 mm thick provide optimal demonstration of the relationship between the tumour and the laryngeal cartilages and other relevant anatomical spaces, although thicker slices may be required if megablocks are used. For supraglottic carcinomas, blocks should include the relationship between the carcinoma and the anterior (submucosal) resection margin at the base of the tongue; blocks taken in the sagittal plane are more appropriate to demonstrate this feature. The description should include the principle site of origin of carcinoma (including any subsites), the extent of involvement of laryngeal cartilages and extra-laryngeal tissues as well as the maximum tumour diameter.[7–10] In the case of a large tumour involving all anatomical subsites of the larynx, it is appropriate to describe the primary site as transglottic. Partial laryngectomy may be perfomed for smaller tumours and trimming procedures for these specimens should follow the same principle as larger resections.

4.3 Selection of blocks for histology of laryngectomy and pharyngolaryngectomy specimens

- One specified tumour block for molecular testing, in which tumour content should be formally assessed.
- Tumour: at least one block per 10 mm diameter of tumour, including one selected to demonstrate the deepest involved tissue plane. The whole tumour should be processed if it is less than 10 mm in size. Megablocks are useful for demonstrating the relationship of tumour with important structures for staging. While they reduce the number of blocks taken it should be noted that the technical complexity for biomedical scientists is high and laboratories may have limited capacity for the processing of megablocks. Taking blocks of fixed tumour prior to decalcification is advised to ensure there is optimum quality tissue for immunohistochemistry and molecular testing if required.
- Blocks should include defined mucosal and soft tissue margins.
- Non-neoplastic mucosa (one block).
- Bone or cartilage if grossly involved by tumour.
- Thyroid if present in laryngectomy. One block is sufficient if the thyroid appears normal. If the thyroid is abnormal, one or more blocks should be taken to confirm or exclude invasion by carcinoma or other pathology.
- Tracheostomy site, if present.

A methodical text-based block key, and/or photographic record of blocks taken should be included either as a print-out or on the laboratory macroscopic photograph archive folder.

Examples of cut up procedures and sampling of key margins and anatomical features are given in Figures 3–7.

[Level of evidence – GPP.]

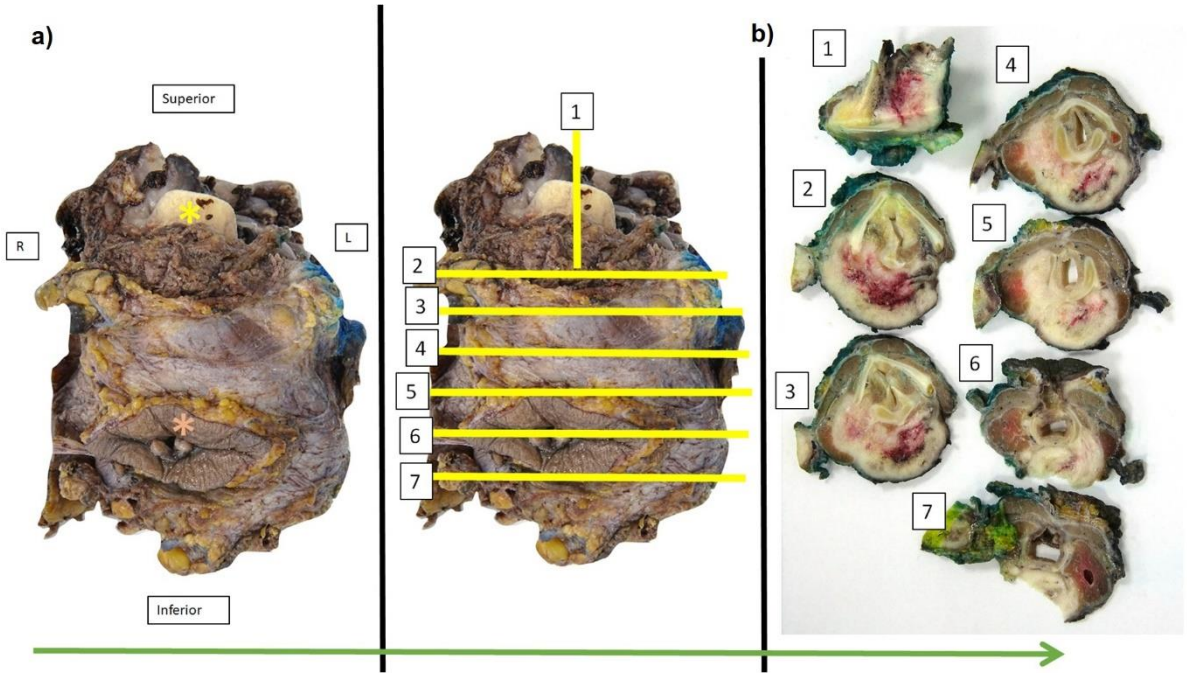

Figure 3. Sampling of laryngopahryngectomy specimen. **3a.** Specimen viewed from the anterior aspect. Epiglottis (yellow star) and tracheostomy site including skin (orange star) are highlighted. **3b.** In this example, the specimen has been sectioned on band saw prior to decalcification in the planes shown in yellow. The resultant slices are seen on the right. If preferred, the specimen can be sectioned on the bench following a period of decalcification in exactly the same planes. Prior to decalcification, it would be prudent to select a block of fixed tumour for embedding prior to decalcification in anticipation of potential immunohistochemistry or molecular testing. The epiglottis is sampled in sagittal plane (slice 1) which allows optimum assessment of the pre-epiglottic space invasion and tongue base margin at the superior aspect of the specimen. Slices 2–7 are taken in transverse plane. The supraglottis corresponds to slice 2. The vocal cords (glottis) are seen in slice 3 and the subglottis corresponds to slices 4–7. The left lobe of thyroid is seen in slices 4–7. The right lobe of thyroid is seen in slices 5–7. In slice 7, the trachea is seen. A more detailed account of the anatomy of each particular laryngeal subsite is given in Figures 4–7. The specimen shows a large hypopharyngeal tumour present in all slices. The tumour is midline/bilateral appears to extend in continuity with the inked posterior specimen limit. Blocks should be selected to determine all core dataset items in particular extent of invasiveness of key anatomical structures and margins. In this example interpretation of the posterior specimen limit is challenging as the surgical ability to resect normal tissue beyond the tumour is hindered by prevertebral fascia.

