

Standards and datasets for reporting cancers

Dataset for histopathology reporting of mucosal malignancies of the oral cavity

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NICE has accredited the process used by The Royal College of Pathologists to produce its Cancer Datasets and Tissue Pathways guidance. Accreditation is valid for 5 years from July 2012. More information on accreditation can be viewed at www.nice.org.uk/accreditation.
For full details on our accreditation visit: www.nice.org.uk/accreditation.

Foreword

The cancer datasets published by The Royal College of Pathologists are a combination of textual guidance and reporting proformas that should assist pathologists in providing a high standard of care for patients and facilitate accurate cancer staging. Guidelines are systematically developed statements to assist the decisions of practitioners and patients about appropriate healthcare for specific clinical circumstances and are based on the best available evidence at the time the document was prepared. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

Each dataset contains **core data items** that will be mandated for inclusion in the Cancer Outcomes and Services Dataset (previously the National Cancer Data Set) in England. Core data items are items 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 90% of reports on cancer resections should record a full set of core data items.

Other, **non-core, data items** are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

Authors are aware that datasets are likely to be read by, *inter alia*, trainees, general pathologists, specialist pathologists and clinicians, and service commissioners. The dataset should seek to deliver guidance with a reasonable balance between the differing needs and expectations of the different groups. The datasets are not intended to cover all aspects of service delivery and reference should be made, where possible and appropriate, to guidance on other aspects of delivery of a tumour-specific service, e.g. cytology and molecular genetics.

The dataset has been reviewed by the Working Group on Cancer Services and was placed on the College website for consultation with the Fellowship from 24 October to 21 November 2011. All comments received from the Working Group and Fellowship were addressed by the authors, to the satisfaction of the Chair of the Working Group and the Director of Publications.

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 Director of Professional Standards and are available on request. The authors of this document have declared that there are no conflicts of interest.

Each year, the College asks the authors of the dataset, in conjunction with the relevant subspecialty adviser to the College, to consider whether or not the dataset needs to be revised.

1 Introduction

1.1 Purpose of the dataset

This document presents the core data that should be provided in histopathology reports on specimens of mucosal malignancies originating in the oral cavity. Malignancies arising in the nose and paranasal sinuses, pharynx and larynx are described in companion datasets, although most of the guidance is the same for each site. The guidance is mainly derived from data on squamous cell carcinomas, which account for 95% of oral malignancies, but similar principles may be applied to the reporting of other mucosal malignancies arising in this anatomical area including adenocarcinomas, neoplasms of minor salivary glands and

neuroendocrine epithelial neoplasms that are important considerations in the differential diagnosis but are not described in detail. Important site-specific and diagnosis-specific recommendations are included as appropriate.

The following stakeholder groups have been consulted:

- 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 Association of Cancer Registries
- the National Cancer Intelligence Network.

Comments from specialist and general histopathologists on the draft document that is being published on the College website will be considered as part of the review of the dataset.

The authors have searched electronic databases for relevant research evidence and systematic reviews on head and neck mucosal malignancies up to April 2011. The recommendations are in line with those of other national pathology organisations (College of American Pathologists, The Royal College of Pathologists of Australasia) and the ENT-UK consensus document for the management of patients with head and neck malignancies [www.entuk.org/publications]. The level of evidence for the recommendations has been summarised according to College guidance (see Appendix E) and indicated in the text as, for example, [*level B*]. No major conflicts in the evidence have been identified and minor discrepancies between studies have been resolved by expert consensus.

No major organisational changes have been identified that would hinder the implementation of the dataset, which is fully integrated with the Cancer Outcomes and Services Dataset, and there are no major financial implications arising from implementation of this guidance.

Optimal reporting of specimens from the head and neck area requires a partnership between the pathologist and surgeon/oncologist.¹ 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 clinicopathological meetings and correlation with pre-operative imaging studies are important in maintaining and developing this partnership.²

The core pathological data are summarised as a proforma, which may be used as the main reporting format or may be combined with free text as required. Individual centres may wish to expand the detail in some sections, e.g. for sites and subsites or to facilitate the recording of data for particular tumour types.

The guidelines should be implemented for the following reasons.

- a. Certain features of invasive mucosal carcinomas (type, size and grade of the primary carcinoma, the pattern of invasion and proximity of carcinoma to resection margins) have been shown to be related to clinical outcome.³⁻¹¹
- b. 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 or chemotherapy¹²
 - monitoring changing patterns of disease, particularly by cancer registries.
- c. These features provide sufficiently accurate pathological information that can be used, together with clinical data, for the patient to be given a prognosis.

- d. To allow the accurate and equitable comparison of surgeons in different surgical units, to identify good surgical and pathological practice, and the comparison of patients in clinical trials.

1.2 Potential users of the dataset

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. 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 Cancer Outcomes and Services Dataset and are collected for epidemiological analysis by Cancer Registries on behalf of the National Cancer Intelligence Network.

1.3 Changes since the second edition

The second edition of this dataset (2005) encompassed mucosal and salivary malignancies and neck dissection specimens. In this revision, separate datasets on mucosal malignancies at each of the main head and neck sites have been produced, alongside datasets on malignant neoplasms arising in the major salivary glands and the dataset on neck dissection specimens for metastatic disease. For convenience, the section on core data required for nodal disease is replicated in each dataset; users should cross-refer to the more detailed discussion in the separate neck dissection dataset. The guidance has been revised to include recent evidence supporting the inclusion of specific data items.

