

Standards and datasets for reporting cancers

Dataset for histopathology reporting of mucosal malignancies of the pharynx

November 2013

Authors: Dr Tim Helliwell, University of Liverpool
Dr Julia Woolgar, University of Liverpool

Unique document number	G111
Document name	Dataset for histopathology reporting of mucosal malignancies of the pharynx
Version number	2
Produced by	Dr Tim Helliwell and Dr Julia Woolgar, University of Liverpool
Date active	November 2013
Date for review	November 2014
Comments	<p>This document supersedes the 2005 document, <i>Datasets for histopathology reports on head and neck carcinomas and salivary neoplasms (2nd edition)</i>.</p> <p>In accordance with the College's pre-publications policy, it was put on The Royal College of Pathologists' website for consultation from 24 October to 21 November 2011. Sixteen items of feedback were received and the authors considered them and amended the document as appropriate. Please email publications@rcpath.org if you wish to see the responses and comments.</p> <p>The authors and sub-specialty advisor reviewed this document in November 2013 and added guidance on SNOMED coding at the end of Section 6.3.</p> <p>Dr Suzy Lishman Vice-President for Advocacy and Communications</p>

The Royal College of Pathologists
2 Carlton House Terrace, London, SW1Y 5AF
Tel: 020 7451 6700
Fax: 020 7451 6701
Web: www.rcpath.org

Registered charity in England and Wales, no. 261035

© 2013, The Royal College of Pathologists

This work is copyright. You may download, display, print and reproduce this document for your personal, non-commercial use. Apart from any use as permitted under the Copyright Act 1968 or as set out above, all other rights are reserved. Requests and inquiries concerning reproduction and rights should be addressed to The Royal College of Pathologists at the above address. First published: 2013



Contents

Foreword	3
1 Introduction	3
2 Specimen request form	6
3 Specimen handling and block selection	6
4 Core data items to be included in the histopathology report	7
5 Non-core pathological data	11
6 Diagnostic coding of primary carcinomas	12
7 Reporting criteria for small biopsy and resection specimens	13
8 Frozen section diagnosis	13
9 Cytological diagnosis of mucosal malignancies	13
10 Specific aspects of individual tumours not covered elsewhere	13
11 Core pathological data for neck dissection specimens	14
12 Criteria for audit of the dataset	15
References	16
Appendix A TNM classification of malignant tumours	21
Appendix B SNOMED codes	23
Appendix C Draft request forms for primary mucosal carcinomas and node dissections	24
Appendix D Reporting proformas	26
Dataset for primary oropharyngeal carcinoma	27
Dataset for primary hypopharyngeal carcinoma	29
Dataset for primary nasopharyngeal carcinoma	31
Dataset for lymph node excision specimens	32
Appendix E Summary table – explanation of levels of evidence	34
Appendix F AGREE monitoring sheet	35



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 nasopharynx, oropharynx and hypopharynx. Malignancies arising in the oral cavity, nose and paranasal sinuses, 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,

undifferentiated nasopharyngeal carcinomas and malignant melanoma, and to 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
- National Cancer Intelligence Network.

Comments from specialist and general histopathologists on the draft document that was published on the College website have been 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. The recommendation that primary carcinomas of the oropharynx are investigated for human papillomavirus implies that the appropriate analytical facilities should be available and funded.

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 proformas that may be used as the main reporting format or may be combined with free text as required. As the core data differ significantly between nasopharynx, oropharynx and hypopharynx, a separate proforma for each primary site has been provided, although the nodal dataset is common to all sites. Individual centres may wish to expand the detail in some sections, e.g. for sites and subsites, to facilitate the recording of data for particular tumour types.

The guidelines 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, a separate dataset on mucosal malignancies at each of the main head and neck sites has 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 proformas have 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.

3.2.1 Nasopharynx

The great majority of nasopharyngeal carcinomas are treated non-surgically so that guidance relating to small biopsies is most appropriate for these tumours.(14) Resection specimens of carcinomas from this area should be carefully orientated by the surgeon so that surgically important resection margins can be appropriately sampled.

3.2.2 Oropharynx

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*.

3.2.3 Laryngopharyngectomy

Horizontal slices 3–5 mm thick provide optimal demonstration of the relationship between the tumour and the laryngeal cartilages, although thicker slices may be required if megablocks are used. For supraglottic carcinomas, blocks should include the relationship between the carcinoma and the anterior (submucosal) resection margin at the base of the tongue; blocks taken in the sagittal plane are more appropriate to demonstrate this feature. The description should include the subsite of origin of carcinoma, and the extent of involvement of laryngeal cartilages and extra-laryngeal tissues.¹⁵

3.2.4 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 if less than 10 mm. If megablocks are used, then the number of blocks will be fewer.
- Blocks of defined mucosal and soft tissue margins.
- Non-neoplastic mucosa (one block).
- Bone surgical margins (if applicable).
- Bone, if involvement by tumour is suspected clinically or on imaging studies.
- Thyroid if present in pharyngolaryngectomy. One block is sufficient if the thyroid appears normal. If the thyroid is abnormal, one or more blocks should be taken to confirm or exclude invasion by carcinoma or other pathology.

