The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for thyroid cancer histopathology reports

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Produced by	Professor Timothy J Stephenson and Dr Sarah J Johnson. Both authors are consultant histopathologists with a special interest in thyroid pathology, and between them have experience in guideline development, postgraduate teaching, provision of expert opinions, case review for national clinical trials, professional leadership through holding office in relevant professional societies, and the external representation of thyroid pathology with the appropriate physician and surgeon organisations and with national sponsors of research and cancer data collection.
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Comments	In accordance with the College's pre-publications policy, this document was on The Royal College of Pathologists' website for consultation from 13 November to 11 December 2013. Forty-two 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. This dataset supersedes the 2010 publication of the same name. **Dr Suzy Lishman** **Vice-President for Advocacy and Communications**

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Foreword

The cancer datasets published by The Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. 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 deviation from them should not necessarily be deemed negligent.

Each dataset specifies either all the **core data items** that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England, or, where the COSD has not yet covered the cancer site, specifies those items which are recommended for inclusion. 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]). The RCPath recommend as a key performance indicator[1] that at least 95% of reports on cancer resections should conform to the cancer dataset. 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 stakeholder organisations have been consulted during the preparation of the dataset:

- British Thyroid Association (www.british-thyroid-association.org), to standardise data items between this document and BTA/Royal College of Physicians' *Thyroid Cancer Guidelines (3rd edition)*
- British Association of Endocrine and Thyroid Surgeons (www.baets.org.uk)
- British Association of Head and Neck Oncologists (www.bahno.org.uk)
- UK Endocrine Pathology Society (www.ukeps.com)
- UK Association of Cancer Registries (UKACR)
- National Cancer Intelligence Network (NCIN) Thyroid Clinical Reference Group.

Supporting evidence and recommendations in this dataset are based on:

- PubMed literature searches (up to July 2013)
- WHO classification, 2004[2]
- NICE *Improving Outcomes Guidance*, 2002[3]
- TNM 7th edition staging classification, 2009.[4]

The supporting evidence is level B to 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 and there are no new major financial or work implications arising from the implementation, compared with the 2010 dataset. However, there are national initiatives to implement structured pathology reporting with the data items within cancer datasets becoming searchable fields within a relational data base,[1] covering most cancers and not just thyroid cancer, which will have resource implications.

A formal revision cycle for all cancer datasets takes place on a three-yearly basis. However, each year, the College will ask 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. 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.

The dataset was reviewed by the Working Group on Cancer Services and was placed on the College website for consultation with the membership from 13 November to 11 December 2013. All comments received from the Working Group and the membership were addressed by the authors to the satisfaction of the Chair of the Working Group 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 Director of Clinical Effectiveness and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

1.1 Endocrine cancer datasets

The management of endocrine tumours is the responsibility of an appropriately experienced MDT. Since these tumours bridge various anatomical divides, they are dealt with by a number of specialist teams. Because several mimics of thyroid carcinomas exist,[5,6,7] the pathologist reporting them should ideally have a special interest in endocrine pathology. Alternatively, he/she should have an interest in endocrine tumours in his/her area of systemic pathology or, if a general pathologist, should participate in a network with the opportunity for specialist pathology review since observer variation is well documented in thyroid tumours[8,9] and the range of prognostic features[10] can require experience in their recognition. The reporting pathologist should either be a core member of the Thyroid Cancer MDT or have access to a pathologist who is a core member, for review purposes.

Each endocrine organ has a separate dataset for its tumours. Although the RCPath's cancer datasets are primarily aimed at collecting core data for the reporting of cancers, the authors propose that the endocrine guidelines should also provide advice on the reporting of benign endocrine tumours and hyperplastic conditions. This has therefore been included with non-core data in section 6.4.

1.2 Thyroid cancer dataset

The proper handling and reporting of the thyroid tumour specimen is important as gross and histological features contribute to the staging of the tumour, and this has implications for prognosis and therapy. There are several systems for staging thyroid tumours. The Royal College of Physicians (RCP) and the British Thyroid Association's guidelines, including their latest (3rd) edition,[10] recommend the use of the 7th edition of the TNM system of staging,[4] using its pathological component with the option of mapping to clinical staging. This mapping is presented in Appendix A for ease of reference.

These proposals for the reporting of thyroid cancers should be implemented for the following reasons:

- pathological staging is important in deciding the correct clinical management of these tumours
- outcome has been shown to be related to particular features (e.g. variants of papillary carcinoma; minimal or wide invasion in follicular carcinoma, presence of capsular or vascular invasion in encapsulated follicular variant papillary carcinoma, presence of vascular invasion in minimally invasive and widely invasive follicular carcinoma[11–13] and the proper definition of poorly differentiated thyroid cancer).[14] These features should therefore be included in histopathology reports to:
    a) provide prognostic information to the surgeon/physician treating the patient
    b) provide accurate data for cancer registration and national datasets.

The following text outlines the approach to be taken in handling specimens. Aspects of best practice in handling thyroid specimens have been reviewed[15] and there are descriptions of the clinically oriented pathology of the thyroid.[16] A synoptic reporting proforma (Appendix C) has been provided as an *aide memoire* for the core data on these neoplasms and as a template for the introduction of structured pathology data. The proforma makes no provision for descriptive commentary on how the data items were arrived at and may be supplemented by a more detailed, free-text report at the pathologist's discretion.

In light of evidence that has emerged since the publication of the previous version of this dataset, the principal changes have been:

- making recommendations on intensity of sampling of different types of thyroidectomy specimen in the clinical circumstances under which these occur, even where these recommendations lie at the Good Practice Point level of evidence only
- rewriting of the sections on papillary carcinoma to adopt a more risk-stratified approach for microcarcinomas and follicular variant papillary thyroid carcinoma (FVPTC)
- rewriting the sections on follicular carcinoma to emphasise the importance of vascular (angio)invasion as an indicator of clinical malignant potential, while de-emphasising the importance of actual number of instances of vascular invasion seen once any has been identified
- adding emphasis and clarity to the identification of extrathyroidal extension of thyroid carcinoma and the recognition of its extent
- alignment of style and terminology with other RCPath cancer datasets
- alignment of terminology with prevailing international trends, e.g. recommendations on terminology for encapsulated follicular patterned lesions are now included
- updating information on the immunohistochemical tests needed for current standard NHS practice
- closer alignment of the dataset with the 3rd edition of BTA/RCP Guidelines.

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 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 and epidemiologists, and facilitates international benchmarking and research.

2 Clinical information required on the specimen request form

This should include full patient details, clinical findings, results of previous cytology[17] and biopsies, and results of imaging investigations. The patient's thyroid hormonal status should be given where relevant, together with details of any hormonal or drug therapy and any familial cancer or endocrine tumour syndromes. The specimen type should be clearly stated. If the operation has resulted in multiple specimens or parts thereof, these should be catalogued explicitly. Any specimens that may be difficult to orientate should have orientation markers attached and these should be described on the specimen request form, with diagrams where words alone will not suffice. Intra-operative findings such as macroscopic extrathyroidal extension of tumour should be stated.

