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 oral cavity

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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. Non-core data items are also 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)
- Ear, Nose and Throat UK (ENT-UK)
- The British Association of Oral and Maxillofacial Surgeons
- The UK and Ireland Association of Cancer Registries

- comments from specialist and general histopathologists on the draft document that was published on the Royal College of Pathologists website were considered as part of the review of the dataset.

The information used by the authors to develop this dataset was obtained by undertaking a search of the PubMed database from January 2010 to October 2022 (inclusive) for relevant primary research evidence and systematic reviews on head and neck mucosal malignancies, either specifically in the oral cavity or generally in the head and neck where these subsites can be separately identified. Key search terms searched included oral cavity (and subsites), clinical trial, prognosis, survival, surgery, chemotherapy, and radiotherapy. 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. They incorporate the core data items and commentary from the International Collaboration on Cancer Reporting (ICCR).[1] 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 will be 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.

All cancer datasets are formally revised every 3 years. However, each year, the College will ask the author of the dataset, in conjunction with the relevant subspecialty 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. This includes all 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, which 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 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, the Working Group on Cancer Services and Lay Advisory Group, and was placed on the College website for consultation with the membership from 8 February to 8 March. 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 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 oral cavity. The protocol applies to all invasive carcinomas of the oral cavity, including the tongue (excluding base of tongue), floor of mouth, buccal and labial mucosae, hard palate, gingiva and vermilion of lip (non-hair bearing). Lymphomas and sarcomas are not included. Neck dissections and nodal excisions are dealt with in a separate dataset and the oral cavity dataset should be used in conjunction with this, 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 oral cavity
- to describe its application in sufficient detail and clarity that pathology 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 multi-disciplinary team (and other clinicopathological) meetings and correlation with pre-operative imaging studies are important in maintaining and developing this partnership and providing optimal care to patients.[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 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 pattern of invasion and proximity of carcinoma to resection margins) have been shown to be related to clinical outcome.[3–8] 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[9,10]
  - monitoring changing patterns of disease, particularly by cancer registries
- 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 aid the selection and comparison of patients in clinical trials.

1.1 Design of this protocol

The College 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 oral cavity (published in 2018).[1] The current protocol includes all of the ICCR cancer dataset elements as well as additional information, elements and commentary. Core ICCR references have been updated to include relevant new information from 2018 to May 2022.

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.

Additional non-core data items that have not been included in the ICCR dataset but are recommended by the College are assessment of the worst pattern of invasion (WPOI) and tumour-infiltrating lymphocytes (TIL).

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 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 oral cavity

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

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

Clinical information should include:

- details of the 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 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.

Details of the legal basis of data sharing with the Cancer Registries can be accessed through the National Disease Registration Service.

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 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 (if containing bone) of the specimen may be helpful to record the extent of the disease and the sites from which tissue blocks are selected. Surgical margins should be painted with an appropriate marker 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. Some additional detail can be found in the relevant sections of the RCPath document *Tissue Pathways For Head and Neck Pathology*.[11] 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 Selection and recording of blocks for histology

In general, oral cavity resection 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.

Note that if the patient has been enrolled in a clinical trial, the trial protocol may dictate specific requirements in the macroscopic examination of the tumour and the selection of blocks. Also, if the specimen has been sampled for biobanking, this should be noted.

Sampling should be as follows:

- at least 1 block per 10 mm diameter of tumour, including 1 selected to demonstrate the maximum depth of invasion. Embed the whole tumour if less than 10 mm. If megablocks are used, then the number of blocks will be fewer.
- blocks of defined mucosal and deep margins
- non-neoplastic mucosa (at least 1 block)
- 1 specified block for molecular testing, in which the tumour content should be formally assessed. It is preferable that a megablock is not used and that this tissue has not been decalcified.

- a methodical text-based block key and/or photographic record of blocks taken should be included.

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

1 ICCR	Descriptor	Core/Non-core	Responses
	Neoadjuvant therapy	Core	Not known Administered Not administered
Neoadjuvant therapy comments: There is no agreed upon system for grading tumour regression in oral squamous cell carcinoma that has been treated with neoadjuvant therapy. However, a history of previous radiotherapy and/or chemotherapy should be included as histologic changes related to the therapy such as necrosis may affect interpretation of the tumour. **RCPath additional comments:** None. *[Level of evidence – GPP.]*			

2 ICCR	Descriptor	Core/Non-core	Responses
	Operative procedure	Core	Not specified Biopsy Resection Other
Operative procedure comments: Important to correlate the type of procedure (excisional biopsy or resection) with the material received for patient safety. Site-specific designations are required for accurate staging and for cancer registration. Modification of the resection, e.g. partial, total should be described. For example: hemi-glossectomy, partial glossectomy; hemi-mandibulectomy, segmental (partial) mandibulectomy; partial maxillectomy, total maxillectomy; selective neck dissection, modified neck dissection.[12,13]			

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	Not specified* Lip Tongue Gingiva Floor of mouth Hard palate Buccal mucosa Buccal vestibule Retromolar trigone Alveolar process Mandible Maxilla Other (specify)

Specimens submitted comments:

The anatomy and surgical interventions of the oral cavity are complex, and it is important to ensure accurate and precise communication between the pathologists and the treating and diagnostic team with respect to exact anatomic site of involvement, tumour laterality and specific operative procedures.[14–16]

The protocol applies to all carcinomas arising at these sites. For large cancers that involve more than 1 site, the primary site of involvement should be recorded.

Mucosal lip. The lip begins at the junction of the vermilion border with the skin and includes only the vermilion surface or that portion of the lip that meets the opposing lip.

Buccal mucosa (inner cheek). Refers to the mucous membrane lining of the inner surface of the cheeks and lips of contact of the opposing lips to the line of attachment of mucosa of the upper and lower alveolar ridge and pterygomandibular raphe.