3.2.5 Trans-oral laser resection specimens

The handling of trans-oral laser resection specimens requires particularly close collaboration between surgeon and pathologist. The main tumour resection may be in one or more parts and it is usual for separate biopsies from resection margins to be submitted for examination. The specimens should be pinned onto a board so that the anatomical relationships between the pieces are maintained and an annotated diagram should indicate the nature of each piece of tissue. The radial and deep margins should be inked to facilitate assessment of the histological sections. The main tumour should be serially sliced and blocked in its entirety. If possible, biopsies from resection margins should be sliced perpendicular to the margin and blocked in their entirety.

[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 for oropharyngeal and hypopharyngeal carcinomas; level B.]

4.2.2 Maximum depth of invasion

The maximum depth of invasion should be recorded in millimetres below the luminal aspect of surface; 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 oropharyngeal 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.^{1,16-23} Reviews and a meta-analysis suggest that 4 mm is the optimal threshold for prediction of cervical node metastasis.^{1,22,24}

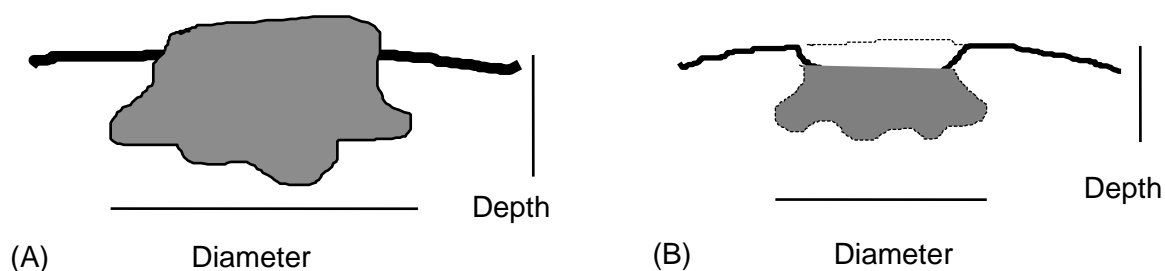


Figure 1: Descriptors of the size of the primary carcinoma for (A) nodular carcinoma and (B) ulcerated carcinoma. Note that depth of invasion refers to the depth of greatest spread in presumed continuity below the top of the adjacent mucosa. For both nodular and ulcerated tumours, the line of the original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

[There is good evidence for the prognostic value of depth of invasion in oropharyngeal carcinomas, level B. Depth of invasion is non-core data for nasopharyngeal and hypopharyngeal carcinomas.]

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 recognised²⁵ 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.²⁵⁻²⁶ The classification of nasopharyngeal carcinomas is described in section 4.2.4.

[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.²⁵ The most aggressive area (at x100 magnification field) is graded as well, moderately or poorly differentiated. This system is widely used and prognostically useful,^{1,19,21,27} even though it suffers from inter-observer variability and sampling problems^{7,28} 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 core data, 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.]

The histological classification of nasopharyngeal carcinomas should follow the WHO guidelines with subdivision into differentiated keratinising and non-keratinising squamous cell carcinomas, and undifferentiated carcinomas.^{14,25}

4.2.5 Pattern of invasion

The pattern of invasion by the carcinoma at its deep margin is of proven prognostic value for oropharyngeal carcinoma^{1,29-30} and the few published studies of tumours at other sites suggest that a similar approach may be of value.^{5,24}

Scoring systems for histopathological features of squamous carcinomas include features related to differentiation and to the tumour/stromal interaction.^{3-5,31} While these have the potential to improve the consistency of reporting, they are not in widespread use and for these guidelines it is suggested that the recording of differentiation and invasive pattern is made separately.

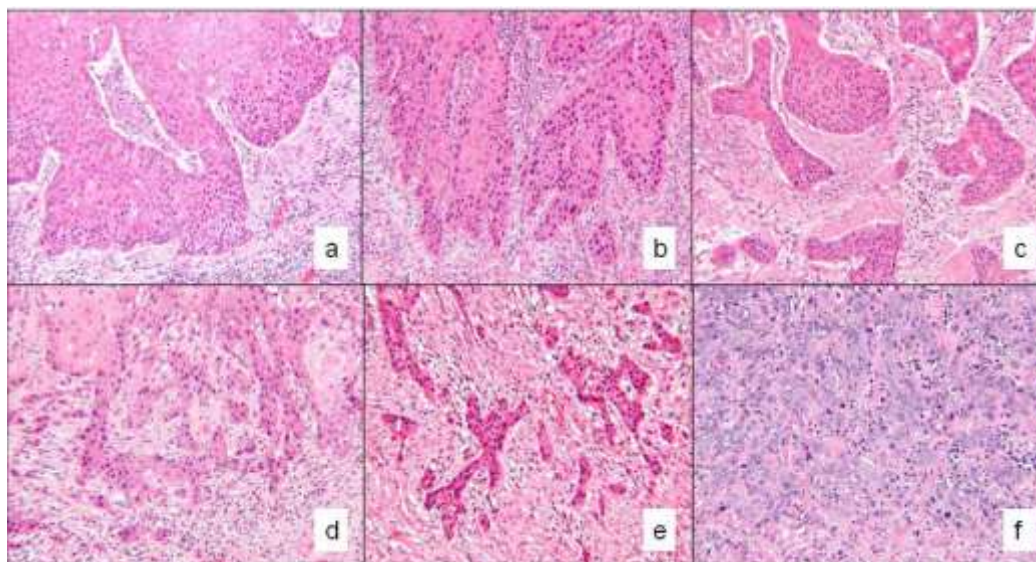
The pattern of tissue invasion by carcinoma is a continuous spectrum of changes. For prognostic purposes, two groups are recognised: carcinomas composed of broad cohesive sheets of cells or strands of cells >15 cells across (Figure 2 a, b and c), and carcinomas composed of narrow strands, non-cohesive small groups or single cells (Figure 2 d, e and f).^{6,31-34}

