

Standards and datasets for reporting cancers

Dataset for the histological reporting of primary invasive cutaneous squamous cell carcinoma and regional lymph nodes

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Comments	<p>This dataset has been revised to include a redesign of the coding appendix and changes to the reporting proformas, including standardisation of terminology and improved clarity to better conform to the NCIN Clinical Outcomes and Services Dataset (COSD) for skin, in particular for AJCC7 staging. It also incorporates updated references relating to tumour subtypes, including text and proforma clarification of keratoacanthomatous lesions.</p> <p>In accordance with the College's pre-publications policy, this document was on the College website for an abridged consultation from 4–18 February 2014. Twenty-one items of feedback were received. 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>Dr Suzy Lishman Vice-President for Advocacy and Communications</p>

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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 (RCPATH) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely 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 are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – 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.

The following organisations were consulted during its preparation and approved the dataset:

- British Association of Dermatologists (BAD) (co-institutional member of the RCPATH Joint Specialty Advisory Committee on Dermatopathology)
- British Society for Dermatopathology (BSD) (institutional member of the RCPATH Joint Specialty Advisory Committee on Dermatopathology)
- National Specialist Dermatopathology External Quality Assessment Scheme (NSDEQA) (member of the RCPATH Joint Specialty Advisory Committee on Dermatopathology)
- National Cancer Intelligence Network (NCIN).

This dataset has been constructed taking into account the new strong evidence base that is contained in and forms the basis for the following new national and international publications. All publications have widespread national and/or international peer acceptance and reflect the current accepted professional standards and practice in skin cancer.

- COSD published by NCIN⁵
- Clinical guidelines published by the British Association of Dermatologists (BAD) and other professional bodies⁶
- World Health Organization (WHO) Classification of Skin Tumours⁷
- Armed Forces Institute of Pathology (AFIP) Atlas of Tumour Pathology⁸
- National Institute for Health and Clinical Excellence (NICE) Guidance on Cancer Series^{9,10}
- National Cancer Peer Review (NCPRI) Program by the Department of Health Cancer Action Team¹¹
- NHS Evidence¹²
- National Comprehensive Cancer Network (NCCN)¹³
- College of American Pathologists (CAP)¹⁴

As well as peer-reviewed scientific publications, consideration has also been given to published evidence and expert opinion on the internet, such as Dermopedia (www.Dermopedia.org).

Evidence for the revised dataset was also obtained by electronically searching medical literature databases for relevant research evidence, systematic reviews and national or international publications on skin cancer up to November 2013. This identified no evidence to alter the views or conclusions of the publications listed above. The evidence has been evaluated according to the modified SIGN guidance and the level of evidence for the recommendations has been summarised according to College guidance (see Appendix F). Most of the supporting evidence is grade C or D or meets the GPP (Good Practice Point) criteria. No major conflicts in the evidence have been identified and any minor discrepancies between evidence 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 COSD, and there are no new major financial or work implications arising from the implementation, compared to the 2002 dataset.

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

The dataset has been reviewed by the WGCS and was placed on the College website for consultation with the membership from 4–18 February 2014. All comments received from the WGCS and membership were addressed by the authors, to the satisfaction of the WGCS Chair and the Vice-President for Advocacy and Communications.

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 Clinical Effectiveness Department and are available on request.

1 Introduction

1.1 Purpose of the dataset

This document provides the dataset for the histological reporting of cutaneous squamous cell carcinoma. It replaces the first edition of the previous dataset of 2002. Although the data items remain largely unchanged, in some instances their current usage has revised implications for treatment, management and prognosis.

The meticulous diagnosis and reporting of cutaneous squamous cell carcinoma is important because histological parameters play a major role in defining patient treatment. Similarly, recording of pathological parameters in the dataset has direct implications for the prognosis of individual patients. The use of datasets (and the background information that forms part of the datasets) in the context of the multidisciplinary team (MDT) meeting is advocated to optimise decisions related to patient treatment, to facilitate regular audit and review of all aspects of the service, to enable the collection of accurate data for Cancer Registries and to provide feedback for those caring for patients with cancer. It is important to have robust local mechanisms in place to ensure that the MDT Clinical Leads and Cancer Registries are

apprised of supplementary or revised histology reports that may affect patient treatment and data collection.

1.2 Changes since the previous edition

The revised dataset is largely based on the previous edition. The main alterations are as follows:

a) Staging

It is essential to accommodate the changes in the international staging of cutaneous squamous cell carcinoma introduced in 2010.

Ideally, staging of cutaneous squamous cell carcinoma should be based on the latest published edition of the tumour, node and metastasis (TNM) categorisation of malignant tumours, published by the International Union against Cancer (UICC).¹ Internationally it has been agreed that this should be identical to the same staging edition published by the American Joint Committee on Cancer (AJCC).² When published, however, it was clear that the UICC 7th edition contained significant differences in relation to skin cancer. These differences, in particular in relation to melanoma, have been partly corrected in a subsequent TNM Supplement.³ The preface contains a statement of policy that the 7th edition of the UICC TNM Classification and Staging is still intended to correspond to the 7th edition of AJCC. Furthermore, in 'Frequently Asked Questions', UICC states for the sake of uniformity that it has adopted AJCC criteria for skin cancer and specifically acceptance of 2 mm as a high-risk feature for non-melanoma skin cancer (except basal cell carcinoma and Merkel cell carcinoma). In the main text, however, UICC has failed to incorporate AJCC high-risk factors, states 4 mm in error and uses different staging definitions for T3 and T4 disease. The latter difference is particularly important as UICC therefore fails to align cutaneous squamous cell carcinoma on the head and neck with cutaneous squamous cell carcinoma at other sites. On that basis, after widespread consultation, The Royal College of Pathologists has advised its members to use the AJCC 7th edition for skin cancer.⁴ For the same reason, a similar decision has been taken by the NCIN.

Several important differences occur in the new AJCC 7th edition.

1. Non-melanoma skin cancer is now divided into two separate chapters with different staging criteria. The two chapters are titled 'Merkel cell carcinoma' and 'Cutaneous squamous cell carcinoma and other cutaneous carcinomas'.
2. There is now no additional tumour staging breakpoint based on diameter for lesions over 20 mm diameter for non-melanoma skin cancer (except Merkel cell carcinoma).
3. As many cutaneous squamous cell carcinomas occur on the head and neck, staging of cutaneous tumours has been aligned with the previous AJCC Head and Neck Staging System. In particular, this has resulted in changes to T3 and T4 staging criteria.
4. Clinical and histological high-risk features are now defined that can upstage from T1 to T2. Although there is some overlap, it should be noted that these high-risk features are not completely identical to those defined by NICE clinical guidelines, as high-risk factors for MDT purposes, patient management and treatment.
5. There is now a new nodal staging system based on the diameter of metastatic deposits and the number and location of nodes involved.
6. AJCC is ambiguous in its definition as to which part of lip applies to cutaneous squamous cell carcinoma staging. In anatomic site, prognostic factors and summary, AJCC states it is hair-bearing lip. In 'high-risk features' it states non-hair bearing lip.

This dataset assumes the latter is a typographical error as AJCC separately defines carcinoma of the lip and oral cavity under Head and Neck TNM staging, to commence at the vermilion border. Head and neck histopathologists should note this anatomical division point as to whether use pT staging for either cutaneous or head and neck squamous cell carcinoma. AJCC lymph node staging for both, however, is similar.

7. It should be noted that AJCC7, and accordingly this dataset, excludes eyelid, penis, vulva and vermilion lip from cutaneous squamous cell carcinoma staging.

b) Core and non-core data items

In contrast to the previous edition of this dataset, data items are now divided into core and non-core types. As defined in the Foreword, core items in The Royal College of Pathologists cancer datasets are robust, evidence-based data items that are required for cancer staging, management and prognosis. These data items are expected to be available routinely for cancer MDT meetings, are recorded by MDT management systems and are used part of the Clinical Lines of Enquiry for the NCPR.

The core and non-core pathological data items are summarised in proforma style, which may be used as the main reporting format or combined with free text as required. The use of proformas and checklists significantly improves the quality of skin cancer histopathology reports.

c) Lymph nodes

The new nodal staging system is included as core data information in a separate reporting proforma.

d) Risk status

National Clinical Guidelines on both squamous and basal cell carcinoma have introduced the concept of risk status in relation to these two malignancies.⁶ In broad terms, high-risk correlates with significantly greater clinical risk for recurrent disease and metastatic potential. The evidence base for this has been endorsed by both NICE and the NHS Cancer Action Team in its publications.^{9,10} Knowledge of risk status is now vital for the correct clinical management and treatment and skin cancer MDT case discussion.