Lower alveolar ridge. This refers to the mucosa overlying the alveolar process of the mandible, which extends from the line of attachment of mucosa in the buccal vestibule to the line of free mucosa of the floor of the mouth. Posteriorly it extends to the ascending ramus of the mandible.

Upper alveolar ridge. This refers to the mucosa overlying the alveolar process of the maxilla, which extends from the line of attachment of mucosa in the upper gingival buccal vestibule to the junction of the hard palate. The posterior margin is the upper end of the pterygopalatine arch.

Floor of the mouth. This is a semilunar space over the mylohyoid and hypoglossus muscles, extending from the inner surface of the lower alveolar ridge to the undersurface of the tongue. The posterior boundary is the base of the anterior pillar of the tonsil. It is divided into 2 sides of the submandibular and sublingual salivary glands.

Hard palate. This is the semilunar area between the upper alveolar ridge and the mucous membrane covering the palatine process of the maxillary palatine bones. It extends from the inner surface of the superior alveolar ridge to the posterior edge of the palatine bone.

Anterior 2-thirds of the tongue (oral tongue). This is the freely mobile portion of the tongue that extends anteriorly from the line of circumvallate papillae to the under-surface (ventral) of the tongue at the junction of the floor of the mouth. It includes the tip of tongue, lateral borders, dorsal surface and ventral tongue.

Retromolar trigone. A triangular shaped region extending distal from the mandibular third molar as the base and attaches to the hamulus of the medial pterygoid process of the sphenoid bone as the apex.

*'Not specified' should be used rarely and only after good effort has been employed to obtain the requisite information.[14–16]

RCPath additional comments:

Surgeons should define the cancer site using these listed sites, and pathology request forms, especially electronic request forms, should be designed with these included.

[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	Tumour site	Core	Not specified* Lip Tongue Gingiva Floor of mouth Hard palate Buccal mucosa Buccal vestibule Retromolar trigone Alveolar process

			Mandible Maxilla Other (specify)
	Tumour laterality	Core	Left Right Bilateral/midline

Tumour site comments:

The comments are as above in datapoint 3.

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
	Tumour maximum dimension	Core	Size (mm)

Tumour dimensions comments:

Tumour dimension is an important component in pathologic staging.[3] 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. At times only microscopic evaluation actually differentiates what clinically (phenotypically) appears to be tumour from what is actual invasion (not dysplasia or inflammation). The maximum depth of invasion should be recorded as core and the discussion should include how/why depth of invasion is different than tumour thickness (see data item 9).[17–25] As for other tissues, measurements are made pragmatically, acknowledging distortion of tissues by fixation and processing.[26]

RCPath additional comments:

Measurement should be provided to a maximum of 1 decimal place, with awareness of the sources of error in such a measurement.

[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 list

Histological tumour type comments:

The major histologic tumour types of squamous cell carcinoma as recognized by the World Health Organization (WHO) classification are squamous cell carcinoma, conventional type, basaloid, papillary, spindle, adenosquamous, acantholytic, lymphoepithelial, verrucous carcinoma and carcinoma cuniculatum. Hybrid lesions exist should be recognised as it may affect prognosis.[27] Subtypes should be assigned for both prognosis and cancer registry.[28–30]

Salivary carcinoma histologic type essentially defines its biologic behaviour and thus influences prognosis, patterns of recurrence and thus clinical management.[31,32] Some carcinoma types (i.e. basal cell adenocarcinoma, conventional acinic cell carcinoma) are more indolent with locoregional recurrence but low nodal and distant metastatic rates.[33]

The major histologic salivary gland carcinomas of minor salivary glands as recognized by the WHO classification are acinic cell carcinoma, adenoid cystic carcinoma, adenocarcinoma not otherwise specified (NOS), (mammary analogue) secretory carcinoma, cystadenocarcinoma, epithelial-myoepithelial carcinoma, mucoepidermoid carcinoma (low, intermediate and high grade), polymorphous adenocarcinoma (low, intermediate and high grade), (hyalinizing) clear cell carcinoma, intraductal carcinoma, carcinosarcoma, myoepithelial carcinoma, oncocytic carcinoma.[8]

Carcinoma ex pleomorphic adenoma is subclassified by type and extent of invasion, the latter including minimally invasive, invasive and intracapsular (non-invasive) cancers. The definition for minimally invasive carcinomas varies, ranging from 1.5 mm to 6 mm. Invasive carcinomas extend beyond 6 mm; non-invasive cancers are completely confined to within the capsule without evidence of penetration into extracapsular tissue. Prior to diagnosing a non-invasive carcinoma ex pleomorphic adenoma, sectioning of the entire lesion for histologic evaluation is recommended to exclude the presence of invasive growth. Prognosis has been linked to the degree of invasion with non-invasive and minimally invasive cancers apparently having a better prognosis than invasive cancers.[34,35]

RCPath additional comments:

Intra-oral pleomorphic adenomas are often incompletely encapsulated/ unencapsulated, and this should be considered in the assessment of invasion in these circumstances.

For mucosal melanoma, please refer to the current ICCR dataset. It is envisaged that a separate 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 ICCR	Descriptor	Core/Non-core	Responses
	Histological tumour grade	Core	Not applicable Cannot be assessed (Gx) Well-differentiated (G1) Moderately differentiated (G2) Poorly differentiated (G3)

Histological grade comments:

Based on the World Health Organization (WHO) classifications, 3 histologic grades of squamous cell carcinoma, conventional type are used: well, moderately or poorly differentiated.[8] The most aggressive or highest grade should be recorded if the tumour has a varied histology. Grading requires the assessment of keratinization, mitotic activity, cellular and nuclear pleomorphism, pattern of invasion and host response.[12,36–39] Squamous cell carcinoma subtypes such as verrucous carcinoma, basaloid squamous cell carcinoma and papillary squamous cell carcinoma are not graded.