[Pattern of invasion may predict nodal metastasis for oropharyngeal and hypopharyngeal carcinomas, level C.]

4.2.6 Distance from invasive carcinoma to surgical margins

Measure the distance histologically in millimetres for both mucosal and deep margins. From a surgical point of view, >5 mm 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.³⁵⁻³⁸ 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.

Figure 2: Patterns of invasion by squamous carcinoma



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.]

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.^{18,39}

[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.^{27,31,40-42}

[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 oropharyngeal 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,²⁵ the system based on grades of squamous intraepithelial neoplasia,⁴³ a two-grade system for the oral cavity⁴⁴ and the Ljubljana classification for laryngeal lesions.⁴⁵⁻⁴⁷ 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.^{36,45,48}

[Level of evidence C.]

4.2.11 Human papillomaviruses (HPV) and head and neck carcinomas

There is substantial evidence to link high-risk human papillomaviruses (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.⁴⁹⁻⁵¹ 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 value⁵²⁻⁵⁴ and HPV status is not core data at other sites.

To allow the stratification of the outcomes of treatment, the HPV status of all oropharyngeal carcinomas should be assessed using validated methods with appropriate controls. The immunocytochemical identification of over-expression of p16 protein is a useful screening method for HPV infection as HPV-associated carcinomas show strong nuclear and cytoplasmic expression of p16 in >70% malignant cells, and p16-negative cases are almost certainly not HPV-associated.^{24,55-57} Carcinomas showing p16 over-expression should have the presence of HPV confirmed by *in situ* hybridisation, if possible. PCR analysis for HPV is not currently recommended as there is a risk of false positive results from formalin-fixed tissues. The report should indicate the methods used to evaluate HPV status (p16 immunocytochemistry and/or *in situ* hybridisation).

[Level of evidence B.]

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 dataset at present.

- Macroscopic growth pattern of carcinoma – exophytic, polypoid, ulcerated or endophytic.
- Type and intensity of inflammatory infiltrate and desmoplastic stromal response.
- Involvement of a tracheostomy (if present).

- 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.^{8,10,35,58-62} 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, with the exception of HPV status.^{10,35,60}

Molecular genetic studies indicate that squamous cell carcinomas are showed marked molecular heterogeneity, offering the possibility for improved prognostic classification and targeted therapies in the future.⁶³⁻⁶⁵

Molecular methods may be used to assess the status of surgical margins;^{36,66} 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.

Epstein Barr virus (EBV) is closely associated with almost all carcinomas of the nasopharynx with higher levels of expression in undifferentiated carcinomas than in keratinising carcinomas.¹⁴ While identification of EBV-associated proteins or RNAs is not in itself of prognostic value, evidence of EBV in nodal metastases may point to a nasopharyngeal primary.

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 tumour thickness 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.⁽⁶⁷⁾ Assessment of the overall adequacy of excision should explicitly include the main resection specimen and separate marginal 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. The surgeon should select the tissue for frozen section diagnosis with care, bearing in mind that it is not usually possible to section material more than 10 mm in diameter.

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

9 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.⁶⁸ 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.²⁵ 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.⁶⁹⁻⁷⁰ 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.^{37,42} For practical purposes, the critical factor influencing the use of adjuvant therapy is involvement of levels IV or V.⁴²

[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.^{1,8,37-38,42,71-75} 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.⁷³ 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 in diameter) is not certain.⁷⁶⁻⁸⁰ 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.⁷⁹⁻⁸⁰ 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.^{79,81} Absolute distinction between these possibilities is not always feasible and, while the TNM classification(13) 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 7 calendar days of the biopsy being taken
 - standard: 80% of all histopathology specimens (excluding those requiring decalcification) will be reported within 10 calendar days of the specimen being taken.