3 Preparation of specimens before dissection

3.1 Gross examination

These specimens are usually sent in formalin, which should be of adequate volume to ensure proper fixation. If received fresh, formalin must be added. Specimens should normally be fixed intact, without slicing, to avoid creating confusion over any tumour capsular penetration or resection margins. For large specimens, after 24 hours of initial fixation, some slicing to aid internal fixation may be undertaken, provided that care is taken to avoid creating false resection margins and tearing intact capsule.

The specimen will usually be described as total (or near-total) thyroidectomy; right or left hemithyroidectomy (+/- isthmus) or isthmusectomy. The nature of the specimen and laterality (in lobectomy specimens) should be noted.

If possible, the specimen should be orientated. The specimen should be measured and described grossly, particularly if there are any unusual features. In total thyroidectomy specimens, measurements of each lobe and isthmus (plus pyramidal lobe if present) should be noted where possible. It should be noted whether the thyroid capsule appears intact on receipt (excluding the intrathyroidal margin on lobectomy specimens). A search should be made for attached parathyroid glands and lymph nodes. The surface of the specimen should be inked/painted.[18]

4 Specimen handling and block selection

4.1 Specimen handling

The specimen should be parallel-sliced (usually transversely) at intervals no thicker than a tissue block, and the cut surfaces of all the slices should be inspected.

The appearance and location(s) of the lesion(s) should be noted. The inclusion of a diagram or photograph in the records with annotation of block selection is best practice. It is important to record the greatest dimension of the lesion (or of the largest lesion, if multiple) as this defines the pT status. If the dimension is ≤20 mm, the macroscopic size should be confirmed or adjusted by the microscopic measurement of size. The presence of macroscopically apparent direct extension beyond the thyroid, which is prognostic *[Level of evidence B],*[19] should be recorded, including which anatomical structures are invaded, to inform the pT3/4 staging. Clearances from the thyroid capsule and relevant resection margins should be measured and noted. The site of any possible parathyroid glands should be noted and they should be processed.

The number and site of lymph nodes submitted or identified in the main specimen should be recorded, and all of the nodes should be completely embedded. Sampling of formal neck

dissections should follow protocols published with the RCPath's 2013 guidelines for tumours of the head and neck (www.rcpath.org/publications-media/publications/datasets/nodal-excisions-neck-dissection-head-neck-carcinomas.htm), which cover the sampling of central/level VI lymph nodes that are often submitted with known papillary carcinoma specimens.

4.2 Block selection

The number of blocks taken will vary according to the tumour type. Tumour type may be known or suspected from any preoperative cytology, enabling appropriate block taking when the specimen is initially dissected. Small biopsies should be embedded in their entirety.

4.2.1 All malignant thyroid tumours

It is possible that the specimen may require extra blocks to be taken after the initial histological diagnosis has been made. This is facilitated by wrapping the remaining slices from each thyroid lobe separately.

The use of megablocks may be considered to show resection margin relationships to large lesions and they may show the entire circumference of tumour capsule of such lesions in one section.

Blocks of the tumour edge and of the thyroid margin closest to the tumour should be taken to assess completeness of excision. Any surgical excision margin within the thyroid (e.g. isthmic margin in a lobectomy specimen) should be processed. Any apparent extrathyroidal extension should be sampled. Apparently normal tissue from the ipsilateral lobe and the contralateral lobe (where present) should be examined carefully for evidence of tumour. Any suspicious areas, such as nodules or pale scarred-looking areas, should be sampled, to detect possible multifocality.

Completion thyroidectomy specimens should be sliced as in section 4.1, with blocks taken from any thyroid lesions, parathyroid glands and lymph nodes. From the background thyroid we suggest one block per 10–20 mm of tissue subject to a minimum of two blocks; these are pragmatic recommendations: no direct evidence for the sampling rates exists.

4.2.2 Papillary carcinoma (PTC)

For papillary carcinoma, there are few published studies regarding sampling. Some recommend that the whole gland is processed.[20] However, a more practical approach is to block the whole tumour if the lesion is ≤30 mm in diameter; if larger, it should be sampled widely enough (as a compromise we suggest at least two blocks per cm diameter of tumour) to permit diagnosis and to assess whether the tumour is of uniform type. Even when no other lesions are identified by naked-eye examination, one block per 10–20 mm of normal-looking tissue should be taken from each lobe. This is to assess whether the lesion is single or multifocal, as multifocal lesions have a poorer outcome *[Level of evidence B]*,[20–23] and to look for other background conditions. The presence of multifocal disease is reflected in the staging and may affect clinical decision-making especially for microcarcinomas (see section 5.3.3); therefore, if one papillary microcarcinoma (≤10 mm; equivalent to stage pT1a)[11] is found, the rest of the specimen should be examined carefully for multifocality.

An encapsulated FVPTC should be sampled as for a follicular neoplasm (section 4.2.3)

[The sampling levels are the authors' compromise recommendations in the absence of specific experimental proof of an ideal sampling rate – Level of evidence: Good practice point.]

4.2.3 Follicular neoplasms

Follicular lesions that are not grossly invasive should be extensively sampled at the interface between the tumour, its capsule and normal gland,[18] to detect capsular and/or vascular

invasion. Some suggest that the total interface is examined histologically in all cases.[24] A more practical approach is to process lesions ≤30 mm in diameter in their entirety and to take at least 10 blocks from larger lesions,[24,25] although more blocks may well be helpful. Where there are multiple nodules, the largest should be processed as described. Any others showing obvious encapsulation should also be sampled, as should those with unusual features, such as solid areas or a pale colour. Follicular lesions that are grossly invasive should be sampled widely enough to allow identification of any poorly differentiated carcinoma,[13] documentation of vascular invasion,[11,12] measurement of distance to resection margins, and recognition of spread beyond the thyroid capsule with documentation of the tissues found to be invaded.

4.2.4 Medullary carcinoma

In cases of medullary thyroid carcinoma, the specimen should be blocked adequately to confirm the diagnosis, recognise the relationship to the thyroid capsule and detect any extrathyroidal extension with definition of which tissues are invaded.[24,25] The non-involved gland may be examined for evidence of C cell hyperplasia (section 5.6) in an attempt to identify familial cases. C cells are usually found in the central parts of the middle and upper thirds of the lobes so these areas should be sampled.

Prophylactic thyroidectomies are submitted for MEN2 or familial medullary thyroid carcinoma patients. These should be sampled in total including any isthmus since the thyroids are relatively small and any tumours may also be small. Calcitonin immunohistochemistry is necessary for identification of lesions suspected of being medullary carcinoma and to confirm the presence of C cell hyperplasia.