The strength of the basis in published evidence for the recommended core data items has been reviewed (see Appendix E). The primary reasons for inclusion of core data are the need for accurate classification and staging and the desire to predict those carcinomas that are likely to recur at local, regional (nodal) or distant sites so that appropriate surveillance, surgery, radiotherapy and/or chemotherapy can be delivered to mitigate the effects of recurrence. TNM staging, in isolation, does not provide sufficient information for management and prognosis¹¹ and additional factors need to be considered. Inevitably, the strength of evidence varies for the prediction of different patterns of recurrence and for survival, and varies between primary tumour sites. To keep the guidance relatively simple, not all possible variations are described in detail and the reader is referred to the cited literature for more information.

The core dataset for squamous cell carcinomas is largely unchanged since the second edition in 2005, although site-specific variations are now more explicitly presented, acknowledging the lack of evidence to support recording tumour thickness in the nasal region and larynx and incorporating evidence of human papillomavirus infection as a core data item for oropharyngeal carcinomas. The 7th edition of the UICC TNM staging system is recommended,¹³ including the separate section on mucosal melanomas.

The reporting proforma has been modified to provide a simpler layout with easily identified options for transfer to an electronic format. For ease of access, the generic head and neck request form and the proforma summary for neck dissections are included with each of the site-specific documents.

1.4 Acknowledgements

For the draft request forms, we are grateful to the late Professor DG McDonald, University of Glasgow, for permission to use the diagrams of the oral cavity and jaws, and to the UICC and Springer-Verlag to use the diagrams of the larynx and neck that are adapted from the *TNM Atlas (3rd edition)*, 1989.

2 Specimen request form

The request form should include patient demographic data, the duration of symptoms, whether surgery is palliative or curative, details of previous histology or pathology reports and the core clinical data items (see section 4). Clinical TNM stage is useful for correlation with pathological findings. A history of previous radiotherapy or chemotherapy should be included, as this may influence the interpretation of the histological changes and should prompt a comment on the extent of any response to treatment. The request form should provide the opportunity for surgeons to provide annotated diagrams of specimens, either as free-hand drawings or on standard diagrams (see Appendix C). Copies of reports that are sent to the Cancer Registries should include the patient's address if possible.

3 Specimen handling and block selection

3.1 Preparation of the specimen before dissection

Resection specimens should be orientated by the surgeon and pinned or sutured to cork or polystyrene blocks. The surgeon should indicate surgically critical margins using metal tags or sutures. Fixation is in a formaldehyde-based solution for 24–48 hours in a container of adequate size (the volume of fixative should be ten times that of the tissue).

Photography and radiography of the specimen may be used to record the nature 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.

3.2 Site-specific considerations and block selection

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.

In general, these specimens may be assessed by cutting the specimen with a large knife into 3–5 mm parallel slices to demonstrate both the relationship of the tumour to mucosal resection margins, and the maximum depth of invasion by the tumour. Specimens from the central and lateral parts of the mouth should be cut in the coronal plane, while specimens from the anterior mouth should be sliced in the sagittal plane. If the tumour is close to bone, the specimen should be decalcified with soft tissue *in situ*.

3.2.1 Selection of blocks for histology

- Tumour: at least one block per 10 mm diameter of tumour, including one selected to demonstrate the maximum depth of invasion; the whole tumour should be processed if it is less than 10 mm in maximum diameter.
- Blocks of defined mucosal and soft tissue margins.
- Non-neoplastic mucosa (one block).
- Bone: if likely to be involved by tumour clinically, on imaging or on macroscopic examination.
- Bone surgical margins (if applicable).

3.2.2 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 of the 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.

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

4 Core data items to be included in the histopathology report

4.1 Clinical data (provided by the surgeon or oncologist)

4.1.1 Site and laterality of the carcinoma

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 UICC nomenclature (see Appendix A).

4.1.2 Type of specimen

The type of specimen should be described as: incisional biopsy, excisional biopsy or resection. The designation of resection specimens may be refined according to site-specific criteria, e.g. partial, total.

[These data are required for accurate staging and for cancer registration.]

4.2 Pathological data

4.2.1 Maximum diameter of tumour

The macroscopic diameter (in millimetres) should be used (Figure 1), unless the histological extent is greater than macroscopically apparent, in which case the microscopic dimension is used. As for other tissues, e.g. breast, measurements are made pragmatically, acknowledging distortion of tissues by fixation and processing.

[Tumour size is the major contributor to stage; level B.]

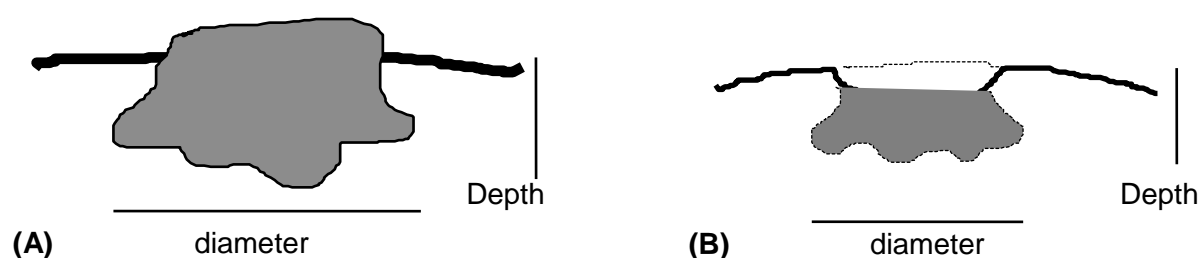


Figure 1: Descriptors of the size of the primary carcinoma for (A) nodular carcinoma and (B) ulcerated carcinoma. Note that depth of invasion refers to the depth of greatest spread in presumed continuity below the top of the adjacent mucosa. For both nodular and ulcerated tumours, the line of the original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