References

1. Woolgar JA. Histopathological prognosticators in oral and oropharyngeal squamous cell carcinoma. *Oral Oncol* 2006;42:229–239.
2. National Institute for Clinical Excellence. *Improving outcomes guidance for head and neck cancer*. NICE, 2004. www.nice.org.uk/nicemedia/pdf/csg_hn_themanual.pdf
3. Anneroth G, Batsakis J, Luna M. Review of the literature and a recommended system of malignancy grading in oral squamous cell carcinomas. *Scandinavian Journal of Dental Research* 1987;95:229–249.
4. Bryne M, Koppang HS, Lilleng R, Stene B, Dabelsteen E. New malignancy grading is a better prognostic indicator than Broder's grading in oral squamous cell carcinomas. *Journal of Oral Pathology and Medicine* 1989;18:432–437.
5. Jakobsson PA, Eneroth CM, Killander D, Moberger G, Martensson B. Histologic classification and grading of malignancy in carcinoma of the larynx. *Acta Radiologica* 1973;12:1–8.
6. Odell EW, Jani P, Sherriff M, Ahluwalia SM, Hibbert J, Levison DA *et al*. The prognostic value of individual grading parameters in small lingual squamous cell carcinomas. *Cancer* 1994;74:789–794.
7. Roland NJ, Caslin AW, Nash J, Stell PM. Value of grading squamous cell carcinoma of the head and neck. *Head Neck* 1992;14:224–229.
8. Kearsley JH, Thomas S. Prognostic markers in cancers of the head and neck region. *Anticancer Drugs* 1993;4:419–429.
9. Snow GB, Annayas A, Vanslooten EA, Bartelink H, Hart AM. Prognostic factors of neck node metastasis. *Clinical Otolaryngology* 1982;7:185–190.
10. Genden EM, Ferlito A, Bradley PJ, Rinaldo A, Scully C. Neck disease and distant metastases. *Oral Oncology* 2003;39:207–212.
11. Takes RP, Rinaldo A, Silver CE, Piccirillo JF, Haigentz M, Jr., Suarez C *et al*. Future of the TNM classification and staging system in head and neck cancer. *Head Neck* 2010;32:1693–1711.
12. Mehanna H, West CM, Nutting C, Paleri V. Head and neck cancer – Part 2: Treatment and prognostic factors. *BMJ*. 2010;341:c4690.
13. Sobin LH, Gospodarowicz MK, Wittekind C. *TNM Classification of malignant tumours (7th edition)*: Wiley-Blackwell, 2009.
14. Wei WI, Sham JS. Nasopharyngeal carcinoma. *Lancet* 2005;365:2041–2054.
15. Helliwell TR. ACP Best Practice No 157. Guidelines for the laboratory handling of laryngectomy specimens. *J Clin Pathol* 2000;53:171–176.
16. Gonzales-Moles MA, Esteban F, Rodriguez-Archilla A, Ruiz-Avila I, Gonzales-Moles S. Importance of tumour thickness measurement in prognosis of tongue cancer. *Oral Oncology* 2002;38:394–397.
17. O-charoenat P, Pillai G, Patel S, Fisher C, Archer D, Eccles SA *et al*. Tumour thickness predicts cervical nodal metastases and survival in early oral tongue cancer. *Oral Oncology* 2003;39:386–390.
18. Suzuki M, Suzuki T, Asai M, Ichimura K, Nibu K, Sugasawa M *et al*. Clinicopathological factors related to cervical lymph node metastasis in a patient with carcinoma of the oral floor. *Acta Otolaryngol Suppl* 2007;559:129–135.
19. Quaedvlieg PJ, Creytens DH, Epping GG, Peutz-Kootstra CJ, Nieman FH, Thissen MR *et al*. Histopathological characteristics of metastasizing squamous cell carcinoma of the skin and lips. *Histopathol* 2006;49:256–264.

20. Pentenero M, Gandolfo S, Carrozzo M. Importance of tumor thickness and depth of invasion in nodal involvement and prognosis of oral squamous cell carcinoma: a review of the literature. *Head Neck* 2005;27:1080–1091.
21. Sparano A, Weinstein G, Chalian A, Yodul M, Weber R. Multivariate predictors of occult neck metastasis in early oral tongue cancer. *Otolaryngol Head Neck Surg* 2004;131:472–476.
22. Huang SH, Hwang D, Lockwood G, Goldstein DP, O'Sullivan B. Predictive value of tumor thickness for cervical lymph-node involvement in squamous cell carcinoma of the oral cavity: a meta-analysis of reported studies. *Cancer* 2009;115:1489–1497.
23. Alkureishi LW, Ross GL, Shoaib T, Soutar DS, Robertson AG, Sorensen JA *et al*. Does tumor depth affect nodal upstaging in squamous cell carcinoma of the head and neck? *Laryngoscope* 2008;118:629–634.
24. Brandwein-Gensler M, Smith RV. Prognostic indicators in head and neck oncology including the new 7th edition of the AJCC staging system. *Head Neck Pathol* 2010;4:53–61.
25. Barnes L, Eveson JW, Reichart P, Sidransky D. *Pathology and Genetics of Head and Neck Tumours*. IARC, 2005.
26. Thariat J, Badoual C, Faure C, Butori C, Marcy PY, Righini CA. Basaloid squamous cell carcinoma of the head and neck: role of HPV and implication in treatment and prognosis. *J Clin Pathol* 2010;63:857–866.
27. Sethi S, Lu M, Kapke A, Benninger MS, Worsham MJ. Patient and tumor factors at diagnosis in a multi-ethnic primary head and neck squamous cell carcinoma cohort. *J Surg Oncol* 2009;99:104–108.
28. Henson DE. The histological grading of neoplasms. *Arch Pathol*. 1988;112:1091–1096.
29. Bryne M. Prognostic value of various molecular and cellular features in oral squamous cell carcinomas: a review. *J Oral Pathol Med* 1991;20:413–420.
30. Crissman JD, Liu WY, Gluckman JL, Cummings G. Prognostic value of histologic parameters in squamous cell carcinoma of the oropharynx. *Cancer* 1984;54:2995–3001.
31. Brandwein-Gensler M, Smith RV, Wang B, Penner C, Theilken A, Broughel D *et al*. Validation of the histologic risk model in a new cohort of patients with head and neck squamous cell carcinoma. *Am J Surg Pathol* 2010;34:676–688.
32. Laramore GE, Scott CB, Schuller DE, Haselow RE, Ervin TJ, Wheeler R *et al*. Is a surgical resection leaving positive margins of benefit to the patient with locally advanced squamous cell carcinoma of the head and neck: a comparative study using the intergroup study 0034 and the Radiation Therapy Oncology Group head and neck database. *Int J Radiat Oncol Biol Phys* 1993;27:1011–1016.
33. Jacobs JR, Ahmad K, Casiano R, Schuller DE, Scott C, Laramore GE *et al*. Implications of positive surgical margins. *Laryngoscope* 1993;103(1 Pt 1):64–68.
34. Zelefsky MJ, Harrison LB, Fass DE, Armstrong JG, Shah JP, Strong EW. Postoperative radiation therapy for squamous cell carcinomas of the oral cavity and oropharynx: impact of therapy on patients with positive surgical margins. *Int J Radiat Oncol Biol Phys* 1993;25:17–21.
35. Slootweg PJ, Hordijk GJ, Schade Y, van Es RJJ, Koole R. Treatment failure and margin status in head and neck cancer. A critical view on the potential value of molecular pathology. *Oral Oncology* 2002;38:500–503.
36. Bradley PJ, MacLennan K, Brakenhoff RH, Leemans CR. Status of primary tumour surgical margins in squamous head and neck cancer: prognostic implications. *Curr Opin Otolaryngol Head Neck Surg* 2007;15:74–81.
37. Laskar SG, Agarwal JP, Srinivas C, Dinshaw KA. Radiotherapeutic management of locally advanced head and neck cancer. *Expert Rev Anticancer Ther* 2006;6:405–417.

