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

# Standards and datasets for reporting cancers

# Dataset for histopathological reporting of testicular neoplasms

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## Foreword

The cancer datasets published by the Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient.

Each dataset contains core data items (see Appendices C–F) 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 95% 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 stakeholders were contacted to consult on this document:

- British Association of Urological Surgeons (BAUS)/BAUS Section of Oncology
- National Cancer Research Institute Teenage and Young Adults (NCRI TYA)/Testis Cancer Clinical Studies Group
- British Association of Urological Pathologists (BAUP)
- UK Association of Cancer Registries (UKACR).

Advice has also been sought from:

- International Society of Urological Pathology (ISUP)
- European Network of Uropathology (ENUP).

### Evidence review

Evidence was sought by review of the previous dataset, and CINAHL (Cumulative Index to Nursing and Allied Health Literature) and PubMed searches reviewing recent articles on risk factors associated with testicular cancer. Recent review articles on testicular cancer were also reviewed. Strength of the data was evaluated according to the modified SIGN guidance (see Appendix G). The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in Appendix H.

Supporting evidence and recommendations in this dataset are also based on:

- PubMed literature searches (up to January 2019)
- WHO Classification of Tumours of the Urinary System and Male Genital Organs, 2016[1]
- International Society of Urological Pathology (ISUP) consensus conference 2015 recommendations[2,3]
- *Datasets for the reporting of neoplasia of the testis: recommendations from the International Collaboration on Cancer Reporting*[4]
- National Institute for Health and Clinical Excellence (NICE) *Improving outcomes in urological cancer*, 2002[5]

- TNM staging classifications (8th edition).[6,7]

Most of the supporting evidence is level C or D at least, or meets the Good Practice Point (GPP) criteria. Evidence is often poor for these relatively rare tumours, usually limited to large cohort studies at best. Disagreements between the authors were settled by discussion, and when no agreement was possible this has been discussed in the text. 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 previous dataset.

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 changes will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Clinical Effectiveness department, Working Group on Cancer Services and Lay Governance Group and was placed on the College website for consultation with the membership from 25 March to 22 April 2020. All comments received from the Working Group and membership were addressed by the authors to the satisfaction of the Chair of the Working Group and the Clinical Lead for Guideline Review.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Clinical Effectiveness department and are available on request. The authors of this document have declared that there are no conflicts of interest.

## 1 Introduction

Testicular cancer is the most common cancer in men under the age of 45. The majority of tumours are germ cell tumours, but there are numerous other types. This makes testicular tumours one of the most diverse areas of human pathology, despite their relative rarity. The picture is complicated by the post-chemotherapy changes that are seen, since many tumours are treated by excision of residual disease after metastasis has occurred. The NICE guidance *Improving Outcomes in Urological Cancer*[5] (www.nice.org.uk) recommended the establishment of a supra-network specialised testicular cancer multidisciplinary team (MDT), serving a population base of 2–4 million and managing 50–100 new patients a year. Patients with testicular cancer diagnosed by local urological multidisciplinary cancer teams should be referred to the specialist supra-network team and the diagnostic slides made available for review. It is expected that lead pathologists reporting testicular tumours and post-chemotherapy residual masses participate in the UK uropathology external quality assurance scheme, which includes testicular neoplasms.

The identification of pathological factors predictive of relapse in patients with disease apparently confined to the testis at presentation (clinical stage I) allows patients at low risk to be offered a range of options including surveillance and, for seminomas, adjuvant carboplatin

is an increasingly popular option over radiotherapy in the UK.[8] For patients with metastatic disease, international collaboration led to the development of an International Consensus Classification, which is based on the primary site, the presence and distribution of metastases, and the level of serum tumour markers alpha-fetoprotein (AFP), human chorionic gonadotrophin (βhCG) and lactate dehydrogenase (LDH).[9] This was subsequently adopted by the TNM classification system.[10]

Patients presenting with metastatic disease and clinical or serological evidence of a germ cell tumour are referred for immediate chemotherapy without prior orchidectomy because of the very rapid doubling times of germ cell tumours. However, in the absence of a testicular lesion, a biopsy may be required to differentiate between a germ cell tumour and other tumour types.

There is a relative lack of top-level evidence supporting the data items in this document. This is because testicular tumours are rare with an extremely high cure rate approaching 98% overall. Therefore, it is fortunately extremely difficult to power studies using death as an end point.[4] Surrogate outcome measures such as clinical stage at presentation are therefore often used. There are few randomised, large-scale, international studies of prognosis and outcome, especially in low-risk tumours. The data from studies needs some scrutiny before deciding whether it can be generalised, for example, to explore whether centralised pathology review and standardised reporting guidance was used. Such measures would be appropriate for tumours managed by supra-regional networks with concentrated pathology expertise. When evidence is limited or absent, items are listed as GPPs determined by the authors' experience.