4.2.2 Maximum depth of invasion

The maximum depth of invasion (in millimetres) below the luminal aspect of surface should be recorded; if the tumour has ulcerated then the reconstructed surface should be used (Figure 1). The aim should be to provide a best estimate of tumour depth; for large carcinomas this may be an approximation. A more detailed comment on the nature of the tissues invaded (mucosa, muscle, etc.) should occur in the 'Comments' sections. Note that depth of invasion, defined in this way, is not the same as tumour thickness which will be larger than depth of invasion in exophytic tumours and smaller in ulcerated tumours. Depth of invasion is significantly related to nodal metastasis for oral T1/T2 carcinomas, although the optimal cut-off point for prognostic purposes is uncertain with 3 mm, 4 mm or 5 mm being suggested by different authors.^{1,14-21} Reviews and a meta-analysis suggest that 4 mm is the optimal threshold for prediction of cervical node metastasis.^{1,20,22}

[There is good evidence for the prognostic value of depth of invasion in oral cavity carcinomas, level B.]

4.2.3 Histological type of carcinoma

These guidelines specifically apply to conventional squamous cell carcinomas. Subtypes of squamous carcinoma, such as papillary, verrucous, basaloid, adenosquamous, acantholytic and spindle cell carcinomas, should be recognised²³ and listed in the core dataset and potential prognostic implications noted in the 'Comments' sections. Basaloid squamous cell carcinomas tend to present with more extensive disease but are also more radiosensitive than conventional squamous cell carcinomas and should be diagnosed using standard criteria.²³⁻²⁴

[Histopathological type is important for cancer registration and prognosis, with strength of evidence varying for different types – level C/D.]

4.2.4 Degree of differentiation (grade)

Grading is based on the degree of resemblance of the carcinoma to the normal epithelium and follows the descriptions in the WHO classification.²³ The most aggressive area (at x100 magnification field) is graded as well, moderately or poorly differentiated. This system is widely used and prognostically useful,^{1,17,19,25} even though it suffers from inter-observer variability and sampling problems.^{7,26} While most squamous 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.

[Histological grade is important for prognostication and prediction of response to adjuvant radiation and/or chemotherapy; level B/C.]

4.2.5 Pattern of invasion.

The pattern of invasion by the carcinoma at its deep margin is of proven prognostic value for oral carcinomas.^{4,6,16,27-28}

Scoring systems for histopathological features of squamous carcinomas include features related to differentiation and to the tumour/stromal interaction.^{3-5,29} While these have the potential to improve the consistency of reporting, they are not in widespread use and it is suggested that the recording of differentiation and invasive pattern is made separately.

The patterns of tissue invasion by carcinoma are a continuous spectrum. For prognostic purposes, two groups are recognised: carcinomas composed of broad cohesive sheets of cells or strands of cells >15 cells across (Figure 2 a,b,c), and carcinomas composed of narrow strands, non-cohesive small groups or single cells (Figure 2 d,e,f).^{6, 29-32}

[Level of evidence is good for oral and lingual carcinomas, level B.]

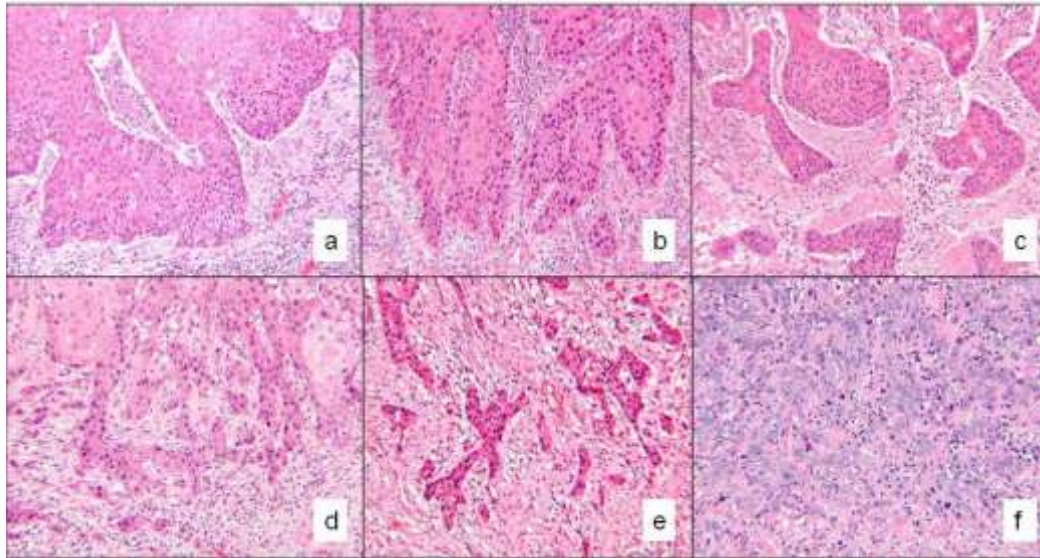


Figure 2: Patterns of invasion by squamous carcinoma

4.2.6 Distance from invasive carcinoma to surgical margins

Measure the distance (in millimetres) histologically for both mucosal and deep margins. From a surgical point of view, > 5mm is clear, 1–5 mm is close and <1 mm is involved. Incomplete resection or the presence of dysplasia at the margin is associated with a significantly increased risk of local recurrence.³³⁻³⁶ In the 'Comments' section it may be noted that if the tumour has an infiltrating pattern of invasive front (or vascular or perineural spread ahead of the invasive front) and a close margin, this may be associated with a high risk of local recurrence. Conversely, it may be acceptable to have a close margin for a well-circumscribed tumour with a cohesive growth pattern.