Grading of minor salivary gland tumours follows the criteria for major salivary gland tumours.[8,33,35]

RCPath additional comments:

Practically, the most aggressive area (at x10 objective field) 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 well-differentiated and poorly differentiated tumours. Where a tumour has a varied appearance, then the highest grade is recorded.

Specific variants of squamous cell carcinoma such as spindle cell, verrucous, basaloid, papillary, and adenosquamous have intrinsic biological behaviours and currently do not require grading.

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

8 ICCR	Descriptor	Core/Non-core	Responses
	Depth of invasion	Core	Depth (mm) Not applicable Cannot be assessed

Depth of invasion comments:

Depth of invasion (DOI) in oral cavity squamous cell carcinoma, particularly of the tongue, has been identified as an important prognostic indicator. DOI is not synonymous with tumour thickness. In the recent American Joint Committee on Cancer (AJCC) the tumour stage (T) has been changed to reflect the importance of DOI.[3] DOI increases T

by 1 step for every 5 mm, whereby T1 is tumour ≤2 cm and DOI ≤5 mm, T2 is tumour ≤2 cm and DOI >5 mm and ≤10 mm or tumour >2 cm but ≤4 cm and ≤10 mm DOI and T3 is tumour >4 cm or any tumour >10 mm DOI. The Union for International Cancer Control (UICC) staging system is similar to the AJCC with 1 exception: if the tumour is >4 cm AND >10 mm DOI then the stage is T4a.[5] DOI measures the invasiveness of the carcinoma. To measure DOI, the basement membrane is identified and an imaginary line is drawn across the tumour. A vertical or plumb line extends to the deepest part of the tumour which represents the DOI. It is important to note that DOI is not synonymous with tumour thickness. An exophytic tumour may be thicker than an ulcerative tumour, but the DOI of the ulcerative lesion may be greater.[3,5,40–44]

RCPath additional comments:

DOI should be stated in mm (to a maximum of 1 decimal place) and is depth of invasion and not tumour thickness (Figure 1). Detailed guidance on measuring DOI provided in references.[43,45,46]

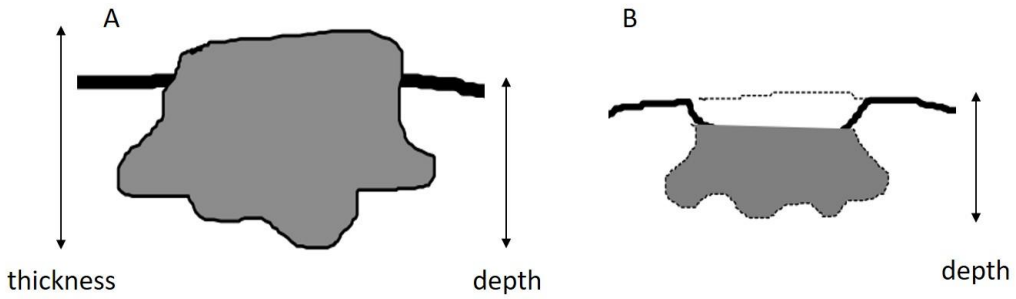

Figure 1: Descriptors of the depth of invasion for (A) nodular carcinoma and (B) ulcerated carcinoma. Note that depth of invasion refers to the depth of greatest spread in presumed continuity below the top of the adjacent mucosa. For both nodular and ulcerated tumours, the line of the original mucosal surface is reconstructed to determine the true thickness.

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

9 ICCR	Descriptor	Core/Non-core	Responses
	Pattern of invasive front	Core	Cohesive Non-cohesive Widely dispersed

Pattern of invasive front comments:

The pattern of invasion in oral squamous cell carcinoma has proven prognostic value and should be reported as cohesive or non-cohesive (see Figure 2). It is important to evaluate the most complex area of tumour-stroma interface (worst area) and ideally assessment should only be made on resection specimens or excisional biopsies. Acknowledgement is made that at times non-surgical treatment decisions are made on incisional biopsy only specimens and consequently the best assessment of pattern of invasion should be noted. Cohesive invasion has been defined in the literature as broad

sheets of cancer cells and/or tumour nests >15 cells across. Non-cohesive invasion shows a spectrum of appearances that includes narrow strands, small groups of <15 tumour cells and single infiltrating tumour cells (as illustrated in the figure 1 below).[40–42, 44] For stage T1/T2 oral squamous cell carcinoma, particularly those arising in the tongue, there is evidence that tumour satellites localized ≥1 mm away from the main tumour or nearest satellite (widely dispersed pattern/ WPOI-5) is a valid adverse prognostic factor.[4,44,47,48]

RCPath additional comments:

An alternative descriptor of the invasive pattern is WPOI.[4,44,47,48] This is a 5-tiered system implemented as part of a histological risk score, to provide more information on the pattern of invasion. 'Cohesive' corresponds to WPOI1, WPOI2 and WPOI3. 'Non-cohesive' corresponds to WPOI4. Widely dispersed corresponds to WPOI5.

The widely dispersed pattern is new to this edition of the dataset, but in all other respects the assessment of the pattern of invasive front and the definitions of the categories is the same as in the previous edition.

As stated above, in order to qualify as widely dispersed a tumour must have a discontinuous tumour satellite that is separated from the main tumour or nearest satellite by 1mm or greater. The separation should be by normal tissue and not tumour-induced fibrosis. The widely dispersed tumour can be of any size or pattern. Tumours can be classified as widely dispersed due to dispersed perineural invasion or dispersed lympho-vascular emboli. Consideration should be given to whether a putative widely dispersed pattern might be a tangential cut through a continuous tumour projection. Examination of sections immediately adjacent to the area of interest may assist in this.