There are changes within this 4th edition of the dataset compared with the 3rd edition, published in 2014, to reflect changing clinical practice including the tendency for the use of surveillance in many patients rather than adjuvant therapy in stage I testicular germ cell tumours (especially in seminoma). Since the 3rd edition, the WHO 2016 classification has been published[1] and the use of this classification system for testicular tumours has been made mandatory. TNM 8 has been published in two forms – Union for International Cancer Control (UICC)[6] and American Joint Committee on Cancer (AJCC).[11] The differences between them for staging of testicular tumours and the rationale for use of a modified version of the UICC version is discussed in the document. This updated staging system results in the designation of a pT2 category for hilar soft tissue and epididymal invasion, which is a change to previous editions where only lymphovascular invasion (LVI) and tunica vaginalis (TV) invasion conferred this category.

## 1.1 Target users and health benefits of this guideline

Although the supra-regional network model of testicular tumours is now well developed,[12] it should be remembered that testicular cancers are usually diagnosed in local hospitals prior to referral to specialist centres. 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 Registration and Analysis Service (NCRAS). Standardised cancer reporting and MDT working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all 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.

The health benefits of conformity to the guidelines and reasons for adoption include:

- subtyping and staging of testicular tumours to determine subsequent clinical management and follow-up

- consistent reporting of pathological risk factors, which vary depending on the tumour subtype and clinical context, to allow patients to make informed decisions about their care
- adoption of a consistent approach to classification and risk assessment of testicular cancers, which is essential for audit and epidemiological studies.

## 2 Clinical information required on the specimen request form

Laterality, the type of specimen (biopsy, simple or radical orchidectomy, lymphadenectomy or post-chemotherapy residual mass), the anatomical origin of lymph nodes and history of prior testicular tumours and treatment should be stated. Information concerning serum tumour markers is extremely helpful and should be encouraged locally. Tumour markers (LDH, AFP, βhCG) should always be available at the time of surgery in all cases of suspected neoplastic disease of the testis. For lymphadenectomies, further clinical information, such as the side of resection, type of resection (template or removal of specific lesion) and orientating sutures, is helpful to allow correlation with the radiological findings. Unlike in lymph node dissection specimens from other sites, there is no requirement for identifying any specific prognostic nodes, such as an apical node.

## 3 Preparation of specimens before dissection

Specimen types include the following:

- radical orchidectomy
- testicular biopsies
- partial orchidectomy
- lymph node excision
- removal of other metastatic lesions (liver, lungs, brain).

### 3.1 Request forms/tracking

Appropriate labelling of request forms and containers must be observed by the requesting clinical team to avoid delays in the booking in of specimens. If available, specimen tracking with bar coding should enable the progress of specimens to be followed during transport and processing in the laboratory, which would help turnaround times to be audited for reporting.

### 3.2 Tissue fixation

- Radical orchidectomy and lymphadenectomy specimens generally require fixation in formalin for 24 hours. Fixative can be slow to penetrate the thick testicular coverings, therefore careful incision into the capsule is extremely helpful for tumour preservation. Although this should ideally be done by the pathologist, it is recognised that delay in incision can lead to poor tissue preservation, which may compromise the most important part of the assessment of testicular tumours (tumour typing). This should be performed by opening the TV (membranes) and slicing through the lateral border of the testis, cutting towards the epididymis, taking care not to affect assessment of hilar soft tissue invasion.
- Because prompt fixation is key, in some centres surgeons or other appropriate members of staff have been educated in careful ‘bivalving’ of the fresh radical orchidectomy specimen. Distortion could make assessment of invasion of some structures (e.g. tunica albuginea) more difficult, but this is considered by the authors of lesser importance than

poor fixation, which leads to difficulties with tumour typing and assessment of genuine LVI versus smear artefact. Measures to reduce distortion of the tumour/hilar soft tissue interface should be taken, e.g. by training staff not to bisect completely through this area to allow the pathologist to complete the incision and assess for hilar soft tissue invasion.