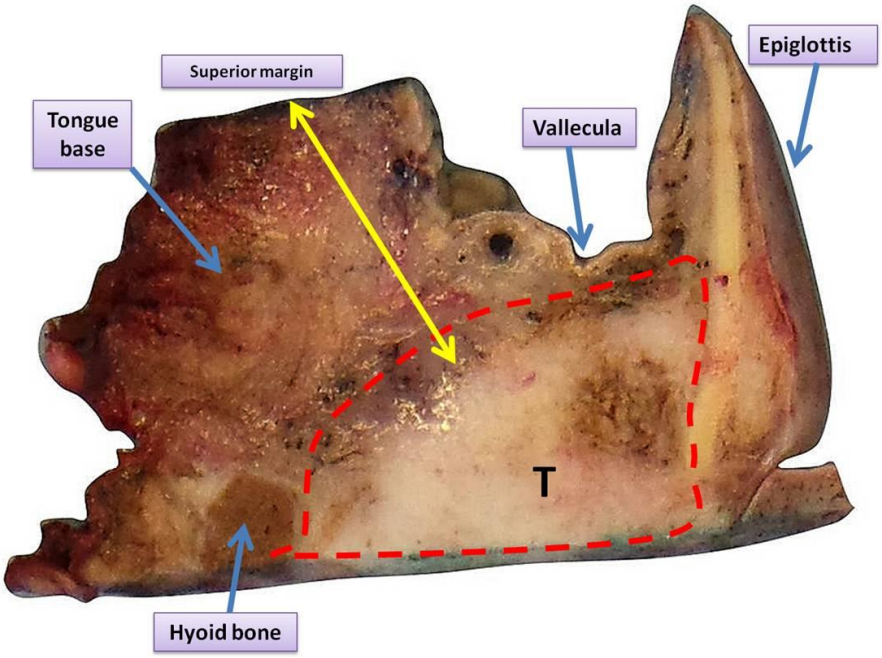

Figure 4. Epiglottis, pre-epiglottic space: key anatomical features. Sagittal section through epilglottis at superior aspect of a laryngopharyngectomy specimen. The pre-epiglottic space (red dashed line) shows invasion by squamous cell carcinoma (T). The yellow arrow demonstrates the nearest superior margin from tumour to the inked tongue base. Epiglottis, hyoid bone, vallecula and tongue base are shown.

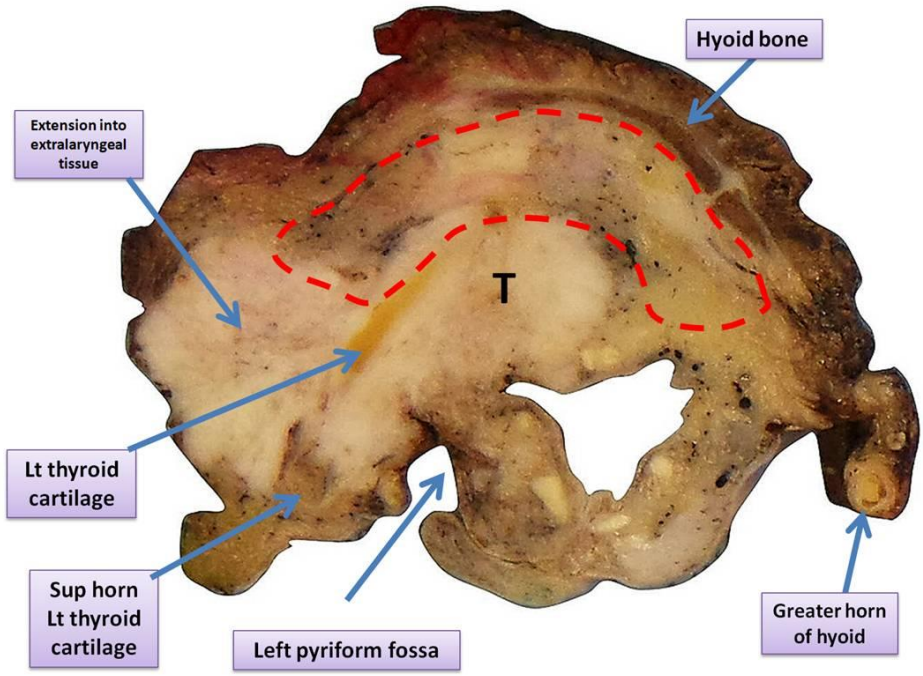

Figure 5. Supraglottis: key anatomical features. Transverse section through the supraglottis of the same specimen. Tumour takes origin from the left pyriform fossa and shows extensive spread into extralaryngeal soft tissue including strap muscle on the left side. The pre-epiglottic space is outlined in red. Tumour is seen infiltrating beyond the left thyroid cartilage. Laryngeal tumours showing extension into extralaryngeal tissues beyond the thyroid cartilage are considered at least pT4a on TNM8 (UICC).