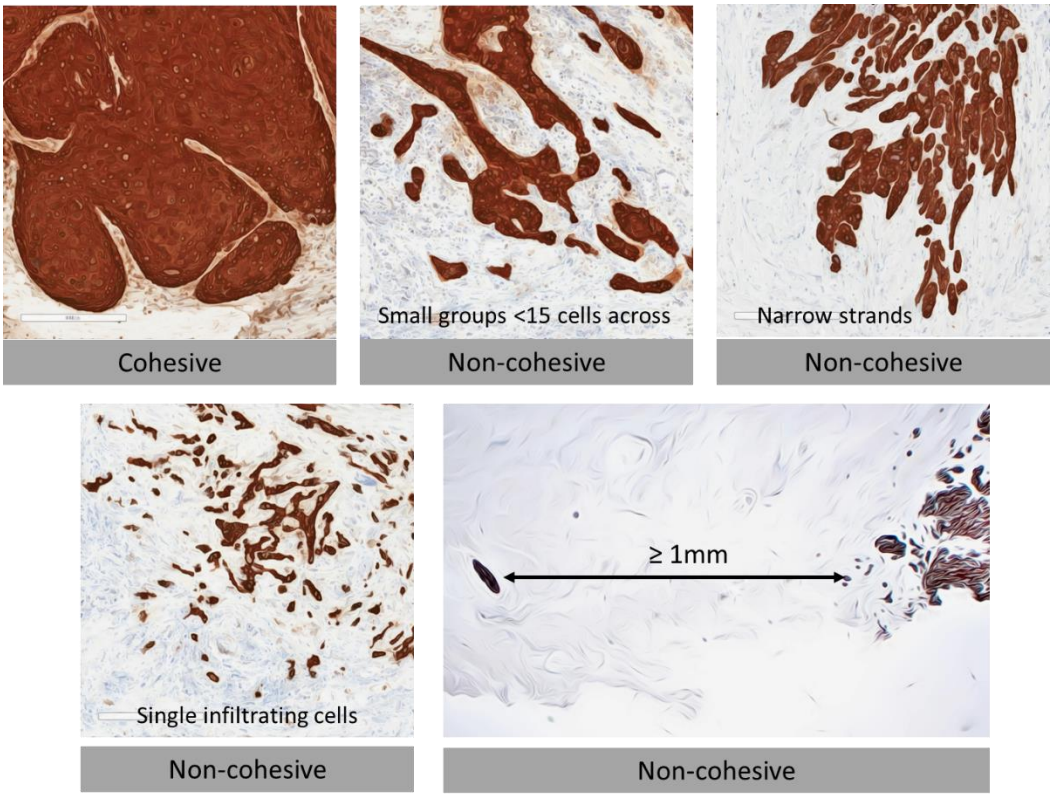

Figure 2: Exemplars of patterns of invasion.

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

10 ICCR	Descriptor	Core/Non-core	Responses
	Bone invasion	Core	Not identified Present Pattern: Erosive Infiltrative Bone involvement Cortical Medullary

Bone invasion comments:

Infiltrative bone involvement by squamous cell carcinoma correlates with a worse prognosis. Bone invasion may be a macroscopic feature, however sampling through the involved bone for histologic examination should be performed to obtain histologic evidence. The presence of bone invasion affects tumour staging and patients with bone invasion often have a worse prognosis. It is important to distinguish superficial cortical bone erosion from infiltrative invasion to the medullary bone as this is critical in accurate tumour staging and is an independent prognostic factor. If bone is resected, then bone margins should be recorded.[20,49]

RCPath additional comments:

Superficial erosion alone of bone / tooth socket by gingival primary is not sufficient to classify a tumour as T4. The presence or absence of involvement of the medullary space of the bone is required for TNM8 and affects overall survival.[49] Recording invasion which is limited to the cortex may also have value, but this does not impact on TNM8 stage. In addition, there is evidence to support describing the pattern of invasion as erosive or infiltrative.

[Level of evidence B – The presence of bone involvement is important for accurate staging of oral cavity malignancies.]

11	Descriptor	Core/Non-core	Responses
ICCR	Perineural invasion*	Core	Not identified Present Ahead of the invasive front: Y/N Cannot be assessed

Perineural invasion comments:

Perineural invasion is associated with a worse prognosis, regardless of nerve size and should be recorded. The presence or absence of perineural and/or endoneural/intraneural invasion may impact subsequent therapy and prognosis.[12,38,50–58]

RCPath additional comments:

There is conflicting literature regarding the importance of perineural invasion only being recorded when it is identified ahead of the invasive front, as suggested in the previous RCPath dataset (2013). In light of this, we suggest that all perineural invasion is recorded, as indicated in the ICCR dataset, but particular emphasis should be made in the report when this is ahead of the invasive front. If possible, a distinction should be made between nerves which have been enveloped by an advancing tumour mass, and true invasion of the perineurium.

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

12	Descriptor	Core/Non-core	Responses
ICCR	Lymphovascular invasion	Core	Not identified Present Cannot be assessed

Lymphovascular invasion comments:

There is a need to distinguish between intravascular tumour embolization and retraction artefact. Positive vascular invasion should be reported only when tumour emboli are identified within endothelial lined spaces. No distinction between venous channels and small lymphatics is required.[36,59]

RCPath additional comments:

None.

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

*Not applicable for nasopharynx.