- Some pathology departments receive radical orchidectomy specimens fresh so tissue can be sampled fresh or fresh frozen for research, which is optimal for nucleic acid quality. This is acceptable as long as sampling does not compromise diagnostic parameters or significantly delay fixation.
- Partial orchidectomies should not usually require incision before fixation as they are smaller and formalin penetrates them well. Incision of partial orchidectomy specimens by the surgeon prior to receipt by a pathologist should be actively discouraged as this will distort the specimen, including most importantly the resection margin and compromise assessment.
- Depending upon personal preference and experience, testicular biopsies may be fixed in Bouin's solution for fertility studies to preserve nuclear morphology.

# 4 Specimen handling and block selection

A synoptic reporting proforma has been added as an *aide memoire* for the main features of these neoplasms (Appendices C and D). The proforma extracts the dataset currently used in diagnosis and staging. This is usually supplemented by a more detailed written report. Aspects of best practice in handling testicular tumour specimens have recently been reviewed as part of broader articles on testicular practice.[2–4,13–15] It is beyond the scope of this document to review the various types of testicular tumours and diagnostic features in detail. The WHO 2016 blue book is the best source for these.[1]

## 4.1 Orchidectomy specimens

Most patients with a clinical diagnosis of testicular tumour undergo a radical orchidectomy, whereby the testis is removed with the tunica, epididymis and a length of spermatic cord via an inguinal approach. Partial orchidectomies may be performed in very specific circumstances, often when the contralateral testis has already been removed, to preserve endocrine function and the potential for natural reproduction.[16] Excision margins or the testicular parenchyma should be inked in these cases. Subcapsular orchidectomies are now rarely performed in the context of prostate cancer. Simple orchidectomies, usually for benign disease, involve the removal of the testis, epididymis and a very short segment of cord via the scrotum. Radical testicular specimens should be orientated by identifying the cord, the slightly more bulbous head of epididymis tapering to the tail of the epididymis, separated from the testis proper by the epididymal sinus.

### 4.1.1 Measuring, opening, inking and sampling

The margin should be inked on a partial orchidectomy specimen to enable its precise recognition microscopically, which is important as involvement may require radical orchidectomy. Photography may be undertaken depending on local facilities and preference.
The testis should be measured in three dimensions and the length of spermatic cord recorded. The terms 'proximal' and 'distal' are best avoided when referring to the cord, as they can cause confusion. A block is taken by the pathologist from the cord resection margin. Some have suggested that this block should be taken prior to incision of the tumour to avoid contamination,[17] however, contamination of the cord margin is rarely a significant issue. It is preferable to rapidly bivalve and fix the testis before the cord margin block is taken. This facilitates good fixation and accurate histological assessment of tumour type. If not already performed, the TV is opened and the testis sliced through the lateral border of the testis, cutting towards the epididymis. The parietal TV can then be reflected and the presence of a hydrocoele and/or adhesions noted. Especially for small tumours, it is necessary to slice

thinly the residual testis. Some pathologists prefer to slice the remaining tissue into 4 mm slices in the horizontal plane, which allows the relationship between the tumour and the rete testis and the tumour and the tunica to be seen clearly.

The greatest dimension of the tumour should be noted. It is also important to note if the tumour is multifocal, as the nodules may be different tumour elements that affect prognosis. However, multifocality per se does not affect prognosis.[4] The size of tumour nodule that constitutes a focus in the literature has not been applied consistently, ranging from ≤1 mm to ≥0.5 mm.[2] If there are multiple tumour nodules, the size of the largest nodule should be quoted as the size of the tumour. This does not affect pT category in the UICC TNM 8th edition. It is noted that in the AJCC TNM 8th edition, for pure seminoma, a size cut-off of >3 cm is used for separating pT1b from pT1a. However, as the recommendation in this dataset is to use UICC (with modifications), this substaging need not be used, although it is possible to include information for subcategorisation in the report if requested by clinicians.

It is important that testicular tumours are sampled generously to accurately identify and quantify tumour elements and identify prognostic factors such as LVI. For example, the finding of a limited non-seminomatous germ cell tumour (NSGCT) component in a tumour that is otherwise seminoma would re-categorise the tumour as a mixed germ cell tumour. It would consequently be managed quite differently as a NSGCT. Based on guidance from ISUP and the AJCC, tumours with a maximum dimension of 2 cm should be embedded in their entirety.[2,6] In addition to this, if the tumour is >2 cm in greatest dimension, ten blocks or a minimum of one to two additional blocks per centimetre, whichever is greater, should be submitted. However, pathologists should strongly consider extensive sampling in specific scenarios. For example, if only seminoma is seen on initial sampling, but the patient has a significantly raised serum AFP, or if microscopic findings are not concordant with the macroscopic impression, more blocks should be taken. Extensive sampling of all tumours that macroscopically appear confined to the testis is recommended as prognostic features such as LVI and pT category are predominantly microscopic observations.