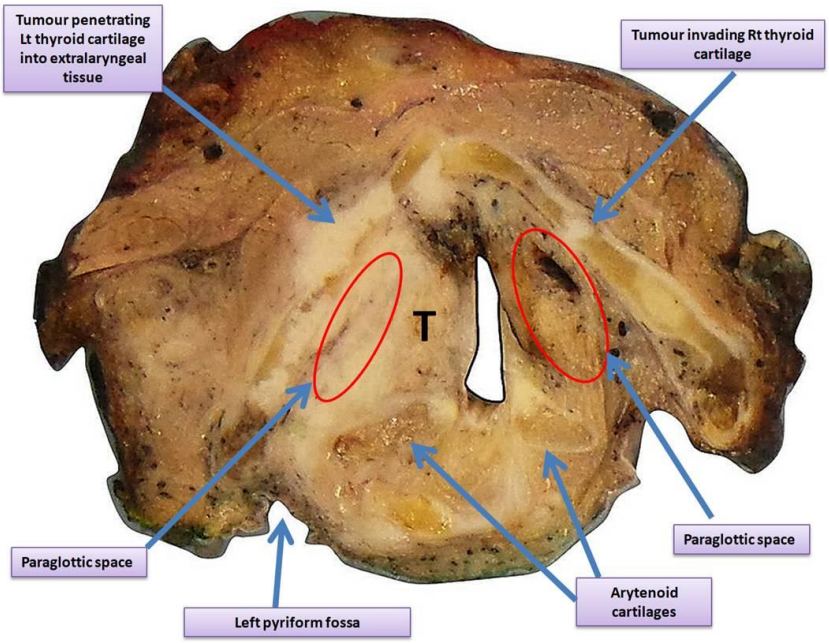

Figure 6. Glottis: key anatomical features. Transverse section through the glottis of the same specimen. There is anatomical distortion with the laryngeal lumen deviated to the right due to extensive tumour mass affecting the left side of the larynx. There is full thickness penetration of the left thyroid cartilage lamina with extension into extralaryngeal soft tissue. The right thyroid cartilage also shows invasion although the external lamina is intact. Both arytenoids are involved by tumour. The left and right paraglottic spaces are highlighted in red.

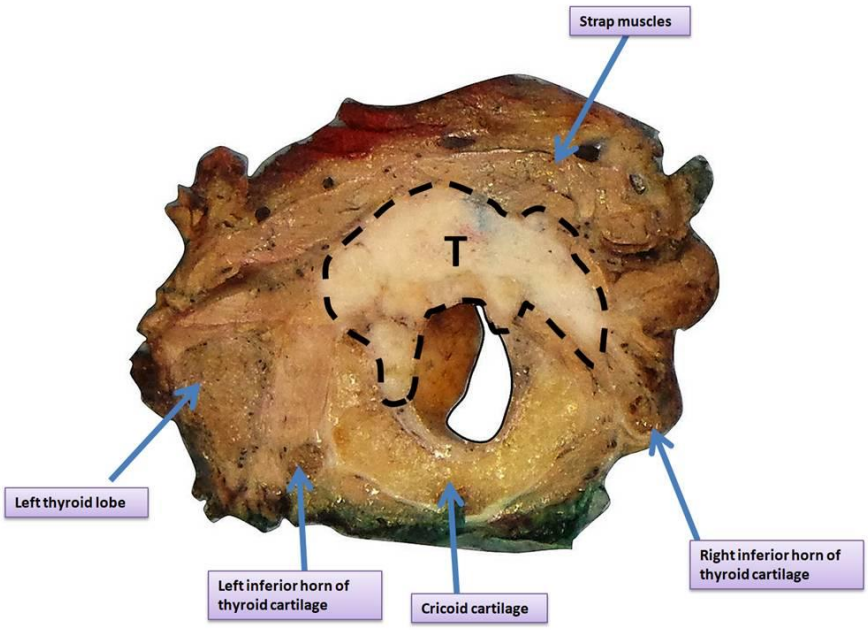

Figure 7. Subglottis: key anatomical features. Transverse section through the subglottis of laryngopharyngectomy specimen. Anteriorly placed tumour mass extends into strap muscles. Cricoid cartilage, left and right inferior horns of thyroid cartilage and left thyroid lobe are also included.

4.4 Trans-oral laser resection specimens

The handling of trans-oral laser resection specimens requires particularly close collaboration between surgeon and pathologist. The main tumour resection may be in one or more parts and it is usual for separate biopsies from resection margins to be submitted for examination. The specimens should be pinned onto a board so that the anatomical relationships between the pieces are maintained and 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 resection margins should be sliced perpendicular to the margin and blocked in their entirety. Small biopsies of the vocal cord are often difficult to orientate and may be pinned onto cork board or affixed to strips of dehydrated cucumber[11] to facilitate handling in the laboratory.

Small excisions may be received in biopsy cassettes sandwiched between small squares of sponge – this technique helps prevents tissue distortion during fixation and keeps specimens flat for easier sectioning. The biopsy cassette technique requires especially close communication between surgeon and pathologist to ensure orientation is preserved.

[Level of evidence – GPP.]

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

5.1 Core data

1 ICCR	Descriptor	Core/Non-core	Responses
	Operative procedure	Core	Biopsy Resection Other Not specified

Operative procedure commentary:

The nature of the operative procedure will influence the required level of detail in the pathological report. Diagnostic/incisional biopsies will usually generate a limited set of data items compared to excision/resection specimens: for example, the status of resection margins does not require detailed consideration for diagnostic biopsies except for very small carcinomas where the entire cancer may be present in the diagnostic specimen.

RCPath additional comments:

If a neck dissection specimen is submitted, please use the separate RCPath dataset: *Dataset for Histopathology Reporting of Nodal Excisions and Neck Dissection Specimens Associated with Head and Neck Carcinomas*.[3]

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

2	Descriptor	Core/Non-core	Responses
	Specimens submitted	Core	Hypopharynx Laryngopharyngectomy Other, specify Larynx Endolaryngeal excision Transoral laser excision Supraglottic laryngectomy Supracricoid laryngectomy Total laryngectomy Vertical hemilaryngectomy, specify side Partial laryngectomy, specify type Other, specify Not specified*

Specimens submitted commentary: The pathologist needs to be informed about the nature of surgery (type of specimen) so that their description and dissection are focused on selecting appropriate tissues to guide accurate cancer staging.[7–10]

*'Not specified' should be used rarely and only after good effort has been employed to obtain the requisite information.

RCPath additional comments: None.