5 Core data items

5.1 Macroscopic data items

Specimen type should be documented.

The location (right, left or isthmus), number, size and relationship to resection margins of any tumours should be recorded. Naked-eye evidence of invasive growth needs to be noted and also thyroid capsule breach, and extension into perithyroidal tissues should be recorded (all of the features to be confirmed by microscopy).

[All of these features are important for prognostication – Level of evidence B.]

5.2 Microscopic data items

There are a number of features that should be documented in all tumours, and specific features relating to the individual tumour types. Differentiated tumours may contain a minority component of more poorly differentiated tumour. Reports should specifically state whether or not any foci of poorly differentiated carcinoma have been found, as they may confer a worse prognosis *[Level of evidence B].*[13,26,27] Such poorly differentiated components may be recognised by tumour necrosis and elevated mitotic count,[14] as well as by growth pattern. Only when *poorly differentiated* carcinoma constitutes the *majority (>50%)* of the tumour should the overall classification change. However, where there is *any* focus of *anaplastic change*, the tumour should be classified overall as undifferentiated/anaplastic[28] (further, all anaplastic carcinomas are defined as stage pT4). *[Level of evidence B.]*[4]

5.2.1 Microscopic data items common to all malignant thyroid tumours

- Type of malignancy.
- Single lesion or multifocal.

- Maximum dimension of carcinoma (largest if multifocal). The dimension is that of the microscopically proven carcinoma, based upon a reconciliation of the macroscopic and microscopic findings. That is to say, not all 'tumour' or 'tumours' noted macroscopically prove to be carcinomas and, conversely, carcinoma extent or numbers found microscopically can be greater than those suspected macroscopically.
- Presence of vascular invasion (any definite endothelial-lined space).
- Extension into extrathyroidal tissues, which should be identified, and whether the extension is macroscopic or microscopic.
- Closest distance to surgical resection margin, which informs the R stage of the tumour.
- Site and number of lymph nodes retrieved, and number of those involved.
- Pathological confirmation of distant metastases.
- SNOMED codes, in a version approved by the local cancer registry.

[All of these features are important for prognostication – Level of evidence B.] [29,30,31]

5.2.2 Notes on lymph node metastases

The total number of lymph nodes sampled and the number involved are required because the yield and the ratio of those involved to not involved has been shown to be prognostic in papillary thyroid carcinoma.[32,33,34]

The site of lymph nodes is required because the exact site involved affects staging and can have prognostic implications.[33]

[All of these features are important for prognostication – Level of evidence B.]

There is some evidence that extranodal extension in lymph node metastases and the size of lymph node metastases may be adverse prognostic factors, but there is insufficient evidence to include these yet as core items.[29,34]

5.2.3 Notes on R stage of tumour

Resection (R) stage is defined in TNM as follows, with suggested interpretation for pathologists:

RX Cannot assess presence of residual primary tumour: this may need to be used in a disrupted specimen when excision margins cannot be assessed.

R0 No residual primary tumour: this is used by the pathologist when there is definite non-tumour tissue between the tumour and the surgical specimen margin microscopically. There is no defined number of mm required, but the distance should be stated in the report.

R1 Microscopic residual primary tumour: this is used by the pathologist when there is any microscopic presence of tumour at the painted surgical specimen margin.

R2 Macroscopic residual primary tumour: ideally this needs to be indicated by the surgeon, but the pathologist may be able to interpret this from the macroscopic specimen. Irrespective of who identifies it, it must be subject to microscopic validation due to the possibility that, for example, fibrosis may be mistaken for tumour.

Recognition of even microscopic involvement of surgical margins, including when it is in the context of a likely responsive tumour having radio-iodine ablation, has been shown to be prognostic. *[Hence R stage is important for prognostication – Level of evidence B.]*[35]

5.2.4 Notes on extrathyroidal extension (ETE)

There is no defined anatomical thyroid capsule, but rather a discontinuous pseudocapsule.[31,36] The defining features of ETE are therefore: growth of tumour in extrathyroidal tissue, e.g. adipose tissue, skeletal muscle; growth beyond last normal thyroid follicles; desmoplastic and inflammatory reaction.[37] Macroscopically detected ETE is more adversely prognostic than microscopically detected ETE in PTC.[19] Recognition of ETE can be difficult and subjective, especially in the isthmus.[32, 37, 38]

ETE should be classified as 'microscopic' (one needed the microscope to see it) versus 'macroscopic' (it was noticed intraoperatively or on naked-eye examination and later confirmed by microscopy), as these are prognostic. For example, tumours with macroscopic ETE have a higher recurrence rate (RR) (52%) and lower disease-free survival (DFS) than those with microscopic ETE. For microscopic ETE, the recurrence rate has been reported as 21% and DFS not significantly different from no ETE (13%), but more lymph node metastases occur, and vascular invasion and positive margins are more common.[19,37] 'Minimal' ETE (normally requiring microscopy to see it and defined in TNM as tumour has breached the thyroid capsule and microscopy shows it to be invading the first soft tissue immediately beyond the capsule, e.g. fibro-adipose tissue) is staged as pT3 and needs to be distinguished from what is variously described in the literature as major/massive/marked (can be seen macroscopically), as anything non-minimal adversely affects morbidity and mortality.

Direct invasion of a parathyroid gland is uncommon, but it is suggested this be regarded as minimal ETE.[19, 37]

[ETE is important for prognostication – Level of evidence B.]

5.3 Papillary thyroid carcinoma (PTC)

The key defining feature for papillary carcinoma is recognition of its nuclear changes. Recognition of qualifying nuclei for PTC, especially in follicular-patterned lesions, is known to be highly subjective even among 'experts'.[8] The most reliable and reproducible nuclear feature[8,39] are clearing, grooves, overlapping and crowding, membrane irregularity and enlargement. Architectural changes will also be present; by definition, the formation of true papillae in the classical variant, and even follicular variant papillary thyroid carcinoma (FVPTC) has subtle architectural abnormalities, such as tubular or complex – elongated, branching, slit-like – follicular shapes. In establishing a diagnosis of FVPTC when there are none of the architectural changes of PTC present and one is relying entirely on nuclear features, those nuclear features must be obviously present and in more than just a single microscopic focus.

[All of these features are important for prognostication – Level of evidence B.]

5.3.1 Notes on clinical papillary carcinoma

These tumours present clinically as thyroid masses or with lymph node metastases. A number of variants of papillary carcinoma have been defined, including the follicular variant (FVPTC) (which requires subclassification as to whether it is encapsulated, see section 5.3.2), the encapsulated variant and the solid variant. The non-encapsulated FVPTC, encapsulated classical PTC and solid variant of PTC are all thought to have a similar prognosis to the classical PTC.