13 ICCR	Descriptor	Core/Non-core	Responses
	Margin status: invasive carcinoma	Core	Involved (specify) Not involved (distance) Cannot be assessed
	Margin status: in situ carcinoma/HG dysplasia	Core	Involved (specify) Not involved (distance) Cannot be assessed

Margin status comments:

All surgical margins should be measured in millimetres histologically for both mucosal and deep margins. In the comments section, acknowledgement should be made how the surgical margin was measured, for example if the margin was submitted from the tumour bed margin at the time of the operative procedure rather than from the surgical specimen.[6,7,60,61] The presence of high-grade dysplasia/carcinoma in situ at the margin is associated with an increased risk of local recurrence and this should be recorded. The definition of a close margin is not standardised but in the oral cavity from a surgical point of view >5 mm is clear and 1–5 mm is close while <1 mm is involved. Acknowledgement is made of fixation and processing distortion on measurements which may cause tissue shrinkage including the surgical margin.[26] Acknowledgement is also made of any laser or electrocautery associated tissue distortion such as cellular and nuclear polymorphism, nuclear hyperchromatism, epithelial cell separation, collagen denaturation, etc. on measurements including the surgical margin.[62–64] Any bone resection margins should be identified and comment on the presence or absence of carcinoma at these margins should be provided.[20] Dysplastic changes include abnormal cellular organisation, increased mitotic activity, and nuclear enlargement with pleomorphism.[6,7,12,38,39,42,60,61,65] Although terminology varies, using the 2022 WHO criteria for oral dysplasia, dysplasia limited to the lower 1-third of the epithelium is generally referred to as mild dysplasia.[39] Moderate dysplasia is defined as cytological atypia extending to the middle third of the epithelium and severe dysplasia extends to the upper third of the epithelium. Carcinoma in situ is considered synonymous with severe dysplasia. Currently, the use of a binary grading system similar to laryngeal dysplasia has been proposed but to date lacks validation in the oral cavity. In a binary system, low-grade dysplasia includes mild dysplasia and mild–moderate dysplasia. The term high grade dysplasia includes moderate dysplasia, severe dysplasia and carcinoma in situ.[39]

Reporting of surgical margins for carcinomas of the minor salivary glands should follow those used for squamous cell carcinoma of oral cavity.

RCPath additional comments:

While the method above is favoured for margin assessment, an additional method for recording the residual tumour 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

If both systems are 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 0.0 mm from the margin in the main specimen, but additional margin biopsies are clear.

Measurement should be provided to a maximum of 1 decimal place, but pragmatically, with awareness of the sources of error in such a measurement. Caution must be exercised in the assessment margins where there is laser or electrocautery artefact. Where significant, this should be acknowledged as a source of error in the measurements of the surgical margin.

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

Tumour focality comments:

True multifocal or synchronous oral cavity carcinomas are rare. Patients with oral squamous cell carcinomas have a high incidence (2–3%) of developing a second primary lesion however these are usually metachronous lesions. The theory of field cancerisation whereby contiguous genetically altered areas of mucosa lead to the development of neoplasms have been supported by studies evaluating clonality and other molecular markers. Proliferative verrucous leucoplakia has the propensity of developing multifocal tumours. It is rare to have multiple tumours disconnected but not uncommon to have more than 1 squamous cell carcinoma connected via dysplasia. The location, proximity to dysplastic epithelium, depth and nodal status remain important. Tumour focality seems to be a standard not just for staging and pathology but for clinical trials and treatment considerations.[66–69]

RCPath additional comments:

None.

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

NC2	Descriptor	Core/Non-core	Responses
	Tumour other dimensions	Non-core	Size (mm)

Tumour dimensions comments

Tumour dimension is an important component in pathologic staging.[3] 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. At times only microscopic evaluation actually differentiates what clinically (phenotypically) appears to be tumour from what is actual invasion (not dysplasia or inflammation). The maximum depth of invasion should be recorded as core and the discussion should include how/why depth of invasion is different than tumour thickness (see data item 9).[17–25] As for other tissues, measurements are made pragmatically, acknowledging distortion of tissues by fixation and processing.[26]

RCPath additional comments:

If possible, microscopic measurement should be provided to a maximum of 1 decimal place, but pragmatically, with awareness of the sources of error in such a measurement.

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

NC3	Descriptor	Core/Non-core	Responses
	Co-existent pathology	Non-core	None identified Dysplasia In situ carcinoma Other (specify)

Coexistent pathology comments:

The most common sites of dysplasia with the highest risk of malignant transformation are lateral and ventral tongue, floor of mouth and lower lip. Dysplastic changes include abnormal cellular organisation, increased mitotic activity including abnormal forms, and nuclear enlargement with pleomorphism. Although terminology varies, dysplasia limited to the lower 1-third of the epithelium is generally referred to as mild dysplasia (low-grade dysplasia), dysplasia limited to the lower 2-thirds as moderate dysplasia and dysplasia involving the full thickness as severe dysplasia/carcinoma in situ.[65,70] However, when moderate dysplasia has marked cytologic atypia, then often the lesion will be upgraded to severe dysplasia. The term high-grade dysplasia includes moderate and severe dysplasia and carcinoma in situ. A recently described subset of oral dysplasia is positive for high-risk HPV. The epithelium exhibits full-thickness dysplastic changes with karyorrhexis and apoptosis and the cells are strongly positive for p16 by Immunohistochemistry.[71]

Proliferative verrucous leucoplakia (PVL) is a distinct form of oral precancer of unknown aetiology with a multifocal presentation and a progressive course with high recurrence rates and malignant transformation in as many as 70% of cases.[72,73] This diagnosis requires adequate clinical information. Subepithelial fibrosis is a characteristic of oral

submucous fibrosis and increased fibrosis is associated with an increased risk of epithelial dysplasia.[74] Some inherited genetic mutations are associated with a higher risk of oral cancer development including Fanconi anaemia, Li-Fraumeni syndrome and dyskeratosis congenita.[8] Care must be taken to rule out reactive atypia which can be seen in epithelium adjacent to ulcers and with fungal infections.

RCPath additional comments:

Use of the WHO 2022 scheme for grading epithelial dysplasia as mild, moderate or severe is recommended. With respect to the grading of epithelial dysplasia, using thirds of the epithelial thickness is insufficiently nuanced to capture the breadth of architectural and cytological atypia seen in epithelial dysplasia. This concept should be used with caution.