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

3	Descriptor	Core/Non-core	Responses
	Specimen dimensions	Core	Maximum dimension__ mm

Specimen dimensions: The size of a resection specimen is useful as it places the size of the tumour into the operative context. In those rare instances where specimens may be mislabelled, the size of the tissue may help to resolve any discrepancies.

RCPath additional comments:
It is sufficient to record the maximum specimen dimensions in the macroscopic description only. Additional specimen dimensions (in mm) may be recorded as a non-core item.

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

4	Descriptor	Core/Non-core	Responses
	Tumour site	Core	Cannot be assessed No macroscopically visible tumour OR Hypopharynx Piriform sinus Postcricoid Pharyngeal wall (posterior and/or lateral) Larynx, supraglottis Epiglottis

			Lingual aspect Laryngeal aspect Aryepiglottic fold Arytenoid False vocal cord/fold Ventricle Larynx, glottis True vocal cord/fold Anterior commissure Posterior commissure Larynx, subglottis Left Right Midline Laterality not specified Other, specify
	Tumour laterality	Core	Left Right Bilateral/midline

Tumour site comments:

Accurate documentation of the laterality and site of the tumour avoids errors in the delivery of therapy. The site of the primary tumour is a key determinant in clinicopathological staging systems for hypopharynx and larynx.

For carcinomas that involve more than one site, the principal site of involvement should be recorded and coded; this may not be the site of origin. If required, the involvement of associated sites can be noted to help in later data analysis. Sites and subsites should be recorded according to the Union for International Cancer Control (UICC) nomenclature.[5]

RCPath additional comments: None.

[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 dimensions	Core	Maximum tumour dimension (largest tumour) ___ mm

Tumour dimensions comments:

The macroscopic diameter (in millimetres) should be used unless the histological extent is greater than macroscopically apparent, in which case the microscopic dimension is used. As for other tissues, measurements are made pragmatically, acknowledging distortion of tissues by fixation and processing.[5,6,12–14]

For larynx, several sites rely on the presence or absence of vocal cord mobility to determine T stage; in these circumstances, only a provisional pT stage can be offered (at least pT1a, for example).

RCPath additional comments: Additional tumour dimensions (in mm) may be recorded as a non-core item.

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

6	Descriptor	Core/Non-core	Responses
	Histological tumour type	Core	Squamous cell carcinoma, conventional type Squamous cell carcinoma, variant types Adenosquamous carcinoma Basaloid squamous cell carcinoma Papillary squamous cell carcinoma Spindle cell squamous cell carcinoma Verrucous squamous cell carcinoma Lymphoepithelial carcinoma Neuroendocrine carcinoma Well differentiated neuroendocrine carcinoma Moderately differentiated neuroendocrine carcinoma Poorly differentiated neuroendocrine carcinoma Small cell neuroendocrine carcinoma Large cell neuroendocrine carcinoma Combined (or composite) neuroendocrine carcinoma, with squamous or adenosquamous component Carcinomas of minor salivary glands Adenoid cystic carcinoma, specify grade Mucoepidermoid carcinoma, specify grade Other, specify

Histological tumour type comments:

Histopathological type is important for cancer registration and prognosis, with strength of evidence varying for different types. Verrucous and papillary carcinomas tend to have a good prognosis while adenosquamous carcinomas have a worse prognosis than conventional and spindle cell carcinomas. For most of the variants of squamous cell carcinoma, surgery with adequate margins is the main treatment. In some tumours, such as large cell neuroendocrine carcinomas, a combination of irradiation and chemotherapy is indicated.

All tumours of the hypopharynx, larynx and trachea should be typed based on the most recent edition of the World Health Organization (WHO) Classification of Head and Neck Tumours.[4,15–24]

RCPath additional comments:

For mucosal melanoma, please refer to the current ICCR dataset.[25] It is envisaged that an RCPath dataset will follow in due course.

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

7	Descriptor	Core/Non-core	Responses
	Histological tumour grade	Core	Not applicable GX: Cannot be assessed G1: Well differentiated G2: Moderately differentiated G3: Poorly differentiated Other, specify

Histological grade comments:

Although human papillomavirus (HPV)-associated carcinomas arising in the oropharynx are graded differently from conventional (non-HPV) carcinomas (see ICCR *Carcinomas of the nasopharynx and oropharynx* dataset),[26] there is insufficient evidence to justify this approach in the hypopharynx and larynx. The recommendation is that HPV assessment should not be performed except for basaloid carcinomas. The conventional grading system for classical squamous cell carcinomas should be used for all tumours at these sites.

Grading is based on the degree of resemblance of the carcinoma to the normal epithelium and follows the descriptions in the WHO classification.[4] The most aggressive area 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 problems. While most squamous cell carcinomas will be moderately differentiated, it is important for prognostication to separate tumours based on differentiation. Where a tumour has a varied appearance, then the highest grade (poorest differentiation) is recorded as a core data item, while the predominant pattern may be recorded as non-core data.

Squamous cell carcinoma variants (basaloid, adenosquamous, spindle cell) are considered to have intrinsic biological potential and are not graded.

For the grading of salivary-type tumour arising from mucosal glands, please refer to the ICCR *Carcinomas of the major salivary glands* dataset for descriptors.[27]

RCPath additional comments: Grading is based on the degree of resemblance of the carcinoma to the normal epithelium and follows the descriptions in the WHO classification.[4] The most aggressive area (at x100 magnification field) is graded as well, moderately or poorly differentiated. This system is widely used and prognostically useful although it suffers from inter-observer variability, sampling problems and does not always correspond to prognosis.[1,24,27–29] 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 (poorest differentiation) is recorded as a core data item, while the predominant pattern may be recorded as non-core data.[30–35]

Although human papillomavirus (HPV)-associated carcinomas arising in the oropharynx are graded differently from conventional (non-HPV) carcinomas there is insufficient evidence to justify this approach in the hypopharynx and larynx. The recommendation is that HPV assessment should not be performed except for basaloid carcinomas, particularly in the upper hypopharynx in which the disease may represent regional extension of an oropharyngeal primary.[36–39]

Squamous cell carcinoma variants (basaloid, adenosquamous, spindle cell) are considered to have intrinsic biological potential and are not graded.[40,41]

For the grading of salivary-type tumour arising from mucosal glands, please refer to the ICCR *Carcinomas of the major salivary glands* dataset[27] for descriptors.