[Margin status is a predictor of local recurrence and may require consideration of adjuvant therapy, level B/C.]

4.2.7 Vascular invasion

The presence or absence of vascular invasion should be mentioned if it is an obvious feature on medium magnification examination of the tumour. 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.

Vascular invasion is a relatively weak predictor of nodal metastasis.^{16,37}

[Level of evidence D.]

4.2.8 Nerve invasion

The presence or absence of invasion of the perineural plane ahead of the invasive front of the carcinoma should be recorded, regardless of the size of the nerve. Perineural invasion predicts local recurrence, nodal metastasis and survival and may indicate a need for adjuvant therapy.^{25,29,38-40}

[Perineural invasion predicts more aggressive disease, level B.]

4.2.9 Bone invasion

The involvement of maxillary or mandibular bone may be by non-invasive erosion of the cortex, or diffuse infiltration of medullary intertrabecular and perineural tissues.¹³ If bone

invasion is present, the presence or absence of carcinoma at the bone margins should be recorded.

[The presence of bone involvement is important for accurate staging of oral malignancies, level B].

4.2.10 Severe dysplasia/*in-situ* carcinoma

Epithelial dysplasia forms a continuous spectrum of appearances, from mild to severe dysplasia/carcinoma *in situ*. Detailed discussion of the criteria and reproducibility of grading systems is not part of these guidelines and consensus has not been reached on the most clinically appropriate and reproducible grading system. The options include the standard WHO system,²³ the system based on grades of squamous intraepithelial neoplasia,⁴¹ a two-grade system for the oral cavity⁴² and the Ljubljana classification for laryngeal lesions.⁴³⁻⁴⁵ Severe dysplasia and carcinoma *in situ* are generally regarded as synonymous and are associated with a high risk of progression to carcinoma.

It is important to exclude hyperplastic lesions and to recognise that the presence of surface keratin does not influence grading. Invasive carcinoma may arise from surface epithelium showing cytological abnormalities less than those of classical severe dysplasia, sometimes even when changes are limited to the basal zone of keratinocytes.

The presence of moderate dysplasia or severe dysplasia/carcinoma *in situ* adjacent to the primary carcinoma and within 5 mm of the resection margins (where it may predict local recurrence) should be recorded.^{34,46-47}

[Level of evidence C.]

5 Non-core pathological data

These features should be included as part of a comprehensive description of a carcinoma and the surrounding tissues. Some are preferences of individual centres or are considered to be of uncertain prognostic significance at most sites in the head and neck region and therefore are not part of the data set at present.

- Macroscopic growth pattern of carcinoma – exophytic, polypoid, ulcerated or endophytic.
- Type and intensity of inflammatory infiltrate and desmoplastic stromal response.
- Response to previous therapy such as necrosis, dystrophic calcification and a foreign body reaction to debris (if applicable).
- Results of other investigations, e.g. flow cytometry, molecular and immunocytochemical studies.

5.1 Molecular markers

Molecular markers – including measures of cell proliferation and nuclear DNA content, the expression of involucrin, blood group antigens, cell adhesion molecules and oncogenes, and the intensity of neoangiogenesis – have been investigated as potential prognostic factors. These features generally correlate with cellular differentiation but do not provide any consistent independent prognostic information.^{8,10,33,48-52} While molecular markers predictive of tumour behaviour or response to therapy may be important pathological data in the future, current surgical practice does not demand their inclusion in the core data set.^{10,33,50}

Molecular genetic studies indicate that squamous cell carcinomas show marked molecular heterogeneity, offering the possibility for improved prognostic classification and targeted therapies in the future.⁵³⁻⁵⁵

Molecular methods may be used to assess the status of surgical margins;^{34,56} these methods may identify histologically inapparent residual carcinoma or preneoplastic field cancerisation but require further validation and assessment of clinical relevance.

Immunocytochemical studies may help to resolve differential diagnostic problems. Most antibodies lack a precise tissue or neoplastic specificity, so that a combination of appropriate results is required to make a diagnosis. These results should always be consistent with the haematoxylin and eosin appearances.

5.2 Human papillomaviruses (HPV) and head and neck carcinomas.

There is substantial evidence to link high-risk human papilloma viruses (particularly HPV16) to a subset of oropharyngeal carcinomas. HPV-associated carcinomas are usually non-keratinising, arise in the tonsils or base of tongue, and tend to have better overall and disease-free survivals than non-HPV associated carcinomas.⁵⁷⁻⁵⁹ Although there is currently insufficient evidence to modify treatment intensity in these patients, this is a subject of active research. The association between HPV and oral and laryngeal carcinomas is less strong and does not currently have clear prognostic value⁶⁰⁻⁶² and HPV status is not a core data item at sites other than oropharynx.

[Level of evidence B.]

6 Diagnostic coding of primary carcinomas

6.1 pT status

pT status should be recorded according to the UICC guidelines¹³ (see Appendix A).

6.2 SNOMED T code

SNOMED T code(s) should be recorded for primary site(s). A list of T codes against site and subsite is provided in Appendix B.

6.3 SNOMED M and P codes

SNOMED M and P codes should be used to describe the morphological diagnosis and diagnostic procedure (see Appendix B). It is recommended that the code for non-keratinising squamous cell carcinoma (M80723) is used for the typical HPV-associated oropharyngeal carcinomas rather than the other options of basaloid or squamous cell carcinoma NOS.