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

NC4	Descriptor	Core/Non-core	Responses
ICCR	Ancillary studies	Non-core	Not performed Performed (specify)

Ancillary studies comments:

In most cases, further studies are not required for the diagnosis. Epithelial immunohistochemical markers may be required for poorly differentiated or spindle cell carcinoma including AE1/AE3, CK5/6, p63 and p40.[75] Lymphoepithelial squamous cell carcinoma in the oral cavity is rare and although not all cases are Epstein-Barr virus (EBV)-positive, EBV-encoded small RNAs (EBERs) studies are indicated.[76] There is currently no role for routine HPV high risk type testing in oral squamous cell carcinoma.[77–79]

RCPath additional comments:

None.

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

6.1 RCPath additional non-core items

NC5	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

TIL Comments:

There is accumulating evidence that tumour-infiltrating lymphocytes (TIL) have 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),[80–83] but simple semi-quantitative TIL assessment on H&E sections has consistently shown clinical validity as a prognostic marker in both HPV- and HPV+ oral and oropharyngeal cancers.[80,83,84] 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.[83,85] Although in comparison oral tumours contain lower TIL levels, with a smaller proportion of tumours containing high TIL levels, this feature is similarly prognostic.

As yet, there is no consensus for a common TIL scoring system across different cancers, and it is clear that 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.[84] 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).[80,83] Assessment is made under low-power magnification, ideally from a full-face H&E section (small biopsies may not account for infiltrate heterogeneity) and taking into account 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, 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, the majority 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 the 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/PD-L1 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.]

7 Diagnostic coding and staging

7.1 General comments

Pathological staging should be undertaken using UICC TNM8 (Appendix B). It is also useful to note that multiple separate foci of invasion are commonly identified in the oral cavity, particularly where the tumour has arisen on a background of field change. UICC TNM8 rule 5 states that the tumour with the highest T category should be categorised and the multifocal nature noted by the suffix (m) or the number of invasive foci noted in parenthesis.

7.2 Staging

15 ICCR	Descriptor	Core/Non-core	Responses
	Pathological staging (UICC TNM8)	Core	See Appendix 2 for TNM

Pathological staging comments:

By American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) convention, the designation T refers to a primary tumour that has not been previously treated. Both staging systems integrate depth of invasion (DOI) into the T categories. Similar to skin malignancies, DOI is significantly associated with disease-free survival.[86] Per the AJCC 8th edition, specific instructions are given to measure DOI. To measure DOI,[5] the basement membrane is identified and an imaginary line is drawn across the tumour. A vertical or plumb line extends to the deepest part of the tumour which represents the DOI. It is important to note that DOI is not synonymous with tumour thickness. An exophytic tumour may be thicker than an ulcerative tumour, but the DOI of the ulcerative lesion may be greater. An important point to highlight is that the UICC 8th edition does not specify how DOI should be measured.[5] In addition as outlined under Depth of invasion, UICC staging system is similar to the AJCC with 1 exception: if the tumour is >4 cm AND >10 mm DOI then the stage is T4a. Superficial erosion alone of bone/tooth socket by primary gingival tumour is not sufficient to classify a tumour as T4a[5] which requires invasion into medullary bone.

RCPath additional comments:

Some ongoing Clinical Trials may be using an earlier version of the TNM classification (e.g. TNM7). If this applies, then an earlier staging scheme can be added, in addition to TNM8.

[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 a biopsy specimen 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 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.[87]

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

11.1 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.[88–90] However, a number of different anti-PD-L1 clones (for example SP142 and 22C3) are available from different manufacturers and the published trials have examined specific clones linked to the activity of specific anti-PD-L1 immunotherapy agents.[88] Moreover, these tests use different algorithms and cut-offs to identify which patients are more likely to benefit from each immunotherapeutic agent. 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.

11.2 Cancer-associated fibroblasts

High levels of cancer-associated fibroblasts (CAF) are associated with poor prognosis in numerous cancer types, including oral and oropharyngeal cancer.[19,91–95] Although CAF has become accepted terminology, these cells have also been referred to as peritumour fibroblasts and myofibroblasts. Different CAF subtypes exist, although historically the term has been used to refer to cells with a myofibroblastic phenotype; smooth muscle actin (SMA)-positive, contractile cells that secrete extracellular matrix. In tissues, these can be identified as SMA-positive spindle cells producing a collagen-rich, desmoplastic stroma. Notably, the *mesenchymal* molecular subgroup, which accounts for around a quarter of HNSCC cases, is defined by high CAF levels (subgroups – basal, mesenchymal, classical,

atypical).[96] Consistent with their association with poor prognosis, CAF have many tumour-promoting functions with recent studies identifying an association between high CAF levels and resistance to anti-PD1/PD-L1 immunotherapy.

A 2017 meta-analysis of 12 oral cancer studies that quantified CAF using SMA immunohistochemistry concluded that high levels of stromal CAF is significantly associated with decreased disease-free and overall survival (HRs – 3.32 and 2.16 respectively; both P<0.0001).[92] Consistent with this, high CAF levels are frequently associated with other parameters of poor prognosis, including depth and pattern of invasion, lymph node metastasis, extracapsular spread and low levels of infiltrating T-cells.[91–95, 97–100]

As yet, there is no consensus for a common CAF scoring system. The largest HNSCC study found the prognostic utility of a 3-group semi-quantitative scoring system, scoring tumours as CAF^{high} (>50% of tumour stroma SMA-positive), $CAF^{moderate}$ (5–50% of tumour stroma SMA-positive) and CAF^{low} (<50% of tumour stroma SMA-positive).[95] Combining CAF^{high} and $CAF^{moderate}$ groups to generate a 2-group scoring system retains prognostic significance.[93] Assessment is made under low-power magnification. SMA immunoreactivity can vary greatly between different areas of the same tumour and ideally assessment should be made from a full-face section (very small biopsies may not account for stromal heterogeneity). Other studies have found that the presence of SMA-positive CAF at the tumour infiltrative front are more prognostic than in the tumour centre.[100]

12 Criteria for audit

The following are recommended by the RCPath as 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):

- 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. NHS trusts are 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 7 and 10 calendar days of the procedure

  - standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days

- 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 multidisciplinary team (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 will 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; these are, therefore, currently considered acceptable.