Cystic PTC by convention is assigned a diameter which equates to that of the cyst containing it, but insufficient data exists to state whether its prognosis is really that which would be expected from the diameter of the cyst, or just that of the tumour within the cyst.

The prognosis of PTC is better than that of follicular thyroid cancer. However, if the confounding effects of age and extent of tumour at diagnosis are removed, survival rates are

comparable.[31–40] The rationale for requiring histological subtype data as core is that within the papillary thyroid carcinoma group, poorer prognosis is associated with specific histological types.[41–45] There is evidence that the tall cell and columnar variants may show more aggressive behaviour.[45–47] The outcome of the diffuse sclerosing variant is a matter of debate.[48] As with follicular tumours, an oncocytic variant is also recognised but this should only be diagnosed when the characteristic nuclear features of papillary carcinoma are present. Papillary architecture in a follicular oncocytic tumour should not be misinterpreted.[49–52]

The adverse histological subtypes of the rare tall cell and the even rarer columnar cell PTC variants, defined by their cell height to width ratio and their detailed nuclear features, should be specifically mentioned if present in other than occasional small foci.[23] To prevent over-diagnosis of the variant, we suggest a stringent approach to diagnosis of the tall cell variant, whereby a height to width ratio of 3x is required in the majority (> 50%) of the tumour.

The other core data items required because they are prognostically significant are:

- tumour size and number[18,20,24]
- presence of vascular invasion[37,50]
- extrathyroidal invasion[31,35]
- lymph node metastases[29–34]
- distant metastases.[4,13]

[All of these features are important for prognostication – Level of evidence B.]

5.3.2 Notes on follicular variant papillary thyroid carcinoma (FVPTC)

By definition, this tumour shows exclusively or almost exclusively follicular architecture yet with papillary thyroid carcinoma nuclei.[53,54] They may present clinically and often yield indeterminate pre-operative cytology.[55,56]

The threshold for referring lesions thought to be FVPTC to an expert thyroid pathologist should be low. In the hands of such pathologists, and in laboratories regularly performing immunohistochemistry on such tumours, the expression of recognised markers of papillary carcinoma, including its variants, can be useful in the identification of FVPTC. The markers found to be useful include cytokeratin 19, high molecular weight cytokeratins, HBME1 and CD56.[57,58]

Prognostically important subtypes exist[59,60] and the report should state clearly which diagnostic label applies.[61–67]

- **Encapsulated:** the clinical behaviour and molecular genetics are more like those of the follicular adenoma/follicular carcinoma group of tumours. They should be assessed as for follicular neoplasms, on the presence or absence of capsular and vascular invasion:[50,51]
  - encapsulated and non-invasive; the diagnosis depends solely on nuclear features (versus follicular adenoma), although partially developed architecture of papillary carcinoma may be present. There is no/or at least a very low risk of recurrence or metastasis, with emerging evidence that conservative management (lobectomy) is adequate
  - encapsulated with invasion; see sections 5.4.1 and 5.4.2 regarding diagnosing capsular and vascular invasion respectively. Capsular invasion alone does not appear to affect long-term outcome and evidence is emerging that thyroid lobectomy alone may be enough, even in this group of patients.[67] Encapsulated, well-differentiated, follicular-patterned thyroid carcinoma does not play a significant role in the fatality rate from thyroid carcinoma.[67] Vascular (angio)invasion is needed for these tumours to behave as low-grade malignancy, and even then

behaviour is still indolent but distant metastasis can occasionally occur, and without lymph node involvement.[68]

- **Non-encapsulated or infiltrative:** the clinical behaviour and molecular genetics are more like those of classical papillary thyroid carcinoma.
- **Diffuse/aggressive/multinodular variants:** these are rare and occur typically in younger patients. They may be multicentric, and have more frequent vascular invasion, and have a propensity for lymph node and distant metastases.

To bring in a diagnosis of FVPTC, the nuclear features should be diffuse or multifocal (see section 5.3). The nuclear features in FVPTC are best assessed around the edge of the lesion rather than the centre where there are often degenerative changes.

Some thyroid nodules have small, non-contiguous foci individually qualifying as FVPTC within them, posing a dilemma as to whether to regard these as multifocal microcarcinomas or as unifocal and equivalent to the maximum diameter of the whole nodule. The present recommendation, provided that the nuclear features are well developed and clearly distinct from those of the background follicular nodule, based on biological behaviour of the lesions is now to regard these individual foci as microcarcinomas rather than to consider that the whole encapsulated nodule as an eFVPTC.[53,68]

An FVPTC may also show oncocytic change. As with the usual PTC, these are differentiated from oncocytic follicular tumours on the basis of nuclear features.

When a papillary thyroid carcinoma with classical (not follicular) growth pattern is encapsulated, then its behaviour is as for classical PTC – it behaves as non-encapsulated classical papillary thyroid cancer and warrants treatment as such.[68]

[All of these features are important for prognostication – Level of evidence B.]

5.3.3 Notes on papillary microcarcinoma

'Microcarcinoma' is a carcinoma ≤10 mm in diameter, staged as pT1a. They are often found incidentally, in the examination of a hemithyroidectomy/thyroidectomy specimen removed for another disease.[69] Most microcarcinomas are papillary microcarcinomas, but may occasionally be follicular carcinoma or medullary thyroid carcinoma. The remainder of this sections deals with papillary thyroid microcarcinomas (microPTC).

A single classical papillary microcarcinoma discovered incidentally is not thought to have a significant risk of recurrence or metastasis and these should be defined separately.[6,10,38,66] When such a microcarcinoma is identified, any residual thyroid tissue should be examined carefully for multifocal disease. The report must state clearly whether there is unifocal or multifocal carcinoma, as the recommended treatment may differ. Multifocality is found in 26–66.7% of cases and bilaterality in 6.7–66.7%.[10,41,42]

Most microPTCs have an excellent long-term prognosis but there are some exceptions and even occasional deaths. For this reason, this dataset requires the data items said to identify patients who may require more aggressive treatment.

Disease-specific mortality has been reported in the range 0–0.9%, with positive lymph nodes in 12.3–40%, recurrence in 3.8–20% and distant metastases in approximately 0.3%. ETE should be looked for as this technically causes up-staging from pT1a to pT3, although some evidence exists that this may not significantly worsen the prognosis.[70,71]

The clinical markers of potential aggressiveness in papillary microcarcinomas are:

- non-incidental presentation
- positive pre-operative FNA

- lymph node metastases, especially if the presenting feature
- distant metastases
- positive family history
- PET scan positive
- nodules in contralateral lobe
- male gender.

The histological markers of potential aggressiveness in papillary microcarcinomas are:

- multifocal and/or bilateral
- upper half of the size range, i.e. 6 mm or more in diameter
- ETE, especially if macroscopic
- desmoplastic fibrosis and/or infiltrative growth pattern
- poorly differentiated component
- lymphovascular invasion.