38. Langendijk JA, Ferlito A, Takes RP, Rodrigo JP, Suarez C, Strojan P *et al.* Postoperative strategies after primary surgery for squamous cell carcinoma of the head and neck. *Oral Oncol* 2010;46:577–585.
39. Poleksic S, Kalwaic HJ. Prognostic value of vascular invasion in squamous cell carcinoma of the head and neck. *Plast Reconstr Surg* 1978;61:234–240.
40. Fagan JJ, Collins B, Barnes L, D'Amico F, Myers EN, Johnson JT. Perineural invasion in squamous cell carcinoma of the head and neck. *Arch Otolaryngol Head Neck Surg* 1998;124:637–640.
41. Flynn CJ, Khaouam N, Gardner S, Higgins K, Enepekides D, Balogh J *et al.* The value of periodic follow-up in the detection of recurrences after radical treatment in locally advanced head and neck cancer. *Clin Oncol (R Coll Radiol)* 2010;22:868–873.
42. Strojan P, Ferlito A, Langendijk JA, Silver CE. Indications for radiotherapy after neck dissection. *Head Neck* 2010. doi: 10.1002/hed.21599
43. Crissman JD, Sakr WA. Squamous intraepithelial neoplasia of the upper aerodigestive tract. In: Gnepp DR (editor). *Diagnostic Surgical Pathology of the Head and Neck*. Philadelphia: W.B. Saunders, 2000. pp 1–17.
44. Warnakulasuriya S, Reibel J, Bouquot J, Dabelsteen E. Oral epithelial dysplasia classification systems: predictive value, utility, weaknesses and scope for improvement. *J Oral Pathol Med* 2008;37:127–133.
45. Hellquist H, Cardesa A, Gale N, Kambic V, Michaels L. Criteria for grading in the Ljubljana classification of epithelial hyperplastic laryngeal lesions. A study by members of the Working Group on Epithelial Hyperplastic Laryngeal Lesions of the European Society of Pathology. *Histopathol* 1999;34:226–233.
46. Gale N, Kambic V, Michaels L, Cardesa A, Hellquist H, Zidar N *et al.* The Ljubljana classification: a practical strategy for the diagnosis of laryngeal precancerous lesions. *Adv Anat Pathol* 2000;7:240–251.
47. Gale N, Michaels L, Luzar B, Poljak M, Zidar N, Fischinger J *et al.* Current review on squamous intraepithelial lesions of the larynx. *Histopathol* 2009;54:639–656.
48. Lumerman H, Freedman P, Kerpel S. Oral epithelial dysplasia and the development of invasive squamous cell carcinoma. *Oral Surg Oral Med Oral Pathol* 1995;79:321–329.
49. Ramqvist T, Dalianis T. An Epidemic of Oropharyngeal Squamous Cell Carcinoma (OSCC) Due to Human Papillomavirus (HPV) Infection and Aspects of Treatment and Prevention. *Anticancer Res* 2011;31:1515–1519.
50. Mehanna H, Jones TM, Gregoire V, Ang KK. Oropharyngeal carcinoma related to human papillomavirus. *BMJ* 2010;340:c1439.
51. Posner MR, Lorch JH, Goloubeva O, Tan M, Schumaker LM, Sarlis NJ *et al.* Survival and human papillomavirus in oropharynx cancer in TAX 324: a subset analysis from an international phase III trial. *Ann Oncol* 2011;22:1071–1077.
52. Hobbs CG, Sterne JA, Bailey M, Heyderman RS, Birchall MA, Thomas SJ. Human papillomavirus and head and neck cancer: a systematic review and meta-analysis. *Clin Otolaryngol* 2006;31:259–266.
53. Ragin CC, Taioli E. Survival of squamous cell carcinoma of the head and neck in relation to human papillomavirus infection: review and meta-analysis. *Int J Cancer* 2007;121:1813–1820.
54. Torrente MC, Rodrigo JP, Haigentz M, Jr., Dikkers FG, Rinaldo A, Takes RP *et al.* Human papillomavirus infections in laryngeal cancer. *Head Neck* 2011;33:581–586.
55. Robinson M, Sloan P, Shaw R. Refining the diagnosis of oropharyngeal squamous cell carcinoma using human papillomavirus testing. *Oral Oncol* 2010;46:492–496.