7 Reporting criteria for small biopsy and resection specimens

7.1 Small diagnostic biopsies

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/*in situ* carcinoma is present, this should be recorded as it may influence the siting of excision margins. It is not realistic to assess reliably the depth of invasion or presence of vascular invasion in small biopsies.

For larger diagnostic biopsies, the pattern and depth of invasion can be determined.

7.2 Transoral laser resection specimens

In specimens resulting from transoral laser resections of mucosal neoplasms, an estimate of the tumour diameter, thickness and pattern of invasion should be made, incorporating all parts of the specimen. The presence or absence of vascular and perineural invasion should be commented on. The resection margins of the main resection specimen are usually distorted by thermal damage to the tissues and may not be assessable histologically.⁶³ Assessment of the overall adequacy of excision should explicitly include the main resection specimen and separate margin 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 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. When selecting tissue for frozen section analysis, the surgeon should help the laboratory to concentrate on the most relevant areas by submitting tissue less than 10 mm diameter from clinically close margins.

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

9 Cytological diagnosis of mucosal malignancies

Exfoliative or fine needle aspiration of mucosal lesions is rarely used as most lesions are susceptible to conventional biopsy techniques.⁶⁴ Fine needle aspiration may be used for the rapid assessment of bulky intra-oral lesions. Cytological diagnosis of lymph node aspirates is covered in the dataset on neck dissections for head and neck cancer.

10 Specific aspects of individual tumours not covered elsewhere

10.1 Mucosal melanoma

The majority of mucosal malignant melanomas arise in the sinonasal tract, with approximately 25% in the oral cavity and a few at other sites.²³ Even small melanomas tend to behave aggressively, with high rates of recurrence and death. Melanoma should be considered in the differential diagnosis of any poorly differentiated mucosal malignancy and immunocytochemical analysis performed when appropriate.⁶⁵⁻⁶⁶ The 7th edition of the TNM staging system¹³ reflects this aggressive behaviour by designating primary melanomas limited to the mucosa as T3 lesions. Advanced and very advanced mucosal melanomas are classified as T4a and T4b respectively (see Appendix A). *In situ* mucosal melanomas are excluded from staging as they are extremely rare.

11 Core pathological data for neck dissection specimens

A detailed explanation and description of the handling and reporting of neck dissections associated with head and neck malignancies is provided in a companion dataset (see the

'Cancer datasets and tissue pathways' section of www.rcpath.org/publications). For ease of use, the text relating to core pathological data is provided here, and the reporting proforma is in Appendix D.

11.1 Total number of nodes and number of positive nodes

At each anatomical level, record the total number of nodes identified and number of nodes involved by carcinoma.^{35,40} For practical purposes, the critical factor influencing the use of adjuvant therapy is involvement of levels IV or V.⁴⁰

[The number of involved nodes affects staging and the pattern of nodal involvement influences postoperative treatment' level of evidence B.]

11.2 Size of largest metastatic deposit

Note that this is not the same as the size of the largest node. The size of the largest metastasis is a determinant in the TNM staging.¹³

[The size of the largest metastasis is a determinant of TNM stage.]

11.3 Extracapsular spread

Extracapsular spread (ECS) is a manifestation of the biological aggression of a carcinoma and is associated with a poor prognosis.^{1,8,35-36,40,67-71} ECS should be recorded as present or not identified. If present, the node level(s) showing this feature are recorded. Any spread through the full thickness of the node capsule is regarded as ECS and the previous separation into macroscopic and microscopic spread is now considered not to be necessary.⁶⁹ Involvement of adjacent anatomical structures should be recorded separately in the 'Comments' section. If histological evidence of extracapsular spread is equivocal, it should be recorded as 'present'. This should prompt the use of adjuvant radiotherapy.

[Level of evidence B.]

Notes on core data items

11.4 Micrometastases

The prognostic significance of micrometastases (2 mm or less in diameter) is not certain.⁷²⁻⁷⁶ Their presence should be included in the number of involved nodes and TNM coded as pN1(mi) or pN2(mi).

11.5 Isolated tumour cells

The TNM classification includes a category of pN0(i+) for nodes that contain clumps of isolated tumour cells (<0.2 mm diameter or <200 cells in one section).¹³ The prognostic significance of isolated tumour cells is not known for head and neck cancer.⁷⁵⁻⁷⁶ At present, it is suggested that dissection and sectioning protocols are not modified to explicitly search for isolated tumour cells.

11.6 Fused nodes

If there is obvious metastatic disease with fusion (matting) of lymph nodes, record:

- the level(s) of nodes involved by the mass
- the maximum dimension
- an estimate of the number of nodes that might be involved in the mass.

11.7 Isolated nodules of tumour in the connective tissue

Isolated nodules of tumour in the connective tissue may represent discontinuous extensions of the primary tumour, soft tissue metastases or nodal metastases that have destroyed the node.^{75,77} Absolute distinction between these possibilities is not always possible and, while the TNM classification¹³ recommends regarding all deposits that do not have the contour of a node as discontinuous tumour extension, there does not appear to be any evidence for this approach in the head and neck. A practical approach is to regard any tumour nodule in the region of the lymphatic drainage as a nodal metastasis, and to only diagnose discontinuous extension of a carcinoma within 10 mm of the primary carcinoma and where there is no evidence of residual lymphoid tissue.

12 Criteria for audit of the dataset

In keeping with the recommended key performance indicators published by The Royal College of Pathologists (www.rcpath.org/index.asp?PageID=35), reports on head and neck cancers should be audited for the following.