[All of these features are important for prognostication – Level of evidence B.][72]

5.3.4 Terminology of encapsulated follicular-patterned lesions

There is recognised intra- and inter-observer variation in the diagnosis of thyroid cancer on histology, especially for encapsulated follicular-patterned tumours.[8] An alternative terminology of 'well-differentiated tumour of uncertain malignant potential (WDT-UMP)' has been proposed for encapsulated follicular-patterned tumours with equivocal nuclear features of papillary thyroid carcinoma, and for follicular tumours in general with dubious capsular invasion (FT-UMP), but this terminology is not widely accepted internationally.[69,73–76] We consider that its adoption would not confer patient benefit and have opted, rather, to continue with traditional definition of FVPTC but within a risk-stratified approach.[10,66]

5.4 Follicular neoplasms

A follicular neoplasm has no nuclear features of PTC and is defined as follicular carcinoma on the basis of showing capsular and/or vascular invasion.

5.4.1 Notes on capsular invasion

Capsular invasion is characterised by complete penetration of the tumour capsule, which may be hook-like, finger-like or mushroom-shaped, often with capsular blunt-ended breaks.[77–79] Helpful published illustrations exist such as Figure 18A 45 in Chan's chapter in *Diagnostic Histopathology of Tumors (3rd edition)*.[28] Care should be taken in assessing this, as the invading tongue of tumour may stimulate the formation of a neocapsule.[5,8] Occasionally, rounded nodules of follicular tissue with similar morphology to the tumour surrounded by capsule may be seen. These should not be deemed to constitute capsular invasion unless they can be shown (e.g. by extra blocks or extra levels) to connect with the main body of the tumour. Entrapment of groups of cells or follicles in the capsule is not defined as invasion. Pseudo-invasive changes may be seen following FNA,[80,81] especially in oncocytic tumours (see section 5.5). These changes are usually accompanied by inflammation, haemosiderin deposition and/or new fibrosis.[80,81]

[Capsular invasion is a key component of diagnosis – Level of evidence B.]

5.4.2 Notes on vascular invasion

Vascular invasion is defined as invasion of definite blood vessels (i.e. angioinvasion) within the tumour capsule or outwith the tumour in adjacent thyroid tissue. Typically these are medium- or large-sized vessels and possess not only endothelium but also an elastic lamina. The tumour cells should project substantially into the vessel lumen, attach to the luminal aspect of the vessel wall and be covered by endothelium. Thrombus may be present in association with the intravascular tumour.[28,82] The following features do not constitute vascular invasion and their presence is not associated with development of metastases: bulging tumour superficially into the vessel but with intact endothelium, tumour cell clusters with intact endothelium, florid reactive endothelial proliferation and post-FNA artefactual displacement. Helpful published illustrations exist such as Figures 18A 38-40 in Chan's chapter in *Diagnostic Histopathology of Tumors (3rd edition)*.[28,82] Lymphovascular space invasion within the tumour itself does not count as vascular invasion for definition of malignancy or prognosis.

[Vascular invasion important for prognostication – Level of evidence B.]

5.4.3 A risk stratification approach for minimally invasive follicular carcinomas based upon whether vascular invasion is present

Minimally invasive tumours are single, encapsulated nodules showing only focal microscopic vascular and/or capsular invasion. Their invasive growth is not discernible on naked-eye examination. It is important to indicate whether there is only capsular invasion or whether the tumour is angioinvasive.

- Tumours showing **only capsular invasion** have a minimal risk of metastasis. Indeed, if no vascular invasion is demonstrable despite thorough sampling as recommended in this cancer dataset, these tumours will behave virtually as though only a follicular adenoma. No further treatment beyond lobectomy may be appropriate for these cases.[67]
- However, tumours with **any vascular invasion (angioinvasion)** may develop metastases. Their treatment will typically include totalisation thyroidectomy and consideration of TSH suppression and possible radio-iodine. There is controversy as to whether this risk increases with the frequency of vascular involvement, with some studies suggesting that the risk is demonstrably worse if four or more foci of vascular invasion are documented.[12,14] Due to the controversy over where any threshold may lie in the number of blood vessels invaded, this revision of the dataset no longer specifies the number of blood vessels seen to be involved as a core data item.

5.4.4 Widely invasive follicular carcinoma

The tumour is defined as widely invasive when it shows obvious gross invasion or extensive microscopic infiltration of thyroid parenchyma, capsular or extratumoral vessels, or extrathyroidal tissues. In most cases, these are not difficult to recognise. However, where the diagnosis is made on the basis of histology, there are no absolute published criteria for defining the threshold. Some would put otherwise minimally invasive tumours with high incidences (e.g. 10 or more) of demonstrable vascular invasion into this category, although we recommend leaving these in the minimally invasive category with communication in free text about the frequency of vascular invasion found as non-core data, unless evidence on a reliable threshold at which it should be recorded becomes published. Widely invasive tumours have a worse prognosis than the minimally invasive lesions[14] and the prognosis worsens still further in proportion to the number of foci of vascular invasion found.[12]

5.4.5 Recording adverse prognostic features in follicular carcinoma

The extent of any spread of tumour beyond the thyroid 'capsule' (extrathyroidal extension, ETE) has prognostic impact, with macroscopically apparent ETE carrying a worse outcome

than ETE that is only visible microscopically.[83] The extent of ETE (minimal/macroscopic) is also recognised in the TNM staging (see section 5.2.4).

Other variants of follicular carcinoma including clear cell and signet ring cell tumours are described, but there is no evidence that their behaviour is significantly different.[20]

[All of these features are important for prognostication – Level of evidence B.]

5.5 Notes on oncocytic tumours

Oncocytic thyroid tumours (the term 'oncocytic' is preferred to 'Hürthle cell')[6,84] may develop as variants of any thyroid tumour, e.g. follicular adenoma, follicular carcinoma, papillary carcinoma, medullary thyroid carcinoma, poorly differentiated carcinoma.[85] Diagnosing malignancy in them should use exactly the same criteria as for the non-oncocytic types, however, once a diagnosis of malignancy is established, prognosis for oncocytic carcinomas is considered to be worse on a stage-stratified basis than for their non-oncocytic equivalents, largely due to oncocytic carcinomas having poor radio-iodine uptake.

This category should be restricted to tumours which, irrespective of histological pattern, comprise at least 75% oncocytic cells.[20,51,52] Focal oncocytic change can be found in ordinary follicular lesions. The distinction from oncocytic follicular variant of papillary carcinoma is made on the nuclear features, as outlined above.

Care should be taken with interpretation of oncocytic tumours because focal necrosis and scars frequently occur. These may be post-FNA or spontaneous. Such scars are frequent, and do not themselves denote malignancy. They may cause distortion, which can be difficult to interpret and may mimic malignancy. Inspissated colloid calcifies and sometimes mimics psammoma bodies but is located within the follicles.