[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	Not identified OR Involves mucosa Involves paraglottic space Involves pre-epiglottic space Partial thickness invasion of cartilage Full thickness invasion of cartilage

Extent of invasion comments:

In the larynx, the invasion of tissue compartments deep to the mucosa is important for staging. The important tissues for staging purposes are the paraglottic space, the pre-epiglottic space and the thyroid and cricoid cartilages. One of the points of distinction between T3 and T4a carcinomas is whether cartilage invasion is minor (partial) or full thickness. The absolute tumour thickness is non-core for larynx and hypopharynx.

RCPath additional comments:

Knowledge of the radiological staging and judicial macroscopic sampling of key structures may aid determination of the greatest extent of microscopic invasion for a given case. The extent of invasion of the thyroid/cricoids cartilages (inner table only, or full thickness) should be recorded.[1,5,6,43–48] Infiltration of the arytenoid and/or epiglottic cartilage does not influence the T stage. If desired, tumour thickness may be recorded as a non-core data.[49–51]

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

9	Descriptor	Core/Non-core	Responses
ICCR	Perineural invasion	Core	Not identified Present Cannot be assessed

Perineural invasion comments:

The presence or absence of perineural invasion should be recorded, regardless of the size of the nerve.[52–64] Invasion of the perineural plane is a predictor of local recurrence and nodal metastasis and may prompt consideration of adjuvant chemoradiotherapy.

The perineural plane is a potential space between the bundles of axons and the perineurium; the presence of carcinoma around a nerve (external to the perineurium) is not regarded as perineural invasion. There is some evidence that extratumoural perineural invasion is of more importance than intratumoural perineural invasion but this requires confirmation. For this dataset, either intratumoural or extratumoural invasion is regarded as a positive finding.

RCPath additional comments: Quantitative assessment of perineural invasion (particularly the size of affected nerve), as recommended in other RCPath datasets, is not routine practice in reporting of head and neck cancer.

[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 Cannot be assessed

Lymphovascular invasion comments:

Lymphovascular invasion is a relatively weak predictor of nodal metastasis.[65,66] The presence of carcinoma cells within an endothelial-lined space is the essential criterion and should be distinguished from retraction artefact. It is not necessary to distinguish between small lymphatics and venous channels.

RCPath additional comments: While it is important to distinguish between small lymphatics and venous channels in tumours in RCPath datasets relating to different body systems, it is not necessary to differentiate between vessel types in tumours of the larynx and hypopharynx.

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

11	Descriptor	Core/Non-core	Responses
ICCR	Margin status: invasive carcinoma	Core	Involved – Specify margin(s), if possible Not involved Distance from closest margin ___ mm Distance not assessable Specify closest margin, if possible
	Margin status: in situ carcinoma/High grade dysplasia	Core	Involved – Specify margin(s), if possible Not involved Distance from closest margin ___ mm Distance not assessable Specify closest margin, if possible Not applicable Cannot be assessed

Margin status comments: Margin status is a predictor of local recurrence and may require consideration of adjuvant therapy.[67–79] The status of the surgical resection margin should include assessment of both invasive and in situ carcinoma.

A positive margin is one in which the carcinoma is present at the margin while the definition of a 'close margin' varies between published series, typically being regarded as between 3 and 5 mm. For laser resections of glottic carcinomas even 1 mm may be adequate due to the thermal damage of tissue at the margin. It is recommended that the distance from in situ or invasive carcinoma to the closest margin is recorded, if assessable. Note that comment on the deep resection margin of a laryngectomy specimen may be inapplicable unless the tumour extends close to the base of tongue or into the soft tissues of the neck.[80]

RCPath additional comments: Interpretation of the posterior surgical margin in the hypopharynx can be challenging since the true anatomical posterior margin may comprise pre-vertebral fascia thus rendering further surgical excision (or margin revision) impossible. Similarly, interpretation of the posterior margin of laryngectomy specimens can also be complicated particularly in large glottic tumours. Interpretation requires an appropriate level of anatomical knowledge as well correlation with pre-operative radiological images by the pathologist. Close communication between the surgical team and the pathologist would also be advisable. In such instances, it may be more appropriate to refer to the 'posterior specimen limit' rather than the posterior margin.

An alternative method for recording the margin status is to use the UICC Residual Tumour (R) Classification:[5]

- 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.]

5.2 Non-core data items

1	Descriptor	Core/Non-core	Responses
ICCR	Neoadjuvant therapy	Non-Core	Administered Not administered Not known
		Non-core	Type of neoadjuvant therapy

Neoadjuvant therapy commentary:
Information from the surgeon about the use of neoadjuvant therapy will help the pathologist interpret correctly the histologic findings. While the extent of tumour necrosis or post-therapy fibrosis are not currently used as an important guide to management for most types of laryngeal/hypopharyngeal cancer, it is good practice to document the effects of previous treatment as part of a free text report. Pragmatically, an estimate of the amount (% tumour volume) of necrosis or fibrosis can be provided as free text.

RCPath additional comments: None.

[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	Tumour focality	Non-core	Unifocal Bilateral Multifocal, specify number of tumours in specimen Cannot be assessed, specify

Tumour focality comments:
Tumour focality is described as unifocal or multifocal to allow the pathologist to describe the complexity of the disease in some patients.[2]

RCPath additional comments: None.