- 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.
- The use of electronic structured reports or locally agreed proformas (it is assumed that these processes will ensure that 90% of core data items are recorded):
 - standard: 80% of resection specimens will include 100% data items presented in a structured format.
- Turnaround times for biopsies and resection specimens:
 - standard: 80% diagnostic biopsies will be reported within seven calendar days of the biopsy being taken.
 - standard: 80% of all histopathology specimens (excluding those requiring decalcification) will be reported within ten calendar days of the specimen being taken.

References

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Appendix A TNM classification of malignant tumours¹³

General principles

pT – Primary tumour

pTX Primary tumour cannot be assessed

pT0 No evidence of primary tumour

pTis Carcinoma *in situ*

pT1, pT2, pT3, pT4 – increasing size and/or local extent of the primary tumour (see specific sites).

Note that if there is doubt as to which category a tumour should be allocated to, the lower (less extensive) category should be used.

Additional descriptors to be used in special cases. These do not affect the stage groupings but may require separate analysis.

The 'm' suffix indicates the presence of multiple primary tumours in a single site and is recorded in parentheses: pT(m)NM.

The 'y' prefix indicates those cases in which classification is performed during or following initial multimodality therapy (neoadjuvant chemotherapy and/or radiation therapy). The ypTNM categorises the extent of tumour actually present at the time of that examination and is not an estimate of tumour before treatment.

The 'r' prefix indicates a recurrent tumour when staged after a documented disease-free interval, and is identified by the 'r' prefix: rTNM.

The R classifier for residual tumour is available in the TNM system, but is not recommended for use in the setting of head and neck cancers. The method of assessment of margins described in section 4.2.6 is well established and current surgical practice, particularly the use of laser resection, does not require the assessment of macroscopic or microscopic residual disease.

For the pN classification of regional lymph nodes see the dataset on neck dissection specimens

M – Distant metastasis

pM1 Distant metastasis confirmed microscopically.

Note that pM0 and pMX are no longer valid categories.

Site-specific T codes

Lip and oral cavity

T1 Tumour 20 mm or less in greatest dimension.

T2 Tumour 21–40 mm in greatest dimension.

T3 Tumour >40 mm in greatest dimension.

T4 Tumour invades adjacent structures.

T4a Moderately advanced local disease.

Lip: Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth or skin of face, i.e. chin or nose.

Oral cavity: Tumour invades adjacent structures, e.g. through cortical bone of the mandible or maxilla, into deep extrinsic muscles of tongue, maxillary sinus, skin of face.

T4b Very advanced local disease. Tumour invades masticator space, pterygoid plates, or skull base, and/or encases internal carotid artery.

Mucosal malignant melanoma

T3 Mucosal disease

T4a Moderately advanced disease. Tumour involving deep soft tissue, cartilage, bone or overlying skin.

T4b Very advanced disease. Tumour involving brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space or mediastinal structures.

Note that the classification of regional lymph node metastasis differs from that used for squamous cell carcinomas.

NX Regional lymph nodes cannot be assessed.

N0 No regional lymph node metastases.

N1 Regional lymph node metastases present.

Appendix B SNOMED codes

Topographical codes

T-52000	Lip
T-52230	External upper lip (vermilion border)
T-52240	External lower lip (vermilion border)
T-52003	Commissures
T-51000	Oral cavity
T-51300	Buccal mucosa
T-52250	Mucosa of upper and lower lips
T-51030	Cheek mucosa
T-51600	Retromolar areas
T-51010	Bucco-alveolar sulci
T-54920	Upper alveolus and gingiva (upper gum)
T-54930	Lower alveolus and gingiva (lower gum)
T-51200	Floor of mouth
T-51110	Hard palate
T-53000	Tongue
T-53120	Dorsum and lateral borders of anterior 2/3
T-53123	Inferior (ventral) surface

Morphological codes

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

M-80702	Squamous carcinoma <i>in situ</i>
M-80703	Squamous carcinoma
M-80705	Microinvasive squamous carcinoma
M-80713	Keratinising squamous carcinoma
M-80723	Non-keratinising squamous carcinoma
M-80743	Spindle cell squamous carcinoma
M-80753	Adenoid squamous carcinoma
M-85603	Adenosquamous carcinoma
M-87203	Malignant melanoma