For squamous cell carcinoma, risk status is important to decide desirable margin clearance, the duration of follow-up and whether the latter is best undertaken in primary or secondary care.

Accordingly, a new data item is required in the form of a comment as to whether the cancer is of low or high-risk type, based on pathological and known clinical parameters. It is acknowledged that subsequent additional knowledge of clinical high-risk factors, unknown or uncertain at the time of reporting, may upgrade low risk to high risk at a later point in time and in particular during skin cancer MDT discussion.

As already highlighted, although there is some overlap with the high-risk factors defined for AJCC T staging, there are some differences from those used in National Clinical Guidelines and by NICE. Although the latter were published before the AJCC 7th edition, extensive peer consultation considered it inappropriate at this point in time, to align the two sets of definitions. In particular, it was considered that a squamous cell carcinoma below 4 mm in thickness and/or Clark level 4, should not be considered high-risk for MDT purposes.

e) Margins

In the previous edition, peripheral and deep margins over 1 mm were measured as whole integers. This remains as a non-core item in this edition of the dataset. The new core requirement involves measuring <1 mm, 1–5 mm and >5 mm.

1.3 Target users and health benefits of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons and oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and multidisciplinary team (MDT) working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. Collection of standardised cancer specific data also provides information for healthcare providers, epidemiologists, and facilitates international benchmarking and research.

2 Clinical information required on the specimen request form

Provision of clinical information is the responsibility of the clinician submitting a specimen for pathological examination. A range of clinical information, as indicated in the proposed UK National Histopathology Request Form (Appendix C) is required for both the COSD and MDT discussion to document and consider any clinical high-risk factors in relation to management and treatment.

The minimum clinical items regarded as core for the pathology report constitute the site of origin of the specimen and the type of specimen. Other clinical items are recognised to be important but since their provenance is not the primary responsibility of the pathologist, they are listed as non-core items to encourage their collection and inclusion in the histology report.

3 Preparation of specimens before dissection

3.1 Skin specimen

The overall size of the submitted specimen must be measured. When appropriate, and in particular with excision specimens, this should incorporate three dimensions. Any unusual features that could be diagnostically important should be recorded.

The presence, absence or any uncertainty about the existence of a lesion or abnormality to naked eye must be recorded. When a lesion is apparent, measurements should include the maximum diameter and elevation.

Inking the margins of all skin specimens with potential skin cancer should be considered. Standard techniques include the use of substances such as Indian ink, silver nitrate, alcian blue, crayon or commercial preparations. Excepting Mohs' surgery, inking is the best way to obtain a reasonably accurate assessment of surgical margins and thereby lesion clearance. Discretion and flexibility should, however, be applied in this decision. The potential for dye to track and give rise to false margins should be taken into account in the final histopathological assessment. Its routine use in large specimens, especially with a clearly visible small central lesion, is debatable. Even in these circumstances, however, inking may be useful because of the possibility of unexpected microscopic extension of the lesion. It is not necessary to ink curetted specimens, incisional, shave and punch biopsies as these are not performed for excisional purposes.

The examination of specimens submitted to the laboratory with prior designated orientation, by, for example sutures or inking, can be facilitated by the use of different coloured inks on different margins, notching the specimen or the insertion of coloured agar into the processing cassette.

3.2 Regional lymphadenectomy specimens

The generalities of macroscopic neck and axillary block dissection, described for head and neck cancer and breast cancer (www.rcpath.org/publications-media), apply equally to skin cancer. Inguinal dissections can be approached as axillary dissections.

The overall dimensions of the fixed tissue must be described, with particular note of any designated orientation and in particular, any apical node. Nodes should be identified by inspection and palpation. The use of clearing agents is time consuming and increases cost. Accordingly this is not regarded as essential.

3.3 Sentinel lymph node biopsy

AJCC7 does not contain specific advice about sentinel lymph node biopsy for cutaneous squamous cell carcinoma. Where appropriate, the dataset guidance contained in nodal excisions of head and neck carcinomas should be used (www.rcpath.org/publications-media) and modified according to general advice in UICC7.

4 Specimen handling, dissection and block selection

4.1 Skin specimen

Very small specimens may not require trimming. In this situation, however, it must be appreciated that a histological section along the longitudinal axis may not accurately reflect the nearest peripheral margin.

The method of handling excisional biopsies depends on the size of the specimen, whether the lesion can be seen, the position of the lesion on the specimen, the uniformity of the lesion and the type of processing technology. It is recommended that a separate judgement is made on each individual case, taking these variables into account, assisted by the following general comments.

Laboratories using rapid processing technology must ensure that trimmed tissue is no more than 2–3 mm in maximum thickness, whereas those using conventional processing technology can increase this to 4–5 mm.

Specimens that need to be trimmed, and in which the lesion can be seen, should be cut at regular intervals so that the nearest naked-eye margin to the lesion can be assessed histopathologically. For many skin ellipses, this will require transverse rather than longitudinal sectioning. When multiple sections are required, this should be undertaken by the 'sliced bread/toast rack' method.

The more of the specimen examined, the more accurate the assessment of the surgical margins will be. Accordingly, for specimens under 10 mm, it is recommended that most or all of the lesion is examined. For specimens over 10 mm, the extent of sampling should take into account the proximity of the lesion to the margins, maximum lesional thickness, lesional uniformity and any unusual features. When the lesion can be clearly identified, sampling the polar margins of skin ellipses should be discretionary and based predominantly on whether the lesion is close (under 1–2 mm) to the margin or is less than that in the shorter transverse axis.

When the lesion cannot be identified, or there is uncertainty, the whole of the specimen should be sampled. In this situation, the polar ends from the long axis of a skin ellipse should be examined. These can be placed in one or two cassettes, depending on whether orientation of the specimen has been identified clinically.

In some very large specimens, as well as sampling the lesion, the cruciate margins at 3, 6, 9 and 12 o'clock can be sampled, although the limitation in assessing margin clearance should be appreciated.

The requirement for step-levels/sections in any type of specimen is dependent on the requirement to identify a lesion, achieve full-face assessment, establish a diagnosis and assess the margins. Requests for levels at cut up can be used flexibly but with the proviso that laboratory protocols and technical experience must ensure that sufficient material remains in the paraffin block for further investigations if subsequently proved necessary.

Trimmed pieces of tissue of different thickness or the processing of more than two pieces of tissue in one cassette, incurs an increased risk of incorrect orientation and sectioning, with potential loss of diagnostic and margin information.

Re-excision specimens are covered in section 11.2.

4.2 Regional lymphadenectomy specimens

All potential lymph nodes must be removed, blocked and recorded in a manner that permits an accurate microscopic count of lymph nodes, number involved and measurement of the maximum diameter of the largest metastasis. Nodes can be bisected or sliced at 4–5 mm intervals.

The dimensions of the largest macroscopic metastatic deposit should be recorded. Representative sampling is acceptable, taking into account the need to measure the largest metastasis, ascertain whether more than one node is involved and to identify potential extracapsular invasion. Ascertaining the maximum diameter of the largest metastasis should be achieved by adopting a pragmatic approach, using both macroscopic and microscopic information. The lymph node or tumour closest to the surgical margin, within a macroscopic distance of 5 mm, should be identified and sampled.

Inking for the specimen surface is not regarded as essential.

5 Core data items

5.1 Clinical

The minimum clinical items regarded as core for the pathology report are the site of origin and the type of specimen.

5.2 Pathological

5.2.1 Macroscopic

Specimen and lesion size

The three dimensional size of the specimen should be recorded in millimetres. The maximum diameter of all lesions should be recorded in millimetres.

5.2.2 Microscopic

a) Histopathological subtype

This dataset uses a modified WHO classification of squamous cell carcinoma.⁷ In addition, it recognises that the origin of squamous cell carcinoma may be from either surface epidermal or follicular squamous epithelium. Both can have *in-situ* or invasive and low-risk or high-risk variants.

For the purpose of skin cancer MDT management, some subtypes of invasive cutaneous squamous cell carcinoma are regarded as clinically high-risk variants in the National Clinical Guidelines and by NICE.^{6,9} These are specifically defined as acantholytic, desmoplastic and spindle cell variants. These subtypes are associated with an increased risk of local recurrence and/or metastasis. The desmoplastic variant is defined as having a desmoplastic stromal component greater than 30%. Both the National Clinical Guidelines and WHO regard the spindle cell variant of squamous cell carcinoma as a high-risk variant. There is, however, debate about this issue and the AFIP have a slightly different view.⁸ The AFIP accepts spindle cell squamous cell carcinoma developing after radiotherapy as a high-risk variant, but regards spindle cell squamous cell carcinoma arising on light-exposed areas as not having the same aggressive potential. Invasive squamous cell carcinoma with adjacent Bowen's disease is also usually regarded as a high-risk variant, although there is now increasing debate as to whether this should be restricted to non-UV -light exposed areas.