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

3	Descriptor	Core/Non-core	Responses
ICCR	Pattern of invasive front	Non-core	Cohesive Non-cohesive Difficult to determine

Pattern of invasive front comments:

The pattern of invasion by the carcinoma at its deep margin is of proven prognostic value for oral and oropharyngeal carcinomas (non-HPV-associated) and there is limited evidence that a similar approach may be of value to predict nodal metastasis for hypopharyngeal and laryngeal carcinomas. Note that the response for this data item is based on the most complex ('worst') area of the carcinoma. The pattern of invasion is included as a non-core data item as many head and neck pathologists include this in their personal descriptive assessment of carcinomas at all sites and it is convenient to use it for larynx and pharynx as well, for consistency with national dataset, even though this is not supported by robust evidence of clinical impact.

RCPath additional comments: Pattern of invasion may be difficult to adequately assess in small laser resection specimens of limited depth. The 'difficult to determine' option should be reserved for such cases.[81,82]

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

4	Descriptor	Core/Non-core	Responses
ICCR	Co-existent pathology	Non-core	None identified OR Necrotizing sialometaplasia Infection, specify Dysplasia, specify type and grade Hyperplasia, specify Other, specify

Coexistent pathology comments: This is a non-core data item to provide the pathologist with the flexibility to record any other diseases that potential impact on clinical management, such as infections, epithelial dysplasia, hyperplastic processes and necrotising sialometaplasia.

RCPath additional comments: None.

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

5	Descriptor	Core/Non-core	Responses
ICCR	Ancillary studies	Non-core	Not performed Performed (specify)

Ancillary studies comments:

This is a non-core data item that is intended to allow pathologists to record the use of additional relevant investigations, in particular molecular testing, the prognostic and predictive significance of which is uncertain. A section of fixed tumour taken before decalcification processes is recommended to facilitate ancillary studies.

The literature recognises that a very few HPV associated carcinomas may occur in the hypopharynx and larynx, but prognostic relevance is uncertain.[37–40]

RCPath additional comments: None.

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

6 Diagnostic coding and staging

Pathological staging, using the most recent edition of the AJCC/UICC Classification of malignant tumours, is a core item for all cancers of the larynx and hypopharynx[5,6] (currently the 8th edition is employed).

By 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 and, as opposed to the clinical classification, 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 or not 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, then this is sufficient for recording the stage and classification.

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 categorizes the extent of tumour actually present at the time of that examination. The 'y' categorization 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.

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

7 Reporting of small biopsy specimens

When a biopsy specimen is all that is received, elements specific to the biopsy should be reported and the remaining items that are applicable to surgically resected tumours 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 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.

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

9 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.

10 Specific aspects of individual tumours not covered elsewhere

Regarding PD-L1 testing, immunohistochemical assessment for PD-L1 expression can predict response to anti-PD-L1 immunotherapy, although this is variable and has certain limitations.[83,84] However, a number of different anti-PD-L1 clones are available from different manufacturers and the published 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.[83] 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 external quality assessment (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.

11 Criteria for audit

The key assurance indicators (see *Key assurance indicators for pathology services*, November 2019) and key performance indicators (see *Key Performance Indicators – Proposals for implementation*, July 2013) as recommended by RCPath are:

- 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. English trusts were required to implement the structured recording of core pathology data in the COSD
  - standard: 95% of reports must contain structured data
- histopathology cases must be reported, confirmed and authorised within seven and ten calendar days of the procedure

- standard: 80% of cases must be reported within seven calendar days and 90% within ten calendar days.

Further suggested audit standard:

- 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.

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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 have ceased cease 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)	59529006
Squamous cell carcinoma	M-80703	Squamous cell carcinoma, no International Classification of Diseases for Oncology subtype (morphologic abnormality) Squamous cell carcinoma of oral cavity	28899001 733343005
Microinvasive squamous carcinoma	M-80705	Squamous cell carcinoma, microinvasive (morphologic abnormality)	12478003
Keratinising squamous carcinoma	M-80713	Squamous cell carcinoma, keratinizing (morphologic abnormality)	18048008
Non-keratinising squamous carcinoma	M-80723	Squamous cell carcinoma, large cell, nonkeratinizing (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

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
Larynx	T-24100	Larynx, not otherwise specified	
Epiglottis	T-24010	Epiglottis	
Aryepiglottic fold	T-24310	Aryepiglottic fold, laryngeal aspect	
False cords	T-24320	Ventricular bands (false cords)	
Glottis	T-24440	Glottis	
Vocal cords	T-24400	Vocal cords	
Anterior commissure	T-24470	Commissures	
Subglottis	T-24450	Subglottis	
Larynx and pharynx	T-24920	Larynx and pharynx, cs	
Hypopharynx	T-60300	Hypopharynx	
Post cricoid	T-24080	Pharyngo-oesophageal junction (post-cricoid area)	
Piriform fossa	T-60320	Piriform sinus	
Posterior pharyngeal wall	T-60350	Posterior pharyngeal wall	
Pharynx	T-60000	Pharynx	

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 information on staging using UICC TNM 8.

Primary tumour (T)

Supraglottis

T1 Tumour limited to one subsite of supraglottis with normal vocal cord mobility

T2 Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx

T3 Tumour limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, preepiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage

T4 T4a Tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscles of tongue (genioglossus, hypoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, or oesophagus

T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures.

Glottis

T1 Tumour limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility

T1a Tumour limited to one vocal cord

T1b Tumour involves both vocal cords

T2 Tumour extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility

T3 Tumour limited to the larynx with vocal cord fixation and/or invasion of paraglottic space and /or inner cortex of the thyroid cartilage

T4 T4a Tumour invades through the outer cortex of the thyroid cartilage, and/or invades tissue beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscles of tongue (genioglossus, hypoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, or oesophagus

T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures.

Subglottis

T1 Tumour limited to the subglottis

T2 Tumour extends to vocal cord(s) with normal or impaired mobility

T3 Tumour limited to larynx with vocal cord fixation

T4 T4a Tumour invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx e.g., trachea, soft tissues of neck including deep/extrinsic muscles of tongue (genioglossus, hypoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, or oesophagus)

T4b Very advanced local disease, tumour invades prevertebral space, encases carotid artery, or invades mediastinal structures.