Procedure codes

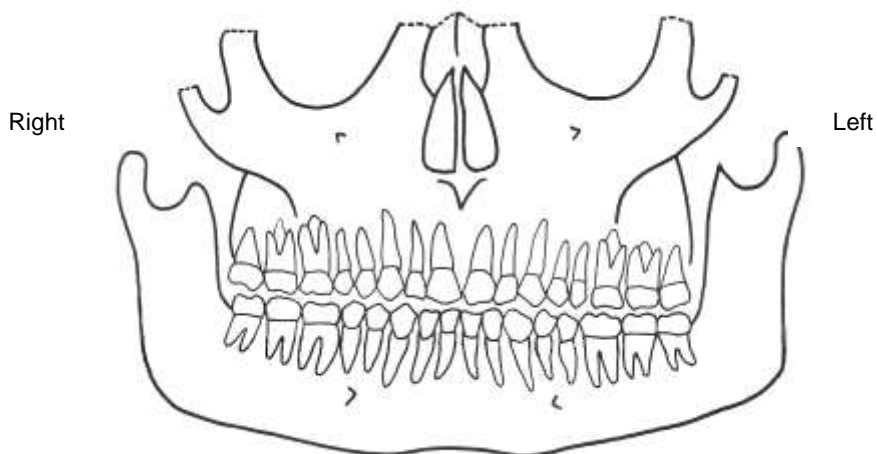
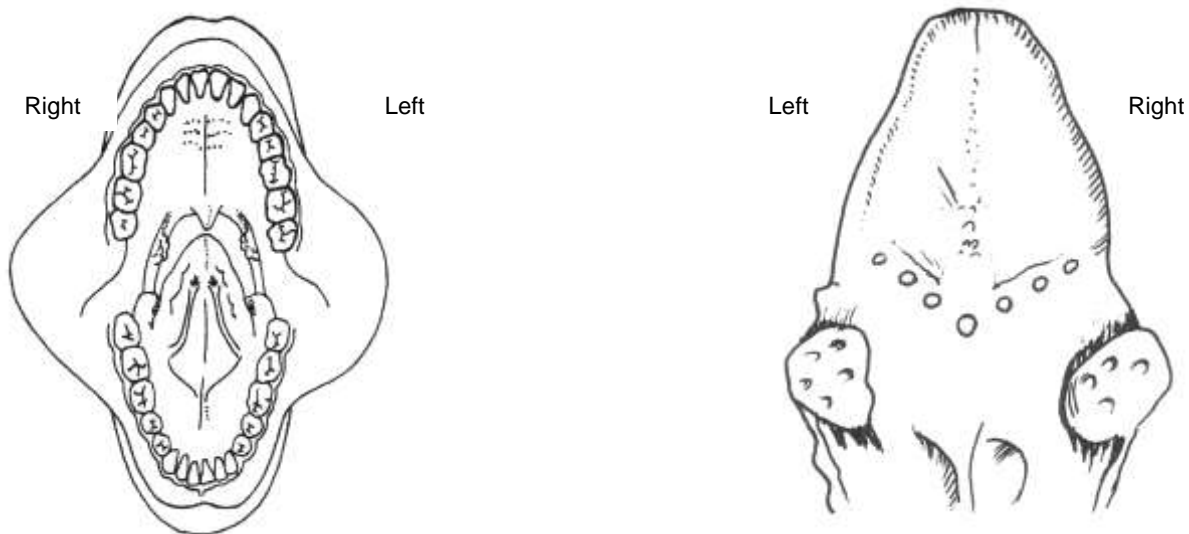
Note: This is not intended to be a comprehensive list of all procedures and other codes should be used as necessary.

P1100	Resection
P1141	Excisional biopsy
P1340	Endoscopic biopsy
P1140	Biopsy, not otherwise specified

Appendix C Draft request forms for primary mucosal carcinomas and node dissections

Surname	Consultant
Forename	Location
Date of birth	
Sex	
Hospital no.	NHS/CHI no.

Relevant medical or dental history	Clinical diagnosis:
Site of lesion	Previous reports (lab no. if known)
Duration of symptoms	
Predisposing factors	Other information:
Date of operation	
Signature	



Left

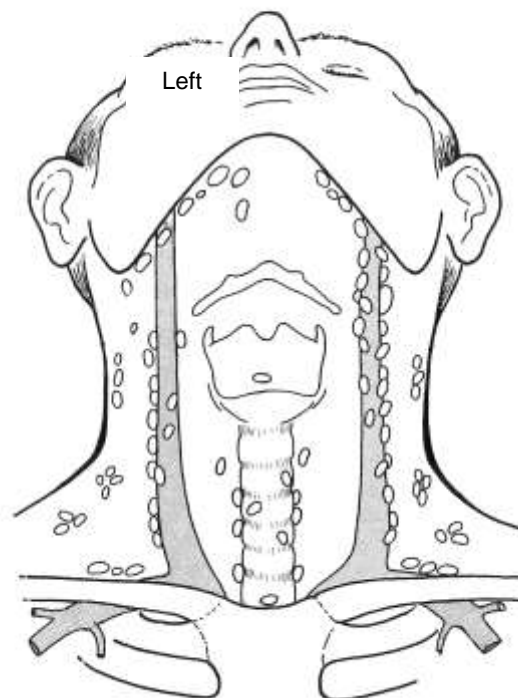
Right



Please tick appropriate boxes:

	Right neck dissection	Left neck dissection
Levels submitted		
I		
II (total)		
IIA		
IIB		
III		
IV		
V		
VI		
Other (specify)		
Non-nodal structures		
Sternomastoid		
Submandibular gland		
Internal jugular vein		
Other (specify)		

Right



Appendix D Reporting proformas

In order to provide flexibility in use, separate reporting proformas are provided for the primary carcinoma and for nodal disease.

It is expected that the proformas will be combined if one operation yields tissue from both the primary site and neck dissection, providing one pathological summary and staging.

The nodal proforma should be edited appropriately, depending on the type(s) of specimen received (sentinel nodes, left and/or right neck dissections).

Dataset for primary oral cavity carcinoma (page 1)

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

CLINICAL DATA

Type of specimen Incisional biopsy Excisional biopsy
Resection Yes No If yes: Partial Total
Clinical TNM stage..... T..... N..... M.....
New primary Recurrence Not known
Previous radiotherapy Yes No Not known
Previous chemotherapy Yes No Not known

Primary tumour

Site..... Subsite(s).....
Right Left Midline
Histological type: Squamous cell carcinoma
Conventional Verrucous Papillary Acantholytic Other (specify)

Other malignancy (specify)

Differentiation Well Moderate Poor

Invasive front Cohesive Non-cohesive

Maximum diameter (mm)
Maximum depth of invasion (mm)
Distance from invasive tumour to mucosal margin (mm) deep margin (mm)

Vascular invasion Yes No
Nerve invasion Yes No
Bone/cartilage invasion Yes No
 If present: Erosive Infiltrating Carcinoma at margin: Yes No
Severe dysplasia Yes No If yes: Dysplasia at margin: Yes No

COMMENTS/ADDITIONAL INFORMATION

Dataset for primary oral cavity carcinoma (page 2)

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

SUMMARY OF PATHOLOGICAL DATA

Tumour site.....
Tumour type.....
pTNM stage pT..... pN.....