56. Stelow EB, Jo VY, Stoler MH, Mills SE. Human papillomavirus-associated squamous cell carcinoma of the upper aerodigestive tract. *Am J Surg Pathol* 2010;34:e15–24.
57. Singhi AD, Westra WH. Comparison of human papillomavirus in situ hybridization and p16 immunohistochemistry in the detection of human papillomavirus-associated head and neck cancer based on a prospective clinical experience. *Cancer* 2010;116:2166–2173.
58. Helliwell TR. Molecular markers of metastasis in squamous carcinomas. *J Pathol* 2001; 194:289–293.
59. Takes RP, Baatenburg De Jong R, Alles MJ, Meevis CA, Marres HA, Kneqt P *et al.* Markers for nodal metastasis in head and neck squamous cancer. *Archives of Otolaryngology Head Neck Surgery* 2002;128:512–518.
60. Genden EM, Ferlito A, Silver CE, Takes RP, Suarez C, Owen RP *et al.* Contemporary management of cancer of the oral cavity. *Eur Arch Otorhinolaryngol* 2010;267:1001–1017.
61. Colella S, Richards KL, Bachinski LL, Baggerly KA, Tsavachidis S, Lang JC *et al.* Molecular signatures of metastasis in head and neck cancer. *Head Neck* 2008;30:1273–1283.
62. Rao VU, Shenoy AM, Karthikeyan B. Role of angiogenetic markers to predict neck node metastasis in head and neck cancers. *J Cancer Res Ther* 2010;6:142–147.
63. Lallemant B, Evrard A, Chambon G, Sabra O, Kacha S, Lallemant JG *et al.* Gene expression profiling in head and neck squamous cell carcinoma: Clinical perspectives. *Head Neck* 2010; 32:1712–1719.
64. Leemans CR, Braakhuis BJ, Brakenhoff RH. The molecular biology of head and neck cancer. *Nat Rev Cancer* 2011;11:9–22.
65. Ziober AF, D'Alessandro L, Ziober BL. Is gene expression profiling of head and neck cancers ready for the clinic? *Biomarkers in Medicine* 2010;4:571–580.
66. Braakhuis BJ, Bloemena E, Leemans CR, Brakenhoff RH. Molecular analysis of surgical margins in head and neck cancer: more than a marginal issue. *Oral Oncol* 2010;46:485–491.
67. Seoane J, Caballero TG, Urizar JM, Almagro M, Mosquera AG, Varela-Centelles P. Pseudodysplastic epithelial artefacts associated with oral mucosa CO2 laser excision: an assessment of margin status. *Int J Oral Maxillofac Surg* 2010;39:783–787.
68. Chute DJ, Stelow EB. Cytology of head and neck squamous cell carcinoma variants. *Diagn Cytopathol* 2010;38:65–80.
69. Shashi Prasad KR, Jones AS, Birchall M, Krajacevic J, Helliwell TR. Immunocytochemical analysis of malignant melanoma of the nasal cavity and sinuses using tissue microarray. *Histopathol* 2007;50:516–519.
70. Nandapalan V, Roland NJ, Helliwell TR, Williams EM, Hamilton JW, Jones AS. Mucosal melanoma of the head and neck. *Clin Otolaryngol Allied Sci* 1998;23:107–116.
71. Greenberg JS, Fowler R, Gomez J, Mo V, Roberts DB, El Naggar AK *et al.* Extent of extracapsular spread. A critical prognosticator in oral tongue cancer. *Cancer* 2003; 97:1464–1470.
72. Ferlito A, Rinaldo A, Devaney KO, MacLennan K, Myers JN, Petruzelli GJ *et al.* Prognostic significance of microscopic and macroscopic extracapsular spread from metastatic tumor in the cervical lymph nodes. *Oral Oncology*. 2002;38:747–751.
73. Woolgar JA, Rogers SN, Lowe D, Brown JS, Vaughan ED. Cervical lymph node metastasis in oral cancer: the importance of even microscopic extracapsular spread. *Oral Oncol* 2003; 39:130–137.
74. Woolgar JA. Detailed topography of cervical lymph-node metastases from oral squamous cell carcinoma. *Int J Oral Maxillofac Surg* 1997;26:3–9.
75. Chuang H-C, Fang F-M, Huang C-C, Huang H-Y, Chen H-K, Chen C-H *et al.* Clinical and pathological determinants in tonsillar cancer. *Head Neck* 2011;33:12:1703–1707.