Hypopharynx

T1 Tumour limited to one subsite of hypopharynx and/or 2 cm or smaller in greatest dimension

T2 Tumour invades more than one subsite of hypopharynx or an adjacent site, or measures larger than 2 cm but not larger than 4 cm in greatest dimension without fixation of hemilarynx

T3 Tumour more than 4 cm in greatest dimension, or with fixation of hemilarynx or extension to oesophagus

T4 T4a Tumour invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus, central compartment soft tissue*

T4b Tumour invades prevertebral fascia, encases carotid artery, or involves mediastinal structures.

*Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

Appendix C Reporting proforma for carcinomas of the larynx and hypopharynx

Surname……	Forenames……..…	Date of birth…….....
Hospital…….……	Hospital no…….....	Sex.....
Date of receipt……..	Date of reporting……..….....	NHS/CHI no……..
Pathologist……..……....	Surgeon…….……	Report no…….....

Operative procedure (core) (select all that apply)

Not specified □ Resection, specify □ Transoral laser microsurgical resection □
Transoral robotic surgical resection □ Other, specify □ ……
Biopsy (excisional, incisional), □ specify ……
Neck (lymph node) dissection[i]□, specify ……Other □ specify……

Specimens submitted (core) (select all that apply)

Not specified □
Hypopharynx □
Laryngopharyngectomy □
Other, specify □……..……

Larynx □
Endolaryngeal excision □ Transoral laser excision□ Supraglottic laryngectomy □
Supracricoid laryngectomy □ Total laryngectomy □
Vertical hemilaryngectomy (specify side) □……,
Partial laryngectomy (specify type) □……,
Other, specify □……

Specimen dimensions

Maximum dimension (core) …….mm

Tumour site (core) (select all that apply)

Cannot be assessed □
No macroscopically visible tumour □
Hypopharynx □ Left □ Right □ Midline □ Laterality not specified □
Piriform sinus□ Postcricoid □ Pharyngeal wall (posterior and/or lateral) □
Other, specify □ ……..……
Larynx, supraglottis □ Left □, Right □, Midline □, Laterality not specified□
Epiglottis □ (Lingual aspect□ Laryngeal aspect□)
Aryepiglottic fold □, Arytenoid □ False vocal cord/fold □
Ventricle □
Larynx, glottis □ Left □, Right □, Midline □, Laterality not specified □
True vocal cord/fold □ Anterior commissure □ Posterior commissure □
Larynx, subglottis □ Left □, Right □, Midline□ , Laterality not specified □
Other □, specify including laterality ……..
Trachea □ Left □ Right □ Midline □ Laterality not specified □
Tumour laterality
Left □, Right □, Bilateral/midline □

Tumour dimensions (core)
Maximum tumour dimension (largest tumour) …….mm
Cannot be assessed, specify ……

Histological tumour type (core)
Squamous cell carcinoma, conventional type □
Squamous cell carcinoma, variant types □ ……
Adenosquamous carcinoma □ Basaloid squamous cell carcinoma □
Papillary squamous cell carcinoma □ Spindle cell squamous cell carcinoma □
Verrucous squamous cell carcinoma □
Lymphoepithelial carcinoma □
Neuroendocrine carcinoma □
Well differentiated neuroendocrine carcinoma □ Moderately differentiated neuroendocrine carcinoma □
Poorly differentiated neuroendocrine carcinoma □ (Small cell type □ Large cell type □)
Combined (or composite) neuroendocrine carcinoma, with squamous or adenosquamous component □
Carcinomas of minor salivary glands □
Adenoid cystic carcinoma □ Mucoepidemoid carcinoma □ Other, specify □……
Other, specify □……

Histological tumour grade (core)
GX: Cannot be assessed □
G1: Well differentiated □
G2: Moderately differentiated □
G3: Poorly differentiated □
Not applicable □ Other, specify □……

Extent of invasion (core)
Larynx
Not identified □ Involves mucosa □ Involves paraglottic space □ Involves pre-epiglotic space □
Partial thickness invasion of cartilage □ Full thickness invasion of cartilage □

Hypopharynx
Tissue layers involved, specify (core) ……..

Perineural invasion (core)
Not identified □ Present □ Cannot be assessed, specify □ ……..

Lymphovascular invasion (core)
Not identified □ Present □ Cannot be assessed, specify □ ……..

Margin status (core)
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/high-grade dysplasia
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 □ Cannot be assessed, specify □ ……

Pathological staging (core) (UICC TNM 8th edition)
TNM Descriptors (only if applicable) specify:

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

Appendix D Reporting proforma for carcinomas of the larynx and hypopharynx in list format

Core/ Non-Core	Element name	Values	Implementation notes
Core	Operative procedure	Multi selection value list (select all that apply): • Not specified OR • Biopsy (excisional, incisional), specify • Resection, 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	Multi selection value list (select all that apply): • Not specified OR • Trachea • Hypopharynx – Laryngopharyngectomy – Other, specify • Larynx – Endolaryngeal excision – Transoral laser excision – Supraglottic laryngectomy – Supracricoid laryngectomy – Total laryngectomy – Vertical hemilaryngectomy, specify side – Partial laryngectomy, specify type – Other, specify	.
Core	Specimen dimensions	Numeric: • Maximum dimension ___ mm	
Core	Tumour site	Multi selection value list (select all that apply): • Cannot be assessed	

Core/ Non-Core	Element name	Values	Implementation notes
		• No macroscopically visible tumour OR • Trachea – Left – Right – Midline – Laterality not specified • Hypopharynx – Left – Right – Midline – Laterality not specified • Piriform sinus • Postcricoid • Pharyngeal wall (posterior and/or lateral) • Other, specify • Layrnx supraglottis – Left – Right – Midline – Laterality not specified • Epiglottis – Lingual aspect – Laryngeal aspect • Aryepiglottic fold • Arytenoid • False vocal cord/fold • Ventricle • Larynx, glottis – Left – Right – Midline – Laterality not specified Single selection value list:	