SNOMED codes

T..... M.....
T..... M.....

Resection of primary tumour Clear Close Involved

Signature:

Date:

Dataset for lymph node excision specimens (page 1)

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

Sentinel node(s)

Levels submitted	I <input type="checkbox"/> IIA <input type="checkbox"/> IIB <input type="checkbox"/> III <input type="checkbox"/> IV <input type="checkbox"/> V <input type="checkbox"/> VI <input type="checkbox"/> other <input type="checkbox"/>									
Node level	No. nodes present	No. positive nodes	ECS present							
I			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
II (total)			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IIA			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IIB			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
III			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IV			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
V			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
VI			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
Other			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
Totals			Yes <input type="checkbox"/>	No <input type="checkbox"/>						

Right neck dissection

Levels submitted	I <input type="checkbox"/> IIA <input type="checkbox"/> IIB <input type="checkbox"/> III <input type="checkbox"/> IV <input type="checkbox"/> V <input type="checkbox"/> VI <input type="checkbox"/> other <input type="checkbox"/>									
Node level	No. nodes present	No. positive nodes	ECS present							
I			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
II (total)			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IIA			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IIB			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
III			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IV			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
V			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
VI			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
Other			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
Totals			Yes <input type="checkbox"/>	No <input type="checkbox"/>						

Left neck dissection

Levels submitted	I <input type="checkbox"/> IIA <input type="checkbox"/> IIB <input type="checkbox"/> III <input type="checkbox"/> IV <input type="checkbox"/> V <input type="checkbox"/> VI <input type="checkbox"/> other <input type="checkbox"/>									
Node level	No. nodes present	No. positive nodes	ECS present							
I			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
II (total)			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IIA			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IIB			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
II			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
III			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
IV			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
V			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
VI			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
Other			Yes <input type="checkbox"/>	No <input type="checkbox"/>						
Totals			Yes <input type="checkbox"/>	No <input type="checkbox"/>						

Dataset for lymph node excision specimens (page 2)

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

COMMENTS/ADDITIONAL INFORMATION

SUMMARY OF PATHOLOGICAL DATA

Tumour type
Tumour site
pTNM stage pN.....
SNOMED codes T..... M.....

Signature: **Date:**

Appendix E Summary table – explanation of levels of evidence

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

Level of evidence	Nature of evidence
A	<p>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</p> <p>or</p> <p>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.</p>
B	<p>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</p> <p>or</p> <p>Extrapolation evidence from studies described in A.</p>
C	<p>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</p> <p>or</p> <p>Extrapolation evidence from studies described in B.</p>
D	<p>Non-analytic studies such as case reports, case series or expert opinion</p> <p>or</p> <p>Extrapolation evidence from studies described in C.</p>
Good practice point (GPP)	<p>Recommended best practice based on the clinical experience of the authors of the writing group.</p>

Appendix F AGREE monitoring sheet

The Cancer Datasets of The Royal College of Pathologists comply with the AGREE standards for good quality clinical guidelines (www.agreecollaboration.org). The sections of this dataset that indicate compliance with each of the AGREE standards are indicated in the table.

AGREE standard	Section of dataset
SCOPE AND PURPOSE	
1. The overall objective(s) of the guideline is (are) specifically described.	1
2. The clinical question(s) covered by the guidelines is (are) specifically described.	1
3. The patients to whom the guideline is meant to apply are specifically described.	1
STAKEHOLDER INVOLVEMENT	
4. The guideline development group includes individuals from all the relevant professional groups.	1
5. The patients' views and preferences have been sought.	Not applicable*
6. The target users of the guideline are clearly defined.	1
7. The guideline has been piloted among target users.	Previous editions
RIGOUR OF DEVELOPMENT	
8. Systematic methods were used to search for evidence.	1
9. The criteria for selecting the evidence are clearly described.	1
10. The methods used for formulating the recommendations are clearly described.	1
11. The health benefits, side effects and risks have been considered in formulating the recommendations.	1
12. There is an explicit link between the recommendations and the supporting evidence.	4
13. The guideline has been externally reviewed by experts prior to its publication.	1
14. A procedure for updating the guideline is provided.	Foreword
CLARITY OF PRESENTATION	
15. The recommendations are specific and unambiguous.	4
16. The different options for management of the condition are clearly presented.	4
17. Key recommendations are easily identifiable.	4
18. The guideline is supported with tools for application.	Appendices A–D
APPLICABILITY	
19. The potential organisational barriers in applying the recommendations have been discussed.	Foreword
20. The potential cost implications of applying the recommendations have been considered.	Foreword
21. The guideline presents key review criteria for monitoring and audit purposes.	1, 12
EDITORIAL INDEPENDENCE	
22. The guideline is editorially independent from the funding body.	1
23. Conflicts of interest of guideline development members have been recorded.	1

* The Lay Advisory Committee (LAC) of The Royal College of Pathologists has advised the Director of Communications that there is no reason to consult directly with patients or the public regarding this dataset because it is technical in nature and intended to guide pathologists in their practice. The authors will refer to the LAC for further advice if necessary.