76. van den Brekel MWM, Stel HV, van der Valk P, van der Waal I, Meyer CJLM, Snow GB. Micrometastases from squamous cell carcinoma in neck dissection specimens. *Eur Arch Otorhinolaryngol* 1992;249:349–353.
77. Ferlito A, Partridge M, Brennan J, Hamakawa H. Lymph node micrometastasis in head and neck cancer: a review. *Acta Otolaryngol* 2001;121:660–665.
78. Devaney KO, Rinaldo A, Ferlito A. Micrometastases in cervical lymph nodes from patients with squamous carcinoma of the head and neck: should they be actively sought? Maybe. *Am J Otolaryngol* 2007;28:271–274.
79. Ferlito A, Rinaldo A, Devaney KO, Nakashiro K, Hamakawa H. Detection of lymph node micrometastases in patients with squamous carcinoma of the head and neck. *Eur Arch Otorhinolaryngol* 2008;265:1147–1153.
80. Seethala RR. Current state of neck dissection in the United States. *Head Neck Pathol* 2009;3:238–245.
81. Jose J, Ferlito A, Rodrigo JP, Devaney KO, Rinaldo A, MacLennan K. Soft tissue deposits from head and neck cancer: an under-recognised prognostic factor? *J Laryngol Otol* 2007;121:1115–1117.

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, 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

Oropharynx

- 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. Tumour invades larynx, deep/extrinsic muscle of tongue, medial pterygoid muscles, hard palate, or mandible
 - T4b Very advanced local disease tumour invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base, or encases carotid artery

Nasopharynx

- T1 Tumour confined to nasopharynx or extends to oropharynx and/or nasal cavity.
- T2 Tumour with postero-lateral parapharyngeal extension.
- T3 Tumour invades bone of skull base and/or paranasal sinuses.
- T4 Tumour with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx or orbit.

Hypopharynx

- T1 Tumour limited to one subsite and/or 20 mm or less in greatest dimension.
- T2 Tumour involves more than one subsite or measures 21–40 mm in size.
- T3 Tumour >40 mm in size or with fixation of hemilarynx or extension to oesophagus.
- T4a Tumour invades adjacent structures (thyroid cartilage, cricoid cartilage, hyoid bone, thyroid gland, oesophagus, central soft tissue).
- T4b Tumour invades prevertebral fascia, encases carotid artery or invades mediastinum.

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-60200	Oropharynx
T-53122	Anterior wall (glosso-epiglottic area)
T-53130	Base of tongue
T-60230	Vallecula
T-60220	Lateral wall
T-61100	Tonsil
T-61240	Tonsillar fossa and pillars
T-61150	Tonsillar pillars
T-60210	Posterior wall
T-60240	Superior wall
T-51120	Inferior surface of soft palate
T-51130	Uvula
T-23000	Nasopharynx
T-23001	Postero-superior wall
T-23002	Lateral wall (includes fossa of Rosenmuller)
T-51122	Inferior wall (superior surface of soft palate)
T-60300	Hypopharynx
T-24080	Pharyngo-oesophageal junction (post-cricoid area)
T-60320	Piriform sinus
T-60350	Posterior pharyngeal wall

Morphological codes

Note: This is not 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
M87203	Malignant melanoma

Procedure codes

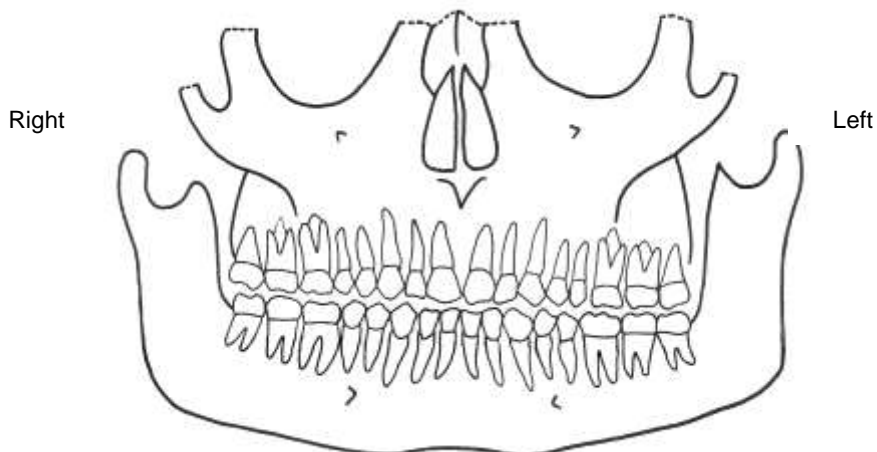
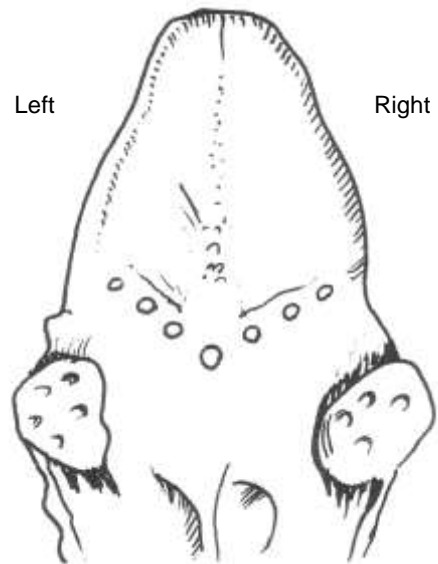
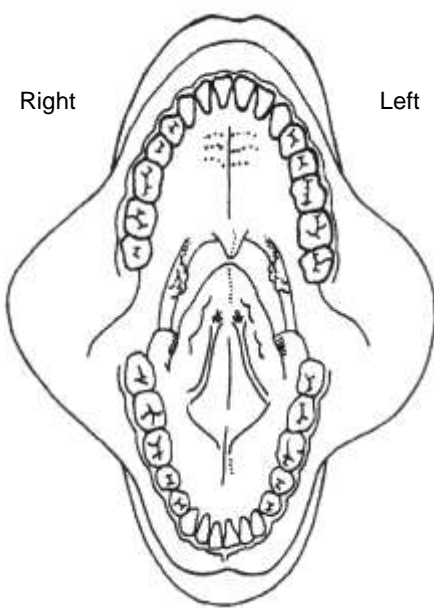
Note: This is not intended to be a comprehensive list of all procedures and other codes should be used as necessary.