Basaloid squamous cell carcinoma is uncommon in the skin but careful distinction must be made from basal cell carcinoma, using appropriate immunohistochemistry (BerEP4 and EMA).^{15,16} These tumours may arise in pre-existing basaloid Bowen's disease and are considered by definition to be poorly differentiated and may be associated with metastasis.¹⁵ They may show weak to focal moderate BerEP4 expression in common with basaloid Bowen's disease but are usually EMA positive (in contrast to the basaloid epithelium of basal cell carcinoma)

If none of the subtype features listed above are present, a squamous cell carcinoma, of surface epidermal origin, is defined in this dataset as being of no special type or classic. Any diagnostic uncertainty with regard to subtype can be entered in the proforma as 'Uncertain' in the 'Other' category.

The Royal College of Pathologists acknowledges the current WHO terminology, which considers keratoacanthoma as synonymous with invasive squamous cell carcinoma of keratoacanthomatous type.⁷ The Royal College of Pathologists, however, similarly acknowledges that there is still considerable national and international debate as to whether keratoacanthoma is truly a pathologically benign or malignant neoplasm. Despite this debate, it is generally recognised that, to date, no one single criterion can make a reliable distinction between squamous cell carcinoma and keratoacanthoma. In each individual case, the diagnosis must be approached by using a constellation of clinical and pathological diagnostic features. The term 'keratoacanthoma' should possibly be avoided in an immunosuppressed patient, in large lesions and in a subungual location, as the latter are all considered to have a greater potential for aggressive behaviour. By clinical definition, a diagnosis of keratoacanthoma must be accompanied by a history of a period of initial rapid growth over a few weeks and subsequent stabilisation or involution over several months. The diagnosis then requires support by the following additional histological features. The whole of the intact lesion should be available for histopathological examination, as this is the only reliable means to accurately assess the overall architecture. The diagnosis should be avoided if there is adjacent surface epidermal involvement or continuity with surface epidermal dysplasia or surface *in-situ* squamous cell carcinoma. The lesion is characterised by an exo-endophytic growth pattern and, in the fully developed stage, there is a central keratin-filled crater-like

appearance and symmetrical peripheral surface epidermal lipping/buttrressing. The silhouette of the periphery is usually gently curving or with blunt down-growths. Although not recognised by all authorities, some consider that there is an early proliferative stage that may display a more infiltrative pattern with increased mitotic activity and prominent pleomorphism. In all areas of the lesion, however, the peripheral zone evolves centrally into distinctive fully maturing cells, with abundant eosinophilic glassy cytoplasm and well-formed keratin. Acantholysis (in the absence of intraepithelial microabscesses) should not be present. The transition from peripheral proliferative to central maturing cells may be quite abrupt. Centrally within the maturing epithelium there should be little nuclear pleomorphism and a normal nuclear/cytoplasmic ratio. Although more nuclear pleomorphism and mitotic figures are permissible in the peripheral zone, solid zones extending beyond the rounded profile or into the subcutis should be absent. Severe and extensive cellular anaplasia must be absent. Atypical mitotic figures must give rise to diagnostic caution, but should not necessarily exclude the diagnosis in an otherwise classic case. In more mature lesions, the central keratin whorls are typically rounded and laminated. There are frequently micro-abscesses within the epithelium, which can include neutrophils and eosinophils. Intraepithelial incorporation of elastic and collagen fibres can be seen both peripherally and centrally, although this feature may also be observed sometimes in invasive squamous cell carcinoma. Perineural and vascular invasion are generally considered to have no adverse effect on prognosis for keratoacanthoma, although larger studies are required. In general, keratoacanthomas show no surface ulceration, no stromal desmoplasia and no extension below the depth of adnexal structures. They may commonly show entrapment of elastic and collagen fibres and a lichenoid inflammatory response. Even in early proliferative lesions, epithelial infiltration from the base of the lesion must be viewed with diagnostic caution.

If these clinicopathological criteria are met, The Royal College of Pathologists is able to endorse diagnostic use of the term 'keratoacanthoma', with its implied expected benign clinical behaviour. This approach also supports clinical guidance from the British Association of Dermatologists, which comments on the benign nature of keratoacanthoma.¹⁷

The Royal College of Pathologists' support for keratoacanthoma as a clinicopathological diagnostic entity also extends, with an appropriate previous clinical history, to the diagnosis of regressing or regressed keratoacanthoma. This lesion often has a crateriform or cystic appearance. There is a lack of epithelial atypia and significant epithelial proliferation, with a frequently attenuated squamous epithelium consequent upon a previous or ongoing lichenoid inflammatory response. There may be an underlying band of dermal fibrosis with granulomas responding to keratin or elastic fibres. The latter may also be seen in the overlying squamous epithelium.

There is also an additional view that keratoacanthoma has the rare potential to transform into classic invasive squamous cell carcinoma.¹⁸

It cannot be overemphasised, however, how difficult the entire area can be diagnostically. Although there is always room for clinical and pathological discretion, completion of a cancer dataset and referral to a skin cancer MDT would not appear essential for a case of classic or regressing/regressed keratoacanthoma that has been diagnosed in the above clinicopathological manner and is completely excised. There must, however, be no hesitation to refer any lesion to a skin cancer MDT that does not appear straightforward or is problematical in some way. This would include any element of clinical or histopathological diagnostic uncertainty, an uncertain or poorly documented clinical history relating to growth and/or potential regression, potential incomplete excision, a fragmented specimen or biopsy, one with perineural or vascular invasion or any case originating from primary care, especially from a non-accredited practitioner in the field of skin cancer. As discussed above, cases in immunosuppressed patients, large or subungual lesions or in association with drug therapy (such as BRAF inhibitors) must also have skin cancer MDT

discussion. Although not regarded as mandatory, it is noted that because of the diagnostic difficulties involved, many centres refer all potential keratoacanthomas and related lesions to a MDT. Some of the above cases may necessitate MDT referral under the diagnostic umbrella term of 'squamoproliferative lesion of uncertain type' (see below), pending further information at the MDT (such as clinical history).

This dataset further adopts an approach that an apparent invasive squamous cell carcinoma, having some but not all features of keratoacanthoma, is best classified as invasive squamous cell carcinoma with some keratoacanthomatous-like features. This is to avoid potential confusion with the WHO term of 'keratoacanthomatous-type of invasive squamous cell carcinoma', regarded as synonymous with keratoacanthoma. It should also be noted that some types of squamous cell carcinoma (such as Ferguson-Smith) can display clinical regression.

Several different types of invasive carcinoma are already recognised to have a follicular origin, such as those arising from follicular derived (sebaceous/pilar or epidermal) cysts, pilomatixoma, tricholemmoma and follicular poroma).

There is, however, increasing support for the diagnosis of a specific follicular variant of squamous cell carcinoma, with *in-situ* and/or invasive growth patterns.^{19,20,21} Diagnostic criteria include an abrupt demarcation of the lesion with rounded peripheral profiles arising from the follicular infundibulum. In pure, compared to hybrid cases, there is an absence of continuity with the surface epithelium, absent surface epidermal dysplasia and absent surface Bowen's disease. Centrally tumours often have multiple infundibular-like downgrowths with central keratin, which is often vertically orientated. Infundibular keratinisation with keratohyaline granules is seen in the superficial parts of the tumour, with tricholemmal keratinisation more deeply. The infundibular connections with the surface epidermis are frequently multiple and particularly apparent at the lateral edges. Most lesions display squamous epithelium (often with relatively mild cellular pleomorphism) but varying clear cell change may be present. Uncommonly lesions are dominated by basaloid cells, which require distinction from basal cell carcinoma (see previously). Subtle peripheral palisading is frequently present, but generally stromal mucin in retraction spaces is not a feature. Central acantholytic spaces containing acidic mucin is a distinctive feature of many lesions. A large number of cases are highly circumscribed and appear to represent *in-situ* lesions, despite being centred on the reticular dermis. Excised lesions that are considered to be *in-situ*, in common with other *in-situ* squamous lesions, do not require skin cancer MDT discussion. The invasive tumour is generally considered to be of low-risk clinical and pathological type, with a very low incidence of recurrence or metastasis, although higher grade variants can occasionally occur. The latter, in particular, relates to lesions with more pleomorphism and more extensive irregular dermal and subcutaneous infiltration. Lesions are usually recognisable without the requirement for histochemistry, although they are typically negative for CD34 (in contrast to tricholemmoma and tricholemmal carcinoma) and negative for HPV (which can be present in follicular poroma). To avoid the pathological allocation of an inappropriate high risk status or tumour stage, there has been a proposal that staging parameters, such as thickness, should be measured in a modified manner, although this approach has yet to be confirmed.²² So-called infundibulo-cystic invasive squamous cell carcinoma appears to be included in the above follicular variant.