5.6 Medullary carcinoma

In best practice, the diagnosis should be confirmed by calcitonin immunoreactivity. In the written histology report it is usual to describe the cellular pattern, but this has no prognostic significance[86] so is omitted from the dataset. The presence of amyloid, confirmed by appropriate histochemical stains, is thought to confer a better prognosis, but does not influence treatment, so again this is omitted from the dataset. Tumour desmoplasia is thought to be an adverse prognostic indicator,[87] but has been omitted from the dataset until there is further confirmation. In less well-differentiated tumours, where calcitonin immunoreactivity is lost, positivity for carcinoembryonic antigen (CEA) may serve as a surrogate marker.[88] Loss of calcitonin immunoreactivity is now considered not to be of adverse prognostic significance.[86,89]

In the syndromes of multiple endocrine neoplasia (MEN) Type 2 and familial medullary thyroid carcinoma (FMTC), medullary carcinoma is often multifocal and preceded/accompanied by C cell hyperplasia.[90] However, the histological evaluation of C cell hyperplasia can be difficult, as the normal range is not properly defined.[91] In addition, extension of the tumour within the gland may produce nodules in the near vicinity. Finally, the presence of C cell hyperplasia may not necessarily correlate with familial disease as there are data to suggest that mild degrees can be found around other tumours and in a variety of other pathological conditions.[86] We suggest, therefore, that this diagnosis is only made when nodules of C cells, confirmed by calcitonin immunoreactivity, are found in blocks that do not contain the main tumour. Diagnosing C cell hyperplasia histologically is optional and now a non-core data item, as clinical guidelines recommend that all newly diagnosed patients with medullary carcinoma be offered genetic testing for RET mutations to detect familial syndromes.[92]

Prophylactic thyroidectomies may be undertaken in MEN2 or FMTC patients (see section 4.2.4).

5.7 Poorly differentiated carcinoma

This group of tumours represents an intermediate degree of differentiation between differentiated follicular cell-derived tumours and anaplastic carcinoma, with insular carcinoma being one particular type of poorly differentiated carcinoma. A useful diagnostic algorithm has been published.[93] This includes follicular cell-derived tumours with necrosis and/or with mitotic counts of 5 or more per 10 hpf.[14] Their growth patterns may be insular (the cells arranged in well-defined nests resembling pancreatic endocrine tumours),[13,94] trabecular or solid.[93] Before the tumour is placed in this category, the 'majority' (>50%)[10] or 'predominant'[14] component should have this appearance. We have, however, included mention of minority components of poorly differentiated carcinoma in the dataset as there is a report that even the presence of a minor component of poorly differentiated carcinoma significantly worsens the prognosis.[27,95] It is also important to note that if the nuclei have the characteristic features of papillary carcinoma and the tumour has a solid growth pattern, it should not be diagnosed as poorly differentiated carcinoma but instead as the solid variant of papillary cancer, which has the prognosis of classical PTC rather than that of poorly differentiated carcinoma.[93]

It is important to recognise poorly differentiated carcinomas as they have a worse prognosis than differentiated carcinoma, although in the few instances where the poorly differentiated carcinoma only shows minimal (visible by microscopy) invasion or is encapsulated, the prognosis is not worsened to the same degree.[14] Poorly differentiated carcinoma usually expresses thyroglobulin, and may or may not respond to radio-iodine treatment.[96] Where there is concern that a poorly differentiated appearing tumour may be C cell derived (i.e. medullary carcinoma), the immunohistochemistry should include CEA and calcitonin antibodies, as the term 'poorly differentiated carcinoma' is reserved for follicular cell-derived tumours.

The presence of better differentiated components should be mentioned in the report as a core data item as there is evidence that the prognosis may be ameliorated by this.[93,95]

[All of these features are important for prognostication – Level of evidence B.]

5.8 Undifferentiated/anaplastic carcinoma

Where a follicular or papillary carcinoma shows even a minor undifferentiated (anaplastic) component, the diagnosis is that of undifferentiated/anaplastic carcinoma.[11,96]

Most undifferentiated tumours will not have a surgical resection, but will be diagnosed by FNA or occasionally by open biopsy. Where a resection is performed, multiple blocks should be taken and immunostaining for thyroglobulin, TTF1 and calcitonin may be performed to attempt to identify a differentiated component. These stains are almost always negative in the anaplastic areas. Immunocytochemistry for cytokeratins (testing for a wide range is recommended) may confirm the epithelial nature.[18,20,23,24] PAX 8 immunostaining may be useful in distinguishing anaplastic thyroid carcinoma (generally positive) from metastatic lung carcinoma (generally negative).[97] Often, however, the diagnosis is one of exclusion achieved through correlation at MDT meeting with imaging, and the most important differential diagnosis to exclude is lymphoma,[98,99] as this has a radically different prognosis and treatment.

The presence of better differentiated components should be mentioned in the report as core data as there is evidence that the prognosis may be ameliorated by this.[93,95]

[All of these features are important for prognostication – Level of evidence B.]

5.9 Mixed/combination tumours

Other rare tumours include mixed follicular/medullary and mixed papillary/medullary carcinomas.[100] These may show immunohistochemical features of both components. All of the tumour types present in a mixed tumour should be recorded in the report as each may require its own specific treatment, e.g. radio-iodine for a follicular epithelial derived carcinoma component.

6 Non-core data items

6.1 Clinical information

The clinical information supplied should be recorded as it was the basis upon which the specimen was interpreted, although it is not core data on the cancer itself and hence does not appear in the reporting proforma.

6.2 Tumour grade

We do not advocate use of tumour grading systems beyond the grades and types in the core data since only the latter have consistently proven to be of clinical significance, although there is emerging evidence that grade, especially presence of the poorly differentiated grade (however defined), may be important in prognosis.[14,93,94] In particular, the finding of a trabecular or solid growth pattern and/or a mitotic count of 1–4 per 10 hpf is thought to be associated with an adverse prognosis,[11] although we recommend treating these items as non-core data unless consistent evidence on their importance emerges.

6.3 Histological subtypes beyond the core data

These may be included to facilitate teaching and research, and to demonstrate to any reviewing pathologist that they have been recognised, but their clinical significance has been proven to be low, compared with the core data.

6.4 Parathyroids

Where possible, parathyroid glands should be identified macroscopically, and processed to confirm their nature and the presence or absence of any pathology. The presence of any parathyroid tissue or glands should be stated in the report, to provide correlation with any clinical concerns over calcium status.[15,16]

6.5 Adjacent thyroid

It is recommended that pathological evidence of autoimmune thyroid disease (AITD) is mentioned in the pathology report. This may help elucidate the relationship between AITD and the pathogenesis of thyroid tumours and is good practice in correlating with clinical status. Incidental neoplasia may be found, such as incidental papillary microcarcinoma, prompting a search for multifocal disease or rendering an already-diagnosed papillary carcinoma multifocal (see section 5.3.3).