Sampling should include all grossly diverse areas (e.g. solid, cystic, myxoid, fibrotic), paying particular attention to haemorrhagic and necrotic areas, which is in contrast to sampling practice in many other tumour types. If the lesion is a scar, then the entire lesion as well as multiple sections from the background testis should be sampled to exclude viable tumour cells and look for germ cell neoplasia in situ (GCNIS).

### 4.1.2 Spermatic cord

While sometimes sections from the midpoint of the cord are taken, this is not mandatory unless a macroscopic abnormality is seen. However, macroscopic examination of the cord to look for abnormalities is necessary in all cases. There is evidence that vascular invasion is not seen in the cord unless it is also present adjacent to the main tumour, therefore it appears unnecessary to perform major blocking of the cord for little additional useful information.[18] Direct infiltration of the spermatic cord results in a pT3 category. The spermatic cord begins at the deep inguinal ring and ends at the posterior border of the testis and does not include the epididymis or hilar fat between the testis and epididymis. Tumours usually first invade the cord adjacent to the head of the epididymis via a route through the rete testis and hilar soft tissues. At the time of gross dissection (and as with the cord margin block, it is optimal to do this prior to opening), a block should be taken where the spermatic cord emerges above the head of the epididymis. If there is direct invasion by the tumour in this block, a category of pT3 can be assigned. It is very important that this block is taken at the time of dissection or the landmarks are lost microscopically in most cases. If the tumour surrounds or invades the vas deferens microscopically, this is also conclusive evidence of spermatic cord invasion and warrants a pT3 category.

Discontinuous involvement of the spermatic cord via a vascular thrombus is currently considered a metastatic deposit (pM1) in the revised TNM 8 (AJCC) system, but not specified in UICC TNM 8. A tumour thrombus within a vessel without invasion is pT2. A study

assessed the impact of classifying discontinuous invasion from involved lymphovascular spaces as pM1 rather than pT3 as per the revised guidance in AJCC TNM 8 and previous 6th and 7th TNM editions. The study categorised 100 germ cell tumours as showing direct spermatic cord invasion (pT3), spermatic cord invasion via spread from discontinuously involved lymphovascular spaces (pT2pM1) or a combination of both (pT3pM1). Using the new guidance, 12% of cases were upstaged (TNM), resulting in a change to the prognostic group (International Germ Cell Cancer Collaborative Group [IGCCCG]) in those cases. Overall, seminomas and NSGCT had a high frequency of advanced clinical stage at presentation, regardless of involvement by direct extension or discontinuous spread from lymphovascular spaces, but there were no statistically significant differences between the groups in either clinical stage at presentation or likelihood of recurrence. However, there was a trend for pM1 patients to have higher recurrence and worst prognosis than pT3 patients.[19] Clearly, this requires study in larger cohorts. In the absence of specific UICC guidance, the authors advise categorising the relatively rare scenario of discontinuous involvement of the spermatic cord via a vascular thrombus as pM1 in line with the practice of the majority of testicular tumour experts internationally.

### 4.1.3 The hilum and epididymis

Blocks should be taken to examine the rete testis, epididymis and hilum to assess involvement by a tumour. Although rete testis stroma invasion does not alter the TNM stage,[6,20] in some centres its presence or absence in seminoma cases affects the information the patient is given on prognosis. It may also affect decisions on adjuvant radiation or carboplatin chemotherapy in stage I disease (often rete testis stroma invasion is present in association with a tumour size of >3–4 cm).

The hilar soft tissue is defined as the site where the rete testis emerges from the testis, including the 0.5 cm diameter of surrounding tissue.[20] It is composed of adipose and loose fibrous connective tissue and is adjacent to the head of the epididymis. It is important to be certain about the location of the origin of the spermatic cord at gross dissection to make the distinction between spermatic cord invasion and hilar soft tissue invasion (see above, the former being pT3 and the latter pT2). At least one block should be taken of hilar soft tissue, but more may be preferable if invasion is suspected.

Invasion of either epididymis or hilar soft tissue confers a pT category of pT2 in the absence of spermatic cord or scrotal invasion; the latter denote categories of pT3 and pT4, respectively. Therefore, the hilar soft tissue and epididymis should be assessed macroscopically for invasion and blocks taken to confirm the findings. Equally, invasion of these structures could be macroscopically subtle but present microscopically, and so they should be sampled in all cases where possible. Some pathologists find the use of mega blocks useful in showing the overall relationship of tumour to local structures, but this is not mandatory.