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

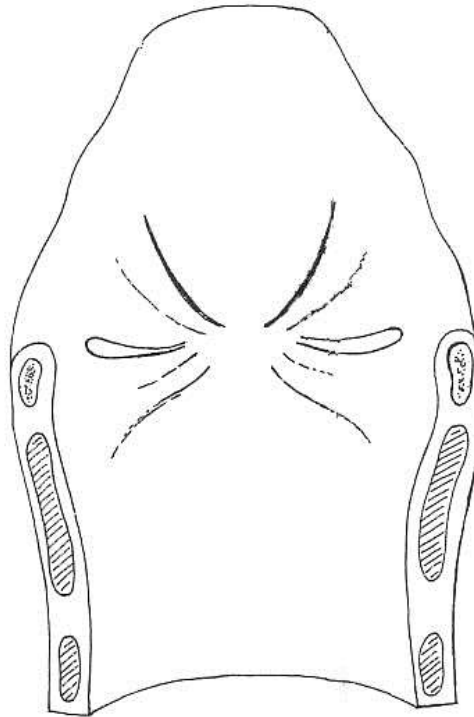
Surname	Consultant
Forename	Location
Date of birth	
Sex	
Hospital no	NHS/CHI no

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

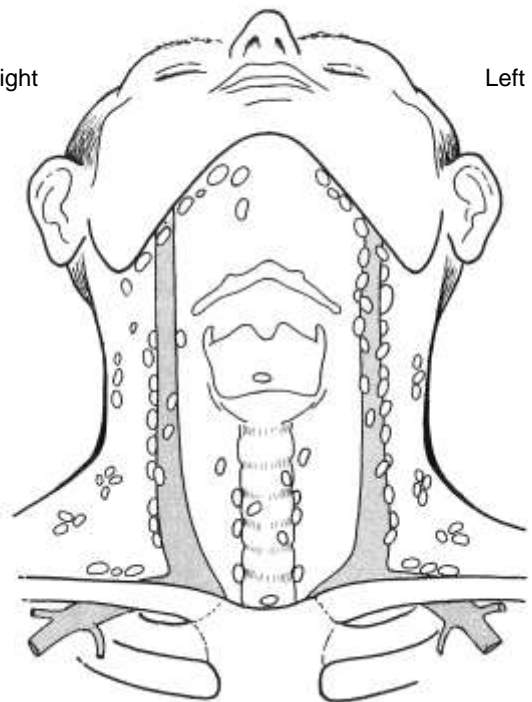


Please tick appropriate boxes:

	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

Left



Right

Left

Appendix D Reporting proformas

In order to provide flexibility in use, separate reporting proformas are provided for the primary carcinomas at each of the main pharyngeal sites 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 oropharyngeal 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/endoscopic 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.....Oropharynx..... 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
HPV status: Not known Negative Positive
p16 testing Negative Positive
ISH testing Negative Positive

Dataset for primary oropharyngeal 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.....

COMMENTS/ADDITIONAL INFORMATION

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 primary hypopharyngeal 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 primary nasopharyngeal carcinoma

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/endoscopic biopsy Resection
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.....Nasopharynx.... Subsite(s).....
Right Left Midline

Histological type:

Squamous cell carcinoma: Yes No Keratinising Non-keratinising
Undifferentiated carcinoma Yes No

Maximum diameter(mm)

Distance from invasive tumour to

 mucosal margin(mm)

 deep margin(mm)

Vascular invasion Yes No

Nerve invasion Yes No

Bone invasion Yes No

COMMENTS/ADDITIONAL INFORMATION

SUMMARY OF PATHOLOGICAL DATA

Tumour site..... Tumour type.....

pTNM stage pT..... pN.....

SNOMED codes

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)	Recommended best practice based on the clinical experience of the authors of the writing group.

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.