It is also recognised by The Royal College of Pathologists that a definitive diagnostic distinction between entities may not always be possible. This may, for example, be between squamous cell carcinoma and keratoacanthoma or between squamous cell carcinoma and pseudocarcinomatous hyperplasia, for example in nodular prurigo or hypertrophic lichen planus. Essentially, these ambiguous/borderline cases represent squamoproliferative lesions of uncertain type (SPLUT). In this situation, each individual case should be reported descriptively in a pragmatic, descriptive, free-text manner and mentioning cancer dataset parameters as appropriate. Such cases should receive skin

cancer MDT discussion but, as with all borderline lesions, it is desirable to minimise use of this category.

As an important practical point it must be remembered that solitary or multiple keratoacanthomas can occur as a Koebner phenomenon at the edge of a previous surgical excision (including those for previous keratoacanthoma or squamous cell carcinoma). Awareness of this biological feature can help circumvent diagnostic confusion and error.

[Different histological subtypes correlate with different clinical risk status – Level of evidence B.]

b) Grade

A poorly differentiated squamous cell carcinoma is a joint high-risk feature to contribute to upstaging from pT1 to pT2 in AJCC7,² and is a solitary high-risk feature for skin cancer MDT management.^{6,9}

Tumour differentiation is a core item for all tumours in the COSD.⁵

Evidence indicates that increasing de-differentiation correlates with an increasing risk of recurrence and metastasis.²

Although AJCC7 lists poorly differentiated as a high-risk feature for staging, its definitions are broad. They are summarised below.

- Low-grade tumours are defined as showing considerable cellular differentiation, uniform cell size, infrequent cellular mitoses and infrequent nuclear irregularity. Intact intercellular bridges are also present.
- High-grade tumours are described as showing poor differentiation, frequent spindle cell characteristics, necrosis and high mitotic activity.

Use of the original Broders method of classifying differentiation was considered in this dataset. Here, four grades are defined using the percentage of well-differentiated tumour present and the surrogate marker for differentiation in this context is usually taken to indicate keratinisation. After consultation, however, a decision was taken to adopt a three-grade classification, which incorporates additional elements such as cytological features and mitotic activity.¹⁵

The three grades are defined as follows.

- Well-differentiated tumours are characterised by squamous epithelium that frequently shows easily recognisable and often abundant keratinisation. The epithelium is obviously squamous and intercellular bridges (prickles) are readily apparent. The tumours display minimal pleomorphism and mitotic figures are mainly basally located.
- Moderately differentiated tumours show rather more structural disorganisation in which the squamous epithelial derivation is less obvious. Nuclear and cytoplasmic pleomorphism is more pronounced and mitotic figures (including abnormal forms) are much more commonly seen. Usually, less keratin formation is evident, often being limited to the formation of keratin pearls (concentric laminated whorls of keratinised squames), horn cysts, and scattered individual keratinised cells.
- In the poorly differentiated variants, it may be difficult to establish the true nature of the lesion unless intercellular bridges are identified or small foci of keratinisation found.

Rarely, the tumour is completely anaplastic and an origin from an overlying dysplastic epithelium may be the only clue to the diagnosis. Here, the immunohistochemical demonstration of keratin expression is often of value.

Unfortunately, AJCC7 provides no guidance as to the percentage of differentiated components required to establish tumour grade. On that basis, this dataset has adopted the widely recognised approach that a tumour should be classified according to its most poorly differentiated region, irrespective of the percentage present.

This approach is also advocated by the National Comprehensive Cancer Network and is used in some other College cancer datasets (such as mucosal malignancies of the oral cavity).¹³ The percentage of various differentiated components can be entered as a non-core dataset item.

[The degree of tumour differentiation correlates with clinical risk status and is a staging determinant – Level of evidence C.]

c) Thickness

A tumour thickness of greater than 2 mm in a cutaneous invasive squamous cell carcinoma is a joint high-risk feature to contribute to upstaging from pT1 to pT2 in AJCC7.² A tumour thickness of greater than 4 mm in invasive squamous cell carcinoma is regarded as a solitary high risk for skin cancer MDT management in National Clinical Guidelines and by NICE.^{6,9} Recording a tumour thickness of 2 mm or more is a site-specific item in the COSD.⁵

It is recognised that increasing thickness of invasive squamous cell carcinoma is associated with increasing metastatic potential. Primary tumours that are 2 mm or less in thickness are not associated with significant metastatic potential and therefore complete excision is usually curative. Tumours over 10 mm are very high risk, with high potential mortality.

In order to conform to AJCC7, tumour thickness must be measured in the same way as Breslow thickness for invasive malignant melanoma (www.rcpath.org/publications-media). It should be measured from the granular layer, or, when present, the ulcer base, to the deepest extent of invasion by contiguous tumour cells. Tumour thickness should be recorded in mm, but whole integers suffice. Tumour thickness can be measured using an ocular micrometer, Vernier scale or an eye-piece measurement graticule. At times, difficulties can be experienced in tumours that are polypoid, exophytic or endophytic. In this situation, a pragmatic approach should be adopted and the difficulty should be mentioned briefly in the report. Although it would be useful to measure thickness in the same way as at other sites, i.e. from the base of the epithelium, this would conflict with the use of AJCC7 and its staging system which is based on Breslow thickness for squamous cell and adnexal carcinomas. Some squamous cell carcinomas have malignant surface epithelium, which displays substantially undulating peaks and troughs with intervening reactive stroma. In this situation, it is recommended that the Breslow thickness is measured from the granular layer in epithelium within the troughs and not the peaks.

The difference in the definition of high risk used for staging in AJCC7 (>2 mm) is noted to be different than the value used in the National Clinical Guidelines and by NICE for skin cancer MDT management (>4 mm). It is noted, however, that in AJCC7, two high-risk features are required for up-staging. In addition, there appears widespread clinical agreement that thickness between 2 and 4 mm, although demonstrating some elevated risk for recurrence and/or metastasis, is not as high a risk or clinically significant as >4 mm as a solitary criterion.

The absence of specific measurement requirements for <2 mm should simplify measurement in cases with very early invasion.

For assessing whether a measurement is >2 or >4 mm, 2 and 4 mm is statistically interpreted to represent 2.0 and 4.0 mm respectively.

On the basis of the above, this dataset recommends measuring thickness as ≤ 2 mm, >2–4 mm or >4 mm.

The difficulty of measuring thickness in follicular derived lesions has been discussed in section 5.2.2 a and clearly additional research requires to be undertaken in this area.²²

[Tumour thickness correlates with clinical risk status and is a staging determinant – Level of evidence B.]

d) Level of invasion

Invasive cutaneous squamous cell carcinoma invading into or beyond the reticular dermis (Clark level 4) is a joint high-risk feature that contributes to upstaging pT1 to pT2 in AJCC7.² Clark levels are defined in detail in the RCPATH melanoma dataset (www.rcpath.org/publications-media).

Invasive cutaneous squamous cell carcinoma extending into or beyond the subcutaneous fat is regarded by the National Clinical Guidelines and NICE as a solitary high-risk determinant for skin cancer MDT management.^{6,9}

Invasion into or beyond the reticular dermis is a site-specific item in the COSD.⁵ The degree of extension beyond the reticular dermis must be specified and, in particular, this includes extension into bone as staging determinants for pT3 and pT4 in AJCC7. These are defined as:

- invasion into facial or cranial bone (maxilla, mandible, orbit, temporal bone) is a solitary determinant to define stage pT3
- invasion of skull base or skeleton (axial or appendicular) is a solitary determinant to define stage pT4.

Both of the latter are also site-specific items for the COSD.⁵

Assessment of the level of invasion in this dataset should now be facilitated by the absence of a requirement to specify invasion into the papillary dermis (Clark level II) or interface between the papillary and reticular dermis (Clark level III).

[The level of invasion is a clinical risk factor and is a staging determinant – Level of evidence B.]

e) Lymphovascular invasion

Evidence to indicate that lymphovascular invasion correlates with recurrence, metastasis or prognosis is limited. Lymphovascular invasion, however, is a descriptor in AJCC7.² It is also a high-risk feature in the National Clinical Guidelines.⁶ The presence of an endothelial-lined space is an essential criterion for lymphovascular invasion, as it is essential to distinguish retraction artefact. As indicated by the AJCC term, it is not necessary to distinguish lymphatic and venous invasion.