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)	28899001
		Squamous cell carcinoma of oral cavity	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**
Lip	T-52000	Lip structure (body structure)	48477009
External upper lip (vermillion)	T-52131	Structure of vermilion border of upper lip (body structure)	128250007
External lower lip (vermillion)	T-52231	Structure of vermilion border of lower lip (body structure)	128251006
Commissures	T-52003	Commissure of lips (body structure)	83299001
Oral cavity	T-51004	Oral cavity structure (body structure)	7462004
Tongue	T-53000	Tongue structure (body structure)	21974007
Tongue dorsum/lateral border	T-53100	Structure of dorsum of tongue (body structure)	66938003
Tongue ventral surface	T-52123	Structure of inferior surface of tongue (body structure)	422005
Buccal mucosa	T-51300	Oral mucous membrane structure (body structure)	113277000
Gingiva (maxilla)	T-54920	Structure of gum of maxilla (body structure)	23114008
Gingiva (mandible)	T-54930	Gum of mandible	304704007
		Gum of maxilla	304703001
Floor of mouth	T-51200	Floor of mouth	36360002
Palate	T-51110	Hard palate	90228003
		Soft palate	49460000
Retromolar	T-51600	Retromolar area	85816001

Mandible	T-10710	Mandible	91609006
Maxilla	T-10180	Maxilla	70925003

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 8, which should be used for all tumours diagnosed after 1 January 2020.

Lip and oral cavity

Primary tumour (T)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in situ

T1 Tumour 2 cm or less in greatest dimension and 5 mm or less depth of invasion*

T2 Tumour 2 cm or less in greatest dimension and more than 5 mm but no more than 10 mm depth of invasion or tumour more than 2 cm but not more than 4 cm in greatest dimension and depth of invasion no more than 10 mm

T3 Tumour more than 4 cm in greatest dimension or more than 10 mm depth of invasion

T4a (Lip) Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (of the chin or the nose)

T4a (Oral cavity) Tumour more than 4 cm in greatest dimension and more than 10 mm depth of invasion or tumour invades through the cortical bone of the mandible or maxillary sinus, or invades the skin of the face

T4b (Lip and oral cavity) Tumour invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery

*Superficial erosion of bone/tooth socket by gingival primary is not sufficient to classify a tumour as T4a.

For regional lymph nodes, refer to the *Dataset for Histopathological Reporting of Nodal Excisions and Neck Dissection Specimens Associated with Head and Neck Carcinomas*.

Regional lymph nodes (N)

NX Regional lymph nodes cannot be assessed.

N0 No regional lymph node metastases.

N1 Regional lymph node metastases present

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

Appendix C Reporting proforma for carcinomas of the oral cavity

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

Neoadjuvant therapy

Information not provided □ Not administered □

Administered □ specify type:

Chemotherapy □ Radiotherapy □ Chemoradiotherapy □

Targeted therapy □ specify if available ……

Immunotherapy □ specify if available ……

Operative procedure (core) (select all that apply)

Not specified □

Resection □ Glossectomy □ Buccal mucosa □ Lip □

Mandibulectomy □ Maxillectomy □ Palatectomy □

Other □ specify.....

Excisional biopsy □ Incisional biopsy □

Neck (lymph node) dissection □, specify ……

Other □ specify……..

Specimens submitted (core) (select all that apply)

Not specified □

Lip □ Tongue □ Gingiva □ Floor of mouth □ Hard palate □ Buccal mucosa □

Buccal vestibule □ Retromolar trigone □ Alveolar process □ Mandible □ Maxilla □

Other □, specify ……

Tumour site (core) (select all that apply)

Not specified □

Lip

Vermilion border upper lip		Left □	Right □ Midline □	Laterality not specified □
Vermilion border lower lip		Left □	Right □ Midline □	Laterality not specified □
Mucosa of upper lip	Left □	Right □	Midline □	Laterality not specified □
Mucosa of lower lip	Left □	Right □	Midline □	Laterality not specified □
Commissure of lip	Left □	Right □		Laterality not specified □

Oral cavity

Lateral border of tongue		Left □	Right □	Laterality not specified □
Ventral surface of tongue, NOS		Left □	Right □ Midline □	Laterality not specified □
Dorsal surface of tongue, NOS		Left □	Right □ Midline □	Laterality not specified □
Anterior 2-thirds of tongue, NOS	Left □	Right □	Midline □	Laterality not specified □
Upper gingiva (gum)		Left □	Right □ Midline □	Laterality not specified □
Lower gingiva (gum)		Left □	Right □ Midline □	Laterality not specified □
Floor of mouth, NOS		Left □	Right □ Midline □	Laterality not specified □
Hard palate		Left □	Right □ Midline □	Laterality not specified □
Buccal mucosa (inner cheek)		Left □	Right □	Laterality not specified □
Retromolar trigone		Left □	Right □	Laterality not specified □

Vestibule of mouth

Maxillary		Left □	Right □ Midline □	Laterality not specified □
Mandibular		Left □	Right □ Midline □	Laterality not specified □

Alveolar process

Maxillary		Left □	Right □ Midline □	Laterality not specified □
Mandibular		Left □	Right □ Midline □	Laterality not specified □
Mandible		Left □	Right □ Midline □	Laterality not specified □
Maxilla		Left □	Right □ Midline □	Laterality not specified □

Other, specify including laterality □

Tumour dimensions (core)

Maximum tumour dimension (largest tumour) …….mm

Cannot be assessed □

Histological tumour type (core)

Multi selection value list (select all that apply):