Incidental microscopic conditions in the background thyroid should be recorded:

- to account for macroscopically described lesions that have prompted block taking
- when they may have affected the clinical and/or radiological impression of tumour extent (e.g. benign, background nodules) and
- when they may have clinical implications for the aftercare of the patient (e.g. thyroiditis).

6.6 Molecular techniques and prognostication

Molecular techniques, e.g. BRAF mutation in the prognostication of PTC, are presently yielding a plethora of publications. Their findings are currently inconsistent to the point that we cannot recommend inclusion of molecular data either as core or non-core items, nor single out any individual publication for citation. Future revisions of the dataset will respond to any consistent findings only when/if they attain significance using the modified SIGN evidence levels (Appendix D), as they would have significant NHS commissioning implications.

7 Diagnostic coding and staging

7.1 Diagnostic coding

Coding is recommended and is useful for data retrieval, workload measurement and audit. SNOMED coding should be applied (see Appendix B).

A comparison of SNOMED systems is given in Table 2 in Appendix B.

7.2 Staging: TNM classification

The 7th edition of TNM is recommended (see Appendix A).[4]

8 Thyroid cytology and reporting of small biopsy specimens

It is beyond the scope of this document to discuss the details of fine needle aspiration (FNA) cytology of thyroid, but most lesions should have had FNA before surgery, so a differential diagnosis may be available. The cytopathologist should be a member of the MDT or have access to a pathologist who is. The descriptive cytology report will inform the clinical decisions on management. We recommend additional use of the numerical categories Thy1–5 as proposed in the guidelines of the RCP/British Thyroid Association,[10] recently updated by the RCPath in consultation with the British Association for Cytopathology and other interested parties.[17]

Molecular and immunohistochemical techniques, e.g. the detection or implication of *BRAF* mutation in the detection of PTC, are showing potential. Future revisions of the dataset will respond to any consistent findings only when/if they reach the appropriate evidence level (Appendix D), as they would have significant NHS commissioning implications.

Needle core biopsies for histology, as with FNA, cannot be used to differentiate follicular carcinoma from adenoma. Their use in thyroid pathology is therefore restricted. They are occasionally used to differentiate between inflammatory/fibrotic conditions and diffusely infiltrating tumours, or for the diagnosis of tumours other than those of follicular type. The report on cancers in needle cores has to be restricted to identifying the tumour type. Vascular invasion should be mentioned if seen. Any tumour grade or special type reported would be provisional because, with the exception of anaplastic carcinoma which can be diagnosed on the basis of a single focus, the other tumour grades and subtypes require some assessment of extent which has to be based on examination of the resected specimen.

9 Reporting of frozen sections

Intraoperative frozen section is occasionally used to confirm the diagnosis of papillary carcinoma, medullary or anaplastic carcinoma, or to identify lymph node involvement. It should not be used to differentiate follicular carcinoma from adenoma.[18,101,102]

10 Criteria for audit of the dataset

The following standards are suggested as some of the criteria that might be used in periodic reviews specific to thyroid pathology service:

- size distribution of tumour maximum diameters as a graph – the standard is that the distribution should be smooth and continuous, with no obvious rounding of measurements, e.g. to nearest 0 or 5 figure
- number of lymph nodes found in specific specimen types
- inter- and intra-observer studies in classification of tumours.

Recommended by the RCPath as key performance indicators:[1]

- proportion of cancers that are reported as structured data (e.g. on a locally developed proforma) reflecting the cancer dataset: 95%
- histopathology specimen report turnaround time: 80% within 7 calendar days, 90% within 10 calendar days.

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Appendix A TNM classification of malignant tumours (7th edition, 2009)[7]

pTX	Primary tumour cannot be assessed
pT0	No evidence of primary tumour
pT1a	≤10 mm, limited to thyroid
pT1b	≤20 mm but >10 mm, limited to thyroid
pT2	>20 mm, ≤40 mm, limited to thyroid
pT3	>40 mm, limited to thyroid or any tumour with minimal extrathyroidal extension, e.g. extension to sternothyroid muscles or perithyroid soft tissues
pT4a	Tumour invades beyond thyroid capsule and invades any of: subcutaneous soft tissues, larynx, trachea, oesophagus, recurrent laryngeal nerve
pT4b	Tumour invades prevertebral fascia, mediastinal vessels, or encases carotid artery.

All anaplastic carcinomas are considered pT4 tumours.

pT4a	Anaplastic carcinoma limited to thyroid
pT4b	Anaplastic carcinoma extends beyond thyroid capsule.

Multifocal tumours (≥ 2 foci) of all histological types should be designated (m), the largest focus determining the classification, e.g. pT2(m).

pNX	Cannot assess regional lymph nodes
pN0	No regional nodes involved
pN1a	Metastasis in level VI (pretracheal, paratracheal and prelaryngeal/Delphian) lymph nodes
pN1b	Metastasis in other unilateral, bilateral or contralateral cervical (levels I, II, III, IV or V) or retropharyngeal or superior mediastinal lymph nodes.

M0	No distant metastases
M1	Distant metastases.

RX	Cannot assess presence of residual primary tumour
R0	No residual primary tumour
R1	Microscopic residual primary tumour
R2	Macroscopic residual primary tumour.

Clinical staging

This is mentioned for ease of reference as it may be mentioned in MDT discussion and in relation to clinical trials, but we recommend that pathology reports include only the pathological TNM staging. The translation of the pathological data into staging differs with the tumour type.[6]

In papillary and follicular carcinoma, there is evidence that prognosis is poorer in older patients and therefore different criteria are applied to patients under 45 years from those to patients aged 45 years and older. In medullary carcinoma, no age stratification applies.

All undifferentiated/anaplastic tumours are regarded as categories within stage IV.

Papillary or follicular under 45 years

Stage I	Any T	Any N	M0
Stage II	Any T	Any N	M1

Papillary or follicular 45 years or over

Stage I	T1a, T1b	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1a	M0
Stage IVA	T1, T2, T3	N1b	M0
	T4a	N0, N1	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Medullary carcinoma

Stage I	T1a, T1b	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T1, T2, T3	N1a	M0
Stage IVA	T1, T2, T3	N1b	M0
	T4a	Any N	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Anaplastic/undifferentiated carcinoma

All are considered stage IV

Stage IVA	T4a	Any N	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Appendix B SNOMED codes

The codes for the more common types are as follows.