Unlike malignant melanoma, there are no international definitions for satellite, microsatellite or in-transit metastasis for cutaneous squamous cell carcinoma. In particular, there are no definitions with regard to size or distance from the primary tumour.

As with Merkel cell carcinoma in the skin, it is recommended that the term 'in-transit metastasis' is used empirically for any metastasis between the primary tumour and regional nodes. If present, this can be specified in the lymphovascular section.

[Lymphovascular invasion can indicate increased risk of local recurrence and metastasis – Level of evidence C.]

f) Perineural invasion

Perineural invasion is a recommended site-specific prognostic factor in AJCC7.² It is a core item in the National Clinical Guidelines⁶ and a site-specific item in the COSD.⁵

Perineural invasion into the skull base is one specific determinant for stage pT4 in AJCC7.² Perineural invasion correlates with a high risk of local recurrence and high clinical morbidity. Perineural invasion does not have prognostic significance in keratoacanthoma (invasive squamous cell carcinoma – keratoacanthomatous type).⁷

There is no evidence to indicate whether perineural invasion in the context of skin applies to intratumoural or extratumoural invasion, including the invading front. Some, however, restrict the term to extratumoural invasion. This information can be included as a non-core item.

In re-excision specimens it is important to ensure that apparent perineural invasion is not so-called 're-excision perineural invasion' (RPI). This reflects the presence of benign perineural epithelial cells in previously biopsied areas, most likely representing reactive/reparative proliferation of traumatised eccrine sweat gland ducts into a plane of lower resistance. Immunohistology can be used to make the distinction.¹⁶

[Perineural invasion can indicate an increased risk of local recurrence and is a staging determinant – Level of evidence C.]

g) Margins

Tumour recurrence and clinical morbidity are influenced by the completeness and adequacy of primary excision. In general, however, use of the words 'complete/incomplete' and 'adequate/inadequate' should be avoided in routine histopathology reports. Unless all of the margins have been examined, it is difficult to be certain about the completeness of excision. The term 'complete' is more acceptable in the context of Mohs' surgery where the peripheral margin has been examined in its entirety. Adequacy implies a degree of clinicopathological judgement and is therefore more applicable in the context of skin cancer MDT discussion. It is well recognised in a significant number of cases where tumour extends to a margin, that there is no residual tumour present on re-excision. This confirms that the term 'incomplete' can be inappropriate in this situation. In non-excision specimens (such as curettings), the term 'edge' may be more appropriate, as the edge may not reflect the true surgical margin.

Although evidence is more robust for peripheral margins, there is broad peer agreement that comments are necessary about the clearance of both peripheral and deep excision margins. The words 'peripheral' or 'radial' rather than 'lateral' are generally preferred, to avoid problems by possible inference of a medial margin. The words 'lateral' and 'medial' may be applicable to specifically defined and designated margins in orientated specimens. Careful consideration has been given as to whether the extent of peripheral and deep clearance should be measured in quantitative terms. It is certainly clinically necessary to have information about whether the peripheral and deep excision margins are clear or involved by tumour. Clinicians invariably also wish to know whether the tumour is close to the nearest margin to evaluate the potential risk of recurrence, the necessity for further treatment and follow-up. 'Close' is, however, a poorly defined term and used

inconsistently for skin cancer treatment and management. The evidence base for the term is also limited. Guidance on adequate *clinical* margins is available in the National Clinical Guidelines and adequacy of clearance is essentially a risk assessment of percentage chance of recurrence, based on margin clearance and low/high-risk status of the tumour. For squamous cell carcinoma this varies between 4 and 6 mm.⁶ Information on histological margins is unfortunately much more limited. Some information is available for basal cell carcinoma, but very little for squamous cell carcinoma. For basal cell carcinoma, the histological definition of 'close', based on recurrence, is variable and has included measurements between 0.31 mm and 0.84 mm or less than 1 high power field. On that basis, it appears that an evidence-based histological definition of close is still awaited. Accordingly, the reporting of margins below 1 mm to one decimal point cannot be routinely supported, although provision of this information remains as a local non-core option.

Consultation with the BAD has revealed strong support for clinical reasons, to know whether squamous and basal cell carcinoma excision margins are histologically involved (0 mm), 'close' as defined below 1 mm, and above 1 mm. Approximately one-third of dermatologists in the East Midlands SHA, when audited, regarded histological margins below 1 mm as effectively involved, although this was not sufficiently consistent to justify adopting the approach in the current dataset.

As a core data element for all cancers, the COSD records whether tumour excision margins are clear by more than 5 mm, clear by greater than 1 mm but less than or equal to 5 mm, or less than or equal to 1 mm but without tumour reaching the margin.⁵ Skin cancer margins should therefore be measured in relation to both 1 mm and 5 mm breakpoints. There is also additional peer support to audit the excision margins of all skin cancer specimens between different Trusts and general practices within a Cancer Network, and between different clinical specialties and clinicians. Measuring resection margins over 1 mm, and histologically to within 1 mm, is one way to facilitate this objective and this could also represent a reasonable surrogate marker for clinical margins as defined in National Guidelines. This dataset recommends measuring peripheral and deep margins histologically as <1 mm, 1–5 mm and >5 mm. Measuring to a whole mm integer over 1 mm is accordingly included as a non-core item.

It is important that assessment of a margin below 1 mm is undertaken on 'full-face' sections, with a low threshold to request additional levels to increase the accuracy of assessment.

It should be noted that margin definitions used for mucosal malignancies of the oral cavity, including vermilion lip (>5 mm clear, 1–5 mm close and <1 mm involved) are not regarded as applicable to cutaneous squamous cell carcinoma, including hair-bearing lip.

This dataset defines margin clearance that is either involved or less than 1 mm as high risk. Using less than 1 mm as the definition takes into account the absence of a strong evidence base in this area and errs on the side of clinical safety, to incorporate different variables such as tumour type, fixation shrinkage, lesion sampling and levels.

[Margin involvement by tumour or the degree of clearance correlates with the risk of clinical recurrence – Level of evidence C.]

h) Maximum diameter

A maximum tumour diameter of greater than 20 mm is a primary determinant in the distinction between stage pT1 and pT2 in AJCC7.² A diameter greater than 20 mm is an important threshold for increased recurrence and metastatic potential. In contrast to AJCC6, there is now considered to be insufficient evidence for an additional 50 mm threshold staging break-point.

Advice on how to measure diameter is not provided in AJCC7. Indeed, it is unclear whether the AJCC7 database uses clinical or histological measurements. To achieve standardisation, however, this dataset advocates a pragmatic approach using both macroscopic and microscopic measurements as deemed suitable and applicable to each individual case.

[Maximum diameter is a primary staging determinant – Level of evidence B.]

i) Pathological risk status for skin cancer

This is largely integrated from AJCC7,² BAD,⁶ NICE,⁹ CPR,¹¹ CAP,¹⁴ AFIP⁸ and NCCN.¹³

High-risk status relates to risk of recurrent disease and/or metastatic potential. The term ‘high risk’ has developed in two different situations and both incorporate clinical and histological parameters. The clinical parameters are covered in clinical items under non-core aspects of the dataset, as their collection is not the primary responsibility of the pathologist.

There are two situations where pathological risk factors present in an invasive squamous cell carcinoma must be known. These are first, clinical and MDT management, and second, in relation to AJCC7 pT2 staging definitions.

a) Clinical and MDT management

The NICE and NCPR criteria for mandatory MDT referral/review are listed in section 11.1. Knowledge of high-risk factors present facilitates MDT decision-making and in particular the extent of desirable margin clearance. It also helps to assess prognosis, decide the duration of follow-up and whether the latter is best undertaken in primary or secondary care.

Although NICE and NCPR list mandatory reasons for MDT referral, any case can be referred to a skin MDT, if considered appropriate, by any member of the skin cancer MDT team. In particular, the latter relates to cases with margins of less than 1 mm. Although a margin of less than 1 mm is not regarded by NICE and NCPR as a mandatory reason for MDT referral/review, each case must still receive careful consideration and be referred to the MDT, if there is any degree of uncertainty over the degree of adequacy of margin clearance.