Squamous cell carcinoma (Single selection value list):

Squamous cell carcinoma, conventional type □

Basaloid squamous cell carcinoma □

Papillary squamous cell carcinoma □

Verrucous carcinoma □

Spindle (sarcomatoid) squamous cell carcinoma □

Adenosquamous cell carcinoma □

Acantholytic squamous cell carcinoma □

Carcinoma cuniculatum □

Lymphoepithelial squamous cell carcinoma □

Other, specify □

Minor salivary gland tumour, specify type ……

Neuroendocrine carcinoma, specify type ……

Other, specify type……

Cannot be assessed, specify ……

Histological tumour grade (core)

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

G2: Moderately differentiated □ G3: Poorly differentiated □

Other, specify □……

Depth of invasion (core)

……mm Not applicable □ Cannot be assessed, specify □ ……

Pattern of invasive front (core)

Cohesive □ Non-cohesive □ Widely dispersed □

Bone invasion (core)

Not identified □ Cortical erosion □ Medullary infiltration □

Cannot be assessed, specify ……..

Perineural invasion (core)

Not identified □ Present □ Ahead of the invasive front? Y □ N □

Cannot be assessed, specify □ ……..

Lymphovascular invasion (core)

Not identified □ Present □ Cannot be assessed, specify □ **……..**

Margin status (core)

Invasive carcinoma

Specify involved margin(s)….

Distance from closest margin…..mm

Specify closest margin….

Margins not assessable □

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 ……..

Pathological staging (core) (UICC TNM 8th edition, only if applicable)

pTNM stage pT.....

Appendix D Reporting proforma for carcinomas of the oral cavity (list format)

Core/ Non-Core	Element name	Values	Implementation notes
Core	**Neoadjuvant therapy**	**Core:** Single selection value list: • Information not provided • Not administered • Administered, specify type Chemotherapy Radiotherapy Chemoradiotherapy Targeted therapy (specify) Immunotherapy (specify)	
Core	**Operative procedure**	**Core:** Single selection value list Resection Glossectomy Buccal Mucosa Lip Mandibulectomy Maxillectomy Palatectomy Other (specify) Excisional Biopsy Incisional Biopsy 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**	Not specified Lip Tongue Gingiva Floor of mouth Hard palate Buccal mucosa Buccal vestibule Retromolar trigone Alveolar process Mandible	.

Core/ Non-Core	Element name	Values	Implementation notes
		Maxilla Other (specify)	
Core	**Tumour site**	**Core:** Single selection value list: Not specified* Lip Vermilion border upper lip Left Right Midline Laterality not specified Vermilion border lower lip Left Right Midline Laterality not specified Mucosa of upper lip Left Right Midline Laterality not specified Mucosa of lower lip Left Right Midline Laterality not specified Commissure of lip Left Right Midline Laterality not specified Tongue Lateral border of tongue Left	

Core/ Non-Core	Element name	Values	Implementation notes
		Right Laterality not specified Ventral surface of tongue, NOS Left Right Midline Laterality not specified Dorsal surface of tongue, NOS Left Right Midline Laterality not specified Anterior 2-thirds of tongue, NOS Left Right Midline Laterality not specified Gingiva Upper gingiva (gum) Left Right Midline Laterality not specified Lower gingiva (gum) Left Right Midline Laterality not specified Floor of mouth Left Right Midline Laterality not specified Hard palate	

Core/ Non-Core	Element name	Values	Implementation notes
		Left Right Midline Laterality not specified Buccal mucosa Left Right Midline Laterality not specified Retromolar trigone Left Right Midline Laterality not specified Buccal vestibule Maxillary Left Right Midline Laterality not specified Mandibular Left Right Midline Laterality not specified Alveolar process Maxillary Left Right Midline Laterality not specified Mandibular Left Right	

Core/ Non-Core	Element name	Values	Implementation notes
		Midline Laterality not specified Mandible Left Right Midline Laterality not specified Maxilla Left Right Midline Laterality not specified Other (specify)	
Core	**Tumour dimensions**	**Core:** Maximum tumour dimension (largest tumour) ___ mm **Core:** Cannot be assessed	
Core	**Histological tumour type**	**Core**: multi value selection list Squamous cell carcinoma Squamous cell carcinoma, conventional type Basaloid squamous cell carcinoma Papillary squamous cell carcinoma Verrucous carcinoma Spindle (sarcomatoid) squamous cell carcinoma Adenosquamous cell carcinoma Acantholytic squamous cell carcinoma Carcinoma cuniculatum Lymphoepithelial squamous cell carcinoma **Other**	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
		Minor salivary gland tumour, (specify) Neuroendocrine carcinoma (specify) Other (specify) **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 • Other, specify • Cannot be assessed, specify	
Core	**Depth of invasion**	**Non-core:** Numeric/Single selection value list: • ___ mm • Not applicable • Cannot be assessed, specify	
Core	**Pattern of invasive front**	**Core**: Single selection value list: • Cohesive • Non-cohesive • Widely dispersed	
Core	**Bone invasion**	**Core**: Single selection value list: • Not identified • Present • Cannot be assessed, specify	
Core	**Perineural invasion**	**Core**: Single selection value list: • Not identified	

Core/ Non-Core	Element name	Values	Implementation notes
		• Present • Ahead of the invasive front • Cannot be assessed, specify	
Core	**Lymphovascular invasion**	**Core**: Single selection value list: • Not identified • 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/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 *** OR • Cannot be assessed, specify	
Core	**Pathological staging** (UICC TNM 8th edition)	**Core**: Choose if applicable: • m – multiple primary tumours	

Core/ Non-Core	Element name	Values	Implementation notes
	TNM descriptors	• r – recurrent • y – post-therapy	
Core	**Primary tumour (pT)**	**Core**: Free text	

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 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 population 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 population 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 population 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 autopsy guidelines of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this autopsy guideline 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	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