Table 1: A comparison of SNOMED 2 or 3 with SNOMED CT codes

Topographical codes	SNOMED 2 or 3	SNOMED CT terminology	SNOMED CT code
Thyroid	T-B6000 (SNOMED 3) T96000 (SNOMED 2)	Thyroid (body structure)	69748006

Table 2: A comparison of SNOMED 2 or 3 with SNOMED CT codes

Morphological codes	SNOMED 2 or 3	SNOMED CT terminology	SNOMED CT code
Papillary carcinoma	M-82603	Papillary adenocarcinoma (morphologic abnormality)	4797003
Papillary microcarcinoma	M-83413	Papillary microcarcinoma (morphologic abnormality)	128674003
Papillary carcinoma, follicular variant	M-83403	Papillary carcinoma, follicular variant (morphologic abnormality)	21968007
Papillary carcinoma, oncocytic variant	M-83423	Papillary carcinoma, oxyphilic cell (morphologic abnormality)	128675002
Papillary carcinoma, tall cell variant	M-83443	Papillary carcinoma, columnar cell (morphologic abnormality)	128677005
Papillary carcinoma, columnar cell variant	M-83443	Papillary carcinoma, columnar cell (morphologic abnormality)	128677005
Follicular carcinoma When oncocytic differ-entiation present, add M82903 to the M83303 already used for the tumour growth pattern	M-83303	Follicular adenocarcinoma (morphologic abnormality)	5257006
Undifferentiated (anaplastic) carcinoma	M-80203	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Squamous cell carcinoma	M-80703	Squamous cell carcinoma, no ICD-O subtype (morphologic abnormality)	28899001
Mucoepidermoid carcinoma	M-83403	Mucoepidermoid carcinoma (morphologic abnormality)	89837001
Medullary thyroid carcinoma	M-83453	Medullary carcinoma with amyloid stroma (morphologic abnormality)	128916007

Morphological codes	SNOMED 2 or 3	SNOMED CT terminology	SNOMED CT code
Spindle cell tumour with thymus-like differentiation (SETTLE)	M-85883	Spindle epithelial tumor with thymus-like element (morphologic abnormality)	128719006
Carcinoma showing thymus-like differentiation (CASTLE)	M-85933	Carcinoma showing thymus-like element (morphologic abnormality)	128720000
Mixed medullary and papillary carcinoma	M-83473	Mixed medullary-papillary carcinoma (morphologic abnormality)	128679008
Mixed medullary and follicular cell carcinoma	M-83463	Mixed medullary-follicular carcinoma (morphologic abnormality)	128678000

Procedure codes (P)

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure.

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

Appendix C Histopathology reporting proforma for thyroid cancer

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

CORE DATA ITEMS
Specimen type

Total thyroidectomy ❑
Left hemithyroidectomy ❑
Right hemithyroidectomy ❑
Isthmusectomy ❑
Biopsy of thyroid ❑
Biopsy/resection of metastasis ❑ (Define site……)
Additional specimens, e.g. lymph node dissection ❑ (Specify..……)

Location of carcinoma

Left lobe ❑ Right lobe ❑ Isthmus ❑ Other ❑ (Specify.....)
No of tumours ..... Single ❑ Multiple (m) ❑ Bilateral (m) ❑
Size.....mm (of largest if multiple)

Cancer type

Papillary carcinoma ❑
Classical PTC ❑
FVPTC ❑
Encapsulated FVPTC ❑
Non-invasive ❑
Capsular invasion only ❑
Vascular (angio)invasion Present ❑ Not identified ❑
Uncertain ❑ Cannot be assessed ❑
Non-encapsulated FVPTC ❑
Diffuse / aggressive / multinodular FVPTC ❑
Microcarcinoma (pT1a):
Single ❑ Multiple (m) ❑ Bilateral (m) ❑
Desmoplastic fibrosis or infiltrative growth pattern present ❑
Incidental finding ❑
Other PTC variant ❑ (Specify.....)
Oncocytic variant Yes ❑ No ❑
Minority poorly differentiated (not anaplastic) component Yes ❑ No ❑

Follicular carcinoma ❑
Minimally invasive ❑
Capsular invasion only ❑
Vascular (angio)invasion Present ❑ Not identified ❑
Uncertain ❑ Cannot be assessed ❑

Widely invasive ❑

Vascular (angio)invasion Present ❑ Not identified ❑
Uncertain ❑ Cannot be assessed ❑

Oncocytic variant Yes ❑ No ❑

Minority poorly differentiated (not anaplastic) component Yes ❑ No ❑

Medullary carcinoma ❑

Poorly differentiated carcinoma (majority (> 50%) of tumour is poorly differentiated) ❑
Differentiated component identified ❑ (Specify)…….....

Undifferentiated/anaplastic carcinoma ❑
Differentiated component identified ❑ (Specify)…….....

Mixed medullary carcinoma with papillary carcinoma ❑
Mixed medullary carcinoma with follicular carcinoma ❑

Angioinvasion / vascular invasion Present ❑ Not identified ❑
Uncertain ❑ Cannot be assessed ❑

Extent

Confined to thyroid (intrathyroidal) ❑

Minimal extrathyroidal extension (seen by microscopy) beyond thyroid capsule into sternothyroid or perithyroidal soft tissues only (pT3) ❑

Tumour invades beyond thyroid capsule into subcutaneous soft tissues, larynx, trachea, oesophagus or recurrent laryngeal nerve; or an anaplastic carcinoma not extending beyond the thyroid capsule (pT4a) ❑

Tumour invades beyond thyroid capsule into prevertebral fascia, mediastinal vessels or encasement of carotid artery, or anaplastic carcinoma extending beyond thyroid capsule (pT4b) ❑

Excision margins

Free of tumour (R0) ❑ Minimum distance .....mm

Microscopic tumour at margin (R1) ❑

Macroscopic tumour at margin (R2) ❑

Lymph nodes

Total number of lymph nodes identified.....

Level VI lymph nodes ❑ Total number ..... Number positive ..... (pN1a)

Other lymph nodes ❑ (Specify site .....)
Total number ..... Number positive ..... (pN1b)

Distant metastasis

Pathological confirmation (pM1) ❑ (Specify site .....)

Stage pT ……. pN ……. pM ……. R …….

SNOMED code TB6 M…….

Signature ……. Date…….……

Appendix D 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	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Level B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Level C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Level D	Non-analytic studies such as case reports, case series or expert opinion or, Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix E 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
5. The patients' views and preferences have been sought	N/A*
6. The target users of the guideline are clearly defined	Foreword
7. The guideline has been piloted among target users	Earlier editions
RIGOUR OF DEVELOPMENT	
8. Systematic methods were used to search for evidence	Foreword
9. The criteria for selecting the evidence are clearly described	Foreword
10. The methods used for formulating the recommendations are clearly described	Foreword
11. The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword
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	Foreword
14. A procedure for updating the guideline is provided	Foreword
CLARITY OF PRESENTATION	
15. The recommendations are specific and unambiguous	3,4,5,7,8,9
16. The different options for management of the condition are clearly presented	5,9
17. Key recommendations are easily identifiable	5,7,8,9
18. The guideline is supported with tools for application	Appendix C
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	10
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 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.