High-risk pathological factors for clinical management

Any one equals high-risk status

A. SCC and stage

- | | | |
|-----|---|--|
| i | Type: acantholytic, desmoplastic, spindle/metaplastic/sarcomatoid
Spindle only if previous radiotherapy
Adenosquamous
SCC with adjacent Bowens | BAD/WHO
AFIP
WHO/AFIP
BAD |
| | RCPATH: any of above | |
| ii | Grade: poorly differentiated
Moderately differentiated | BAD(text)/WHO/AJCC7/NCCN
BAD (table)/NCCN |
| | RCPATH: poorly differentiated | |
| iii | Perineural invasion present | BAD/NICE/WHO/AJCC7/NCCN |
| | RCPATH: perineural invasion present | |

- | | | |
|-----|--|---------------------|
| iv | Lymphovascular invasion present | BAD/CAP |
| | RCPATH: lymphovascular invasion present | |
| v* | Thickness >4 mm | BAD/NICE/NCCN/UICC7 |
| | Thickness >2 mm | AJCC7 |
| | RCPATH: thickness >4 mm | |
| vi* | ≥ Subcutaneous fat | BAD/NICE/WHO |
| | ≥ Reticular dermis | AJCC7/NCCN |
| | RCPATH: ≥ subcutaneous fat (Clark level 5) | |
| vii | TNM pathological (p) stage T2, 3, 4 | BAD/NICE/AJCC |
| | RCPATH: T2, T3, T4 | |

B. Margins

Histological margins

Margins that are involved (0 mm) NICE/BAD

Margins that are less than 1 mm RCPATH/BAD

RCPATH: Margins that are involved (0 mm) or less than 1 mm

* AJCC7 criteria post-dated BAD/NICE/WHO publications.

Upstaging from T1 to T2 in AJCC7, however, requires the presence of at least two of the designated AJCC7 high-risk features (see below). Thickness and Clark level for AJCC7 in particular are noted to be different high-risk factors from BAD/NICE guidelines (greater than 4 mm or Clark level 5 or greater), although only one feature is required for the latter. The RCPATH has adopted the latter in view of strong clinical support in the UK.

The pathology risk status is reported as core items, under the two subheadings of SCC and stage and margin, to provide clinical guidance relating to management, treatment and prognosis. It does not necessarily indicate a requirement for MDT referral or additional treatment. One or both of the latter must be decided on an individual case basis by a clinician and/or within an MDT setting.

Note that a low-risk squamous cell carcinoma using histological criteria may be upgraded to an overall high-risk lesion, when summated with any clinical high-risk features present (supplied by the clinician and/or at an MDT).

[Knowledge of defined high-risk pathological features is required for appropriate clinical management, treatment and MDT discussion – Level of evidence B.]

b) High-risk pathological and clinical features to upstage pT1 to pT2 (AJCC 7).

pT2 is defined as either maximum diameter ≥20 mm, or pT1 (i.e. ≤20 mm) upstaged to pT2 by two high-risk features*.

* These comprise:

- grade: poorly differentiated
- perineural invasion
- thickness > 2 mm
- Clark level ≥ 4
- clinical: ear and hair-bearing (non-glabrous) lip.

[Defined pathological and clinical high-risk features constitute staging parameters – Level of evidence B.]

See Appendix E for a comparison of high-risk pathology factors for clinical and MDT management and AJCC7 pT1 upstaging for < 20 mm maximum diameter.

j) Lymph nodes – number of nodes involved and maximum size of metastatic deposit

The number of involved nodes and the size of largest metastatic deposit are primary pN staging determinants. There are staging breakpoints at 30 and 60 mm. Note that size relates to metastatic deposit and not lymph node. The number of nodes identified and the number of nodes involved are a core requirement in the COSD.⁵ The anatomical site and laterality of the lymph nodes must be recorded.

[The number of nodes involved and maximum size of metastatic deposit are primary staging determinants – Level of evidence B.]

k) Lymph nodes – extracapsular invasion (spread/extension)

This is widely regarded as a manifestation of potential biological aggression and considered to be associated with a worse prognosis. This finding prompts consideration of the use of adjuvant chemotherapy.

[The presence of extracapsular invasion institutes consideration of adjuvant radiotherapy – Level of evidence C.]

l) Lymph nodes – highest/apical node

Clinicians often identify the highest/apical lymph node in lymphadenectomy specimens. If identified, the report must indicate whether this contains a metastatic tumour deposit.

[This information is often requested by clinicians and considered to have some prognostic value – Level of evidence D.]

6 Non-core data items

These can be included to create a more comprehensive report, taking into account local Cancer Network and clinical preferences, audit and research. These data items have been supported during the informal consultation on the dataset.

6.1 Clinical

These are based on the National Clinical Guidelines⁶, core and site-specific items in COSD⁵ and the draft UK National Histopathology Request Form (Appendix C). They also conform to NICE requirements⁹ and can be captured if provided by the clinician.

- Date of surgical procedure
- Grade of clinician undertaking procedure
- Clinical diagnosis/description
- Procedure intention of clinician (diagnostic or therapeutic biopsy)
- Is this a tumour recurrence?
- Previous histology reference number(s)

- Is the patient immunocompromised?
- Is this a tumour arising in an area of radiation or thermal injury, chronic draining sinus, chronic ulcer, chronic inflammation or Bowen's disease?
- Is the tumour arising in an individual genetically predisposed to cancer
- Clinical high-risk factors for skin cancer MDT treatment/management⁹ (any one equals high risk):

Anatomic location – ear and hair-bearing (non-glabrous) lip*	BAD/AJCC7 ^{6,2}
Recurrent or persistent	BAD ⁶
Reduced immune status	BAD ⁶
Genetics	BAD ⁶
Area of radiation, thermal injury, chronic draining sinuses, chronic ulcers or chronic inflammation	BAD ⁶
Arising in non-exposed sites such as perineum, sacrum, sole of foot	BAD ⁶

* Also used in TNM 7 T2 definition (see pathology).

6.2 Pathological

- Tumour growth pattern at closest margin: circumscribed/cohesive, infiltrative/non-cohesive.
- Percentage of well, moderately and poorly differentiated components.
- Tumour thickness measured to nearest 1 mm as a whole integer.
- Margins: below 1 mm measured to nearest 0.1 mm or 0.5 mm.
- Margins: over 1 mm measured to whole mm integer.
- Extent of involvement or closeness at a margin. Here it is useful to know if the tumour abuts or transects a margin and whether the involvement is focal or more widespread. This can be expressed as a distance in millimetres.
- Margins: information on nearest peripheral and deep margins in relation to designated specimen orientation.
- Perineural/lymphovascular invasion: intratumoral, extratumoural, multifocal and distance to nearest margin. Diameter of involved fibre and whether less than 0.1 mm.
- Incisional biopsies: whether subcutaneous fat is present.
- Distance of tumour to nearest margin in lymphadenectomy specimens.
- Blood vessel invasion in lymphadenectomy specimens.
- TNM stage group: minimum on the information available.
- The Royal College of Pathologists recognises that many clinicians and MDTs look for guidance from their histopathologists with regard the probability/likelihood of completeness of tumour clearance. As already discussed, this is a subjective and somewhat visionary area and accordingly cannot be included as a core item. An individually or locally agreed statement of probability of clearance is, however, not unreasonable and accordingly is included as a non-core item, with possible suggested terminology. If used, it must be firmly understood by the clinician and/or MDT that this

is a subjective and not objective assessment, with variation in the degree of potential accuracy.

Suggested terminology could include:

- clearance appears complete
 - clearance appears close but probably complete
 - clearance appears close but possibly complete
 - clearance appears uncertain.
- High-risk status score: a summation of the number of high-risk factors present.

7 Diagnostic coding and staging

TNM and SNOMED are required for the COSD.⁵

7.1 pTNM status

pTNM status must be recorded according to the 7th edition AJCC.²

TNM stage grouping should be deferred until all current TNM information is available and if appropriate after skin cancer MDT discussion.

A stage group can be added to a histopathology report as a non-core item, but the report should indicate that this is the minimum stage group based on the information in the report.

The general principles are:

pT Primary tumour

pTx Primary tumour cannot be assessed

pTis Carcinoma – *in situ*

pT1, pT2, pT3, pT4 – increasing pT stages

Additional descriptors can be used:

- the suffix 'm' indicates the presence of multiple primary tumours at a single site and is recorded in parentheses: pT(m) N M
- the 'r' prefix indicates a recurrent tumour when staging is carried out after a documented disease-free interval. Full details are available in Appendix A.

7.2 SNOMED codes

SNOMED Topography (T) code should be recorded for the site.

SNOMED Morphology (M) code should be recorded for the diagnosis/tumour morphology.

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

A list of applicable T and M codes is provided in Appendix B.

8 Reporting of small biopsy specimens

When a procedure is carried out with the clear intention of establishing a diagnosis (e.g. some punch biopsies, incisional biopsies and some shave or curettings), data items should be restricted to diagnosis and indicators of high-risk status.

9 Reporting of frozen sections

Frozen sections should be limited to Mohs' micrographic surgery where horizontal sections are used to accurately assess margin status. Vertical frozen sections should not be used to assess margins as they are insufficiently representative of the entire margin.