Core/ Non-Core	Element name	Values	Implementation notes
		• True vocal cord/fold • Anterior commissure • Posterior commissure • Larynx, subglottis – Left – Right – Midline – Laterality not specified • Tumour laterality – Left – Right – Bilateral/midline • Other, specify including laterality	
Core	Tumour dimensions	Numeric: • Maximum tumour dimension (largest tumour) ___ mm • Cannot be assessed, specify	
Core	Histological tumour type	Multi selection value list (select all that apply): • Squamous cell carcinoma, conventional type • Squamous cell carcinoma, variant types Single selection value list: • Adenosquamous carcinoma • Basaloid squamous cell carcinoma • Papillary squamous cell carcinoma • Spindle cell squamous cell carcinoma • Verrucous squamous cell carcinoma • Lymphoepithelial carcinoma • Neuroendocrine carcinoma Single selection value list: • Well differentiated neuroendocrine carcinoma	Value list from the WHO Classification of Head and Neck Tumours (2017). 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
		• Moderately differentiated neuroendocrine carcinoma • Poorly differentiated neuroendocrine carcinoma • Small cell neuroendocrine carcinoma • Large cell neuroendocrine carcinoma • Combined (or composite) neuroendocrine carcinoma, with squamous or adenosquamous component • Carcinomas of minor salivary glands Single selection value list: – Adenoid cystic carcinoma, specify grade – Mucoepidermoid carcinoma, specify grade – Other, specify • Other, specify	
Core	Histological tumour grade	Single selection value list: • Not applicable • GX: Cannot be assessed • G1: Well differentiated • G2: Moderately differentiated • G3: Poorly differentiated • Other, specify	
Core	Extent of invasion	**Larynx** Multi selection value list (select all that apply)/numeric: • Not identified OR • Involves mucosa • Involves paraglottic space • Involves pre-epiglottic space • Partial thickness invasion of cartilage • Full thickness invasion of cartilage **Hypopharynx**	

Core/ Non-Core	Element name	Values	Implementation notes
		• Tissue layers involved, specify	
Core	Perineural invasion	Single selection value list: • Not identified • Present • Cannot be assessed, specify	
Core	Lymphovascular invasion	Single selection value list: • Not identified • Present • Cannot be assessed, specify	
Core	Margin status	Single selection value list/text/numeric: **Invasive carcinoma** • Involved – Specify margin(s), if possible • Not involved – Distance from closest margin ___ mm – Distance not assessable – Specify closest margin, if possible **Carcinoma in situ/high-grade dysplasia**** • Involved – Specify margin(s), if possible • Not involved – Distance from closest margin ___ mm – Distance not assessable – Specify closest margin, if possible • Cannot be assessed, specify	**High-grade dysplasia is synonymous with moderate/ severe dysplasia.
Core	Pathological staging (UICC TNM 8th edition) TNM descriptors	Choose if applicable: • m – multiple primary tumours • r – recurrent • y – post-therapy	Reproduced with permission. Source: Brierley, James D, Gospodarowicz Mary K, Wittekind, Christian. *UICC TNM Classification*

Core/ Non-Core	Element name	Values	Implementation notes
			of Malignant Tumours (8th edition), Chichester, UK: Wiley-Blackwell, 2017.
Core	Primary tumour (pT)	Single selection value list: • TX Primary tumour cannot be assessed • Tis Carcinoma in situ	Note that the results of lymph node/neck dissection are derived from a separate dataset.
Core	Primary tumour: Hypopharynx	Single selection value list: • T1 Tumour limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension • T2 Tumour invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension without fixation of hemilarynx • T3 Tumour more than 4 cm in greatest dimension, or with fixation of hemilarynx or extension to oesophageal mucosa • T4a Moderately advanced local disease: tumour invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus, or central compartment soft tissue# • T4b Very advanced local disease: tumour invades prevertebral fascia, encases carotid artery, or invades mediastinal structures	# Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.
Core	Primary tumour: Supraglottis	Single selection value list: • T1 Tumour limited to one subsite of supraglottis with normal vocal cord mobility • T2 Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g. mucosa of base of tongue, vallecula, medial wall of piriform	

Core/ Non-Core	Element name	Values	Implementation notes
		sinus) without fixation of the larynx • T3 Tumour limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage • T4a Moderately advanced local disease: tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx e.g. trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, or oesophagus • T4b Very advanced local disease: tumour invades prevertebral space, encases carotid artery, or mediastinal structures.	
	Primary tumour: Glottis	Single selection value list: • T1 Tumour limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility • T1a Tumour limited to one vocal cord • T1b Tumour involves both vocal cords • T2 Tumour extends to supraglottis and/or subglottis and/or with impaired vocal cord mobility • T3 Tumour limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of the thyroid cartilage • T4a Tumour invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx e.g. trachea, soft tissues of neck including deep/extrinsic muscle of the tongue	

Core/ Non-Core	Element name	Values	Implementation notes
		(genioglossus,hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus • T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures.	
Core	Primary tumour: Subglottis	Single selection value list: • T1 Tumour limited to subglottis • T2 Tumour extends to vocal cord(s) with normal or impaired mobility • T3 Tumour limited to larynx with vocal cord fixation • T4a Tumour invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx e.g. trachea, soft tissues of neck including deep/extrinsic muscles of tongue (genioglossus,hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus • T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures.	

Appendix E Summary table – explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008;337:1832)

Grade (level) of evidence	Nature of evidence
Grade A	At least one 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 (www.agreetrust.org). The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table below.

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	All sections
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	All sections
16 The different options for management of the condition or health issue are clearly presented	All sections
17 Key recommendations are easily identifiable	All sections
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 11
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