The use of frozen sections for a specific clinical diagnostic problem usually cannot be supported as this circumvents the desirable standard of prospective skin cancer MDT discussion and potential patient involvement in the decision making process.

Frozen sections have no role in lymph node assessment.

10 Cytological diagnosis

Cytology has little role in the primary diagnosis of cutaneous squamous cell carcinoma.

Fine needle aspiration cytology and biopsy is an appropriate modality to investigate clinically and/or radiologically abnormal regional lymph nodes for potential metastatic squamous cell carcinoma. Lymph node involvement is discussed in section 9 above and in the RCPATH dataset for the histopathological reporting of nodal excisions associated with head and neck carcinomas (www.rcpath.org/publications-media).

11 Specific aspects of individual tumours not covered elsewhere

11.1 MDT referral

Invasive squamous cell carcinoma cases that must be referred for local skin cancer MDT discussion:^{9,11}

- those involving the excision margin/s
- patients suitable for Mohs' surgery
- cases for nodal dissection or sentinel lymph node biopsy (SNLB – see below)
- immunocompromised patients.

Case to be referred to the specialist/central skin cancer MDT:⁹

- high-risk SCCs that pose management difficulty
- metastatic SCC
- immunocompromised patients
- cases for nodal dissection or SLNB
- patients suitable for Mohs' surgery.

Although defined as a pathological high-risk factor in this dataset, and accordingly requiring careful consideration in each individual case, the MDT referral/review status of lesions with

histological margins of less than 1 mm remains a clinical decision (by a clinician and/or pathologist) or as agreed in any locally agreed protocol.

See Appendix E for a summary of high-risk factors for clinical and MDT management.

11.2 Re-excision specimens

There has been considerable debate as to the extent of the examination that is required of wider local excision specimens for skin cancer. Macroscopic examination is essential. This is the most reliable means to record that the re-excision has been undertaken and also the dimensions of the wider excision specimen. The fixed specimen should also be sliced every 2–4 mm to detect any macroscopic abnormalities such as potential satellite metastases. Each slice with a macroscopic abnormality must be examined histologically, to ensure that margin status can be assessed.

The debate centres on the cost-efficiency of examining an entire specimen which is macroscopically normal when abnormalities were not present at the margins of the index specimen. Some peers consider that this is the only guaranteed way to ensure that residual disease or metastases are not overlooked. Some also consider that the specimen should always be examined in its entirety with a biomedical scientist led cut-up. There does, however, appear to be considerable latitude for discretion in this area. An acceptable compromise would be to sample the specimen in its shortest transverse axis, incorporating the area where the scar appears closest to the margin. This can generally be achieved in 1–4 cassettes of tissue. Clinicians require information about whether the specimen contains a scar and whether the scar is completely excised.

If abnormalities were reported to extend to the resection margins in the index specimen, the specimen should be examined more extensively. For specimens up to 10 mm, the entire specimen should be sampled. Specimens over 10 mm should be sampled pragmatically according to the nature of the original margin involvement.

11.3 Reporting pathologist

NICE and NCPR recommend that, whenever possible, lymph node cytopathology and histopathology resulting from the investigation and treatment of primary skin cancer should be undertaken by the same team of pathologists involved in the reporting of the cutaneous specimens. This is to improve the sensitivity and specificity of investigative pathological methodology and to facilitate skin cancer MDT discussion and audit.^{8,10}

This NICE recommendation relates primarily to inguinal and axillary sentinel lymph node biopsy and lymph node dissections for skin cancer. Head and neck sentinel lymph node biopsy for skin cancer also lies within the competence of specialist dermatopathologists. These topics all lie within the area covered by the National Specialist Dermatopathology EQA. Lymph node dissection of the head and neck and associated reporting, however, must only be undertaken by those having appropriate skills and competence in the area. This is primarily demonstrated by regular practice in the field and participating in an appropriate EQA scheme. In general, this therefore limits head and neck lymph node dissection and reporting to individuals regularly involved in this area of head and neck pathology. Head and neck lymph node dissection must be undertaken and reported according to The Royal College of Pathologists' neck dissection cancer dataset (www.rcpath.org/publications-media/publications/datasets/datasets-TP.htm).

12 Criteria for audit of the dataset

12.1 Recommended by NICE⁹

- Skin cancer excision margins between specialties and clinicians.
- Skin cancer specimens in primary care.
- Histopathology reporting times (see below).
- Audit of all BCCs and SCCs not discussed at the MDT.

12.2 Recommended by the RCPATH as key performance indicators (KPIs)

(see *Key Performance Indicators – Proposals for implementation* (July 2013) on www.rcpath.org/clinical-effectiveness/kpi/KPI):

- Cancer resections must be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPATH cancer datasets. English Trusts are required to implement the structured recording of core pathology data in the COSD by January 2014.

Standard: 95% of reports must contain structured data

- Histopathology cases that are reported, confirmed and authorised within seven and ten calendar days of the procedure.

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

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Appendix A AJCC7 pathological staging of cutaneous squamous cell carcinoma and regional lymph nodes

A1 Cutaneous squamous cell, basal cell carcinoma and adnexal carcinoma but excluding Merkel cell carcinoma and carcinomas of eyelid, vulva and penis

Definitions of TNM

Primary tumour (T)*

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- Tis Carcinoma *in situ*
- T1 Tumour 20 mm or less in greatest dimension and (*with the exception of BCC**) with less than two high-risk features*
- T2 Tumour greater than 20 mm in greatest dimension *or* (*with the exception of BCC**) any size and with two or more high-risk features*
- T3 Tumour with invasion of maxilla, mandible, orbit or temporal bone
- T4 Tumour with invasion of skeleton (axial or appendicular) or perineural invasion of skull base

High-risk features for the primary tumour (T) staging (*except BCC**)

- Depth/invasion >2 mm thickness
Clark level ≥ 4
Perineural invasion
- Anatomic location Primary site ear
Primary site hair-bearing lip
- Differentiation Poorly differentiated or undifferentiated

* Stated in AJCC 7 to rarely apply to BCC and not accordingly not included in staging by The Royal College of Pathologists and NCIN.

Regional lymph nodes (N)

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastases
- N1 Metastasis in a single ipsilateral lymph node, 30 mm or less in greatest dimension
- N2 Metastasis in a single ipsilateral lymph node, more than 30 mm but not more than 60 mm in greatest dimension; or in multiple ipsilateral lymph nodes, none, more than 60 mm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 60 mm in greatest dimension

- N2a Metastasis in a single ipsilateral lymph node, more than 30 mm but not more than 60 mm in greatest dimension
- N2b Metastasis in multiple ipsilateral lymph nodes, none more than 60 mm in greatest dimension
- N2c Metastasis in bilateral or contralateral lymph nodes, none more than 60 mm in greatest dimension
- N3 Metastasis in a lymph node, more than 60 mm in greatest dimension

Distant metastasis (M)

M0 No distant metastases

M1 Distant metastases

A2 Anatomic stage/prognostic groups

Stage	T	N	M
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IV	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T Any	N3	M0
	T4	N Any	M0
	T Any	N Any	M1

Appendix B Cutaneous squamous cell carcinoma SNOMED coding

Topographical codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Skin	T01000	Skin structure (body structure)	39937001
Lymph node	TC4000 (SNOMED 3) T08000 (SNOMED 2)	Structure of lymph node (body structure)	59441001

Morphological codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Invasive squamous cell carcinoma, NOS	M80703	Squamous cell carcinoma, no ICD-O subtype (morphologic abnormality)	28899001
Keratinising squamous cell carcinoma	M80713	Squamous cell carcinoma, keratinizing (morphologic abnormality)	18048008
Non-keratinising squamous cell carcinoma	M80723	Squamous cell carcinoma, large cell, nonkeratinizing (morphologic abnormality)	45490001
Spindle squamous cell carcinoma	M80743	Squamous cell carcinoma, spindle cell (morphologic abnormality)	10288008
Pseudoglandular, acantholytic, adenoid squamous cell carcinoma	M80753	Adenoid squamous cell carcinoma (morphologic abnormality)	85956000
Verrucous squamous cell carcinoma	M80513	Verrucous carcinoma (morphologic abnormality)	89906000
Metastatic squamous cell carcinoma	M80706	Squamous cell carcinoma, metastatic (morphologic abnormality)	64204000
Keratoacanthoma	M72860	Keratoacanthoma – category (morphologic abnormality)	416378000
Keratoacanthoma-like SCC	M80713	Squamous cell carcinoma, keratinizing (morphologic abnormality)	18048008

Procedure

Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

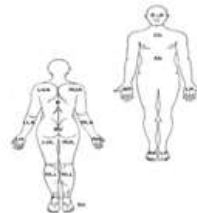
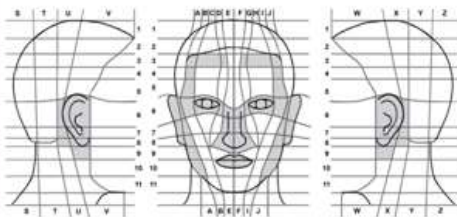
Appendix C Draft UK National Histopathology Request Form for skin biopsies

Devised by the NCIN Skin Site-Specific Reference Group and kindly provided for RCPATH dataset information by the NCIN. Permission for use should be sought from the NCIN. This histopathology request form is approved by the BAD; the mode of national implementation is under consultation.

The UK National Histopathology Request form for skin biopsies

Date of surgical procedure	Please attach patient details
Name of surgeon	
Clinical diagnosis: free text	Grade of surgeon: Nurse, Specialist trainee, Consultant, Hospital Practitioner, Other

Mandatory for Clinician to complete:	First biopsy	Second	Third	Fourth
Site Code as per image (insert LUL etc)				
Clinical Diagnosis (select either BCC, SCC, Melanoma, Atypical Mole, other tumour or other). For inflammatory lesions add clinical details as free text.				
Clinical size of lesion sampled (max diameter) (mm)				
Intention of the surgeon (select biopsy, excision or curative curettage)				
Procedure (select curettage, shave biopsy, punch, incisional biopsy or excision)				
For tumours give measured surgical clinical margin (mm)				
Is this a recurrent tumour?	Y/N	Y/N	Y/N	Y/N
Is the patient immunocompromised?	Y/N			
Is this a tumour arising in areas of radiation or thermal injury, chronic draining sinuses, chronic ulcers, chronic inflammation or Bowen's Disease	Y/N	Y/N	Y/N	Y/N
Is this a tumour arising in a genetically predisposed individual?	Y/N			



Please mark site of samples taken on the above images
For head and neck skin cancers the site code will be made up of the number in the horizontal grid and the letter from the vertical grid (e.g. for a tumour in the middle of the nose that might be code 8E). Where a lesion lies across grid lines then that grid reference in which the greater part of the tumour lies should be used OR if the lesion impacts on a grey shaded area or on the lips then that code should be used. Where the tumour is on the marked lips then the code LIP should be used. For tumours outside the head and neck the letters are indicated on the body map. e.g. a tumour on the left lower arm is LLA).

Free text

Appendix D1 Histopathology reporting proforma for cutaneous invasive squamous cell 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

Clinical site

Specimen type: Excisional biopsy Incisional (diagnostic) biopsy Punch biopsy Shave
 Curettings (Therapeutic) Curettings (Diagnostic) Curettings (Not specified)
 Other Please specify

Macroscopic description

Size of specimen: Lengthmm Breadth....mm Depthmm
 Maximum diameter of lesion:mm Uncertain No lesion seen

Histological data

Subtype: No special type (classic) No special type (classic) with adjacent Bowsens Verrucous
 Acantholytic (pseudoglandular/adenoid/pseudovascular) Desmoplastic
 Spindle/sarcomatoid/metaplastic Keratoacanthomatous-like Follicular
 Adenosquamous (SCC with divergent differentiation) Other (specify).....

Grade: Well-differentiated Moderately differentiated Poorly differentiated
 Uncertain Cannot be assessed

Lesion Thickness: ≤ 2 mm >2 mm Uncertain Cannot be assessed

(If greater than 2 mm: >2–4 mm >4 mm Uncertain Cannot be assessed

Level of invasion ≥ reticular dermis (Clark level 4): No Yes Uncertain Cannot be assessed

If yes, specify tissue/level: Fat (Clark level 5) Muscle Fascia Perichondrium
 Cartilage Paratendon/tendon Periosteum Bone

If bone invasion present:

Invasion of maxilla, mandible, orbit or temporal bone: No Yes (pT3) Uncertain Cannot be assessed

Invasion of skeleton (axial or appendicular): No Yes (pT4) Uncertain Cannot be assessed

Lymphovascular invasion Not identified Present Uncertain Cannot be assessed

Perineural invasion Not identified Present Uncertain Cannot be assessed

If perineural invasion present:

Perineural invasion of skull base: No Yes (pT4) Uncertain Cannot be assessed

Margins

	Involved	Not involved			Uncertain	Not applicable
		<1 mm	1–5 mm	>5mm		
Peripheral	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Deep	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Maximum diameter >20 mm (macroscopic and/or microscopic) No Yes
 Uncertain Cannot be assessed

TNM pathological (p) stage
 (AJCC7).....

Pathological risk status for clinical management
 SCC and stage Low High
 Margins Low High

SNOMED code.....

COMMENTS

Pathologist.....

Date.....

Appendix D2 Histopathology reporting proforma for regional lymph nodes associated with cutaneous invasive squamous cell 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

Anatomical site: Axillary Inguinal Other (specify):.....
 Laterality: Right Left

Histological data

LYMPHADENECTOMY

Number of nodes identified.....

Nodes involved No Yes
 Highest/apical node involved No Yes Not identified clinically

If nodes are involved

IPSILATERAL

Number involved.....

Maximum size of metastasis ≤30 mm >30 mm – ≤60 mm >60 mm
 Extracapsular invasion No Yes Uncertain Cannot be assessed
 Margin not involved No Yes Uncertain Cannot be assessed

CONTRALATERAL

Number involved.....

Maximum size of metastasis ≤30 mm >30 mm – ≤60 mm >60 mm
 Extracapsular invasion No Yes Uncertain Cannot be assessed
 Margin not involved No Yes Uncertain Cannot be assessed

TNM pathological (p) stage (AJCC7) N...

SNOMED code.....

COMMENTS

Pathologist..... Date.....

Appendix E Comparison table of high-risk factors for clinical and NICE/NCPR MDT management and AJCC7 TNM pT1 upstaging

	Clinical and MDT management	AJCC/TNM
	Pathology high risk	High-risk to upstage ≤ 20 mm maximum diameter from pT1 to pT2^a
Minimum number required	One	Two
Clinical criteria	Not included in pathology risk assessment For use by clinician and/or MDT Low-risk pathology may be upstaged by a high-risk clinical factor ^b	Ear or hair-bearing lip
SCC and stage		
Grade	Poorly differentiated	Poorly differentiated
Thickness	> 4 mm	> 2 mm
Level of invasion	\geq Subcutaneous fat	\geq Reticular dermis
Perineural invasion	Present	Present
Lymphovascular invasion	Present	Not applicable
High-grade subtype^c	Present	Not applicable
TNM	pT 2, ^a 3, 4	Not applicable
Margin status		
0 mm (involved)	Present	Not applicable
Less than 1 mm	See note ^d	Not applicable

Notes

- a. The presence of any of the two listed high-risk factors (eg >2 mm thickness with a level \geq reticular dermis) upstages from pT1 to pT2 and results in a high-risk lesion for clinical management /MDT purposes.
- b. Clinical information from a clinician or notes, and/or available at a MDT, can upstage pathology low-risk status to high-risk for NICE/NCPR MDT purposes.
- c. Acantholytic, desmoplastic, spindle/sarcomatoid/metaplastic, adenosquamous or SCC with Bowsens.
- d. Pathological margins less than 1 mm are not defined as high risk by NICE/NCPR for mandatory MDT referral/review. They are, however, regarded as pathologically high risk in this cancer dataset for broader clinical management. The requirement for MDT referral/ review must be considered and decided individually on each case by a clinician and/or pathologist or according to a locally agreed protocol. MDT referral/review should be particularly considered when there is any reasonable uncertainty with regard to the adequacy of margin clearance.

Appendix F Summary table – explanation of levels of evidence

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

Level of evidence	Nature of evidence
Level 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>
Level 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>
Level 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>
Level 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 G AGREE compliance 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.	Foreword,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.	Foreword,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 and local use
RIGOUR OF DEVELOPMENT	
8. Systematic methods were used to search for evidence.	Foreword,1
9. The criteria for selecting the evidence are clearly described.	Foreword,1
10. The methods used for formulating the recommendations are clearly described.	Foreword,1
11. The health benefits, side effects and risks have been considered in formulating the recommendations.	Foreword,1
12. There is an explicit link between the recommendations and the supporting evidence.	5
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.	3,4,5
16. The different options for management of the condition are clearly presented.	4,5
17. Key recommendations are easily identifiable.	3,4,5
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,1
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.	12
EDITORIAL INDEPENDENCE	
22. The guideline is editorially independent from the funding body.	Foreword
23. Conflicts of interest of guideline development members have been recorded.	Foreword

*The Lay Advisory Committee (LAC) of The Royal College of Pathologists has advised 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.