This guidance around the staging of hilar soft tissue and epididymis as pT2 is a departure from the guidance given in the 3rd edition of this dataset in which epididymis invasion was regarded as pT1 (based on UICC TNM 7)[6] and hilar soft tissue invasion was regarded as pT3 based on the limited evidence available at the time.[21] There is growing evidence of the importance of hilar soft tissue invasion and prognosis, for example being associated with metastatic disease at presentation in NSGCT.[22] Less evidence exists to support epididymal invasion as an adverse prognostic factor and this is based on expert consensus as to its importance.[3] There remains no specific published guidance in UICC as to the staging of hilar soft tissue invasion without cord invasion. In our opinion, the possibility of epididymal invasion without adjacent soft tissue invasion is very unlikely. It is almost always seen in association with hilar soft tissue invasion, and we believe can be regarded as pT2. In summary, both hilar soft tissue invasion and epididymal invasion are regarded as pT2.

Careful examination at gross dissection of the tunica albuginea should identify if there is tumour extension through the tunica albuginea and involvement of the TV. Grossly adherent

TV may indicate tumour invasion of the parietal layer. The finding of a macroscopically adherent TV is not specific and can be a result of another process, for example inflammation associated with tumour, rather than the tumour itself. Thus, the TV should be sampled in all cases in which tumour invasion is suspected to confirm this microscopically. Some samples should include tunica albuginea to assess for microscopic visceral TV invasion (penetration) on its external surface. Additionally, the tunica albuginea can reveal foci of LVI. Involvement of either the visceral or parietal TV layers is classified as pT2. TV invasion should not change treatment options in clinical scenarios.

### 4.1.4 Background testis

At least one block should be taken of the background testis to clarify the presence or absence of GCNIS. The WHO 2016 classification of testicular tumours[1] separates those germ cell tumours associated with GCNIS from those that are not. Thus, it is important to identify GCNIS in background testis, although this may not be possible if the tumour has obliterated all the parenchyma. For example, the finding of GCNIS in background testis is incompatible with a diagnosis of teratoma of the pre-pubertal type or other entities with very different natural history, notably spermatocytic tumour or Sertoli cell tumours.[23,24] The reporting of the presence or absence of GCNIS is therefore a core data item.

In summary, the following are noted:

- size of testis in three dimensions and length of spermatic cord
- presence or absence of macroscopically adherent TV
- tumour location (upper pole, midsection or lower pole)
- maximum tumour size
- the appearance (solid or cystic or other) and colour of the tumour
- multifocality, if present, and size of largest focus/nodule
- the relationship of the tumour to the tunica albuginea, rete (if identifiable), epididymis and spermatic cord
- the presence of abnormalities in the residual normal testis
- the presence or absence of abnormalities in the spermatic cord.

## 4.2 Primary lymphadenectomy specimens

Although retroperitoneal lymph node dissections can be performed as an alternative to surveillance or chemotherapy in patients with stage I disease,[25] this is unusual in the UK. Any such specimens are measured in three dimensions. Lymph nodes are identified and described as either macroscopically normal or involved by tumour. The size of any lymph node masses should be noted as this is required for TNM staging. Inking for margins is recommended.

## 4.3 Excision of residual masses after chemotherapy

A complete (template) retroperitoneal lymph node dissection may be performed in many cases, but sometimes only the involved lymph nodes are removed ('lumpectomy').[26] The masses usually consist of single or multiple lymph nodes, but occasionally visceral metastasis may be resected.

Specimens should be measured in three dimensions and inking for margins is recommended. All macroscopically positive lymph nodes or any nodal mass should be measured macroscopically by recording at least the maximum dimension. However, measuring each mass in three dimensions is optimal. The size of any positive lymph nodes may affect the pN

category, with significant cut-offs at 2 cm and 5 cm for the size of lymph node metastases. The number and fraction of involved nodes is important.[27]

Lymph nodes should be dissected and liberally sampled including all areas of different macroscopic appearance in the case of residual masses in post-chemotherapy NSGCT. Generous sampling is recommended with the aim of identifying any viable embryonal carcinoma, yolk sac tumour or choriocarcinoma present or somatic-type malignancy, which may trigger further chemotherapy. Findings of post-chemotherapy teratoma, cystic trophoblastic tumour, fibrosis, necrosis or non-viable tumour would not normally trigger further therapy. Any positive nodes/nodal masses should be comprehensively sampled. At least one block per centimetre of maximum diameter is usual. More may be required to adequately demonstrate macroscopically different areas and interface with surrounding structures. All macroscopically negative lymph nodes should be sampled.

In some cases it may be desirable to embed the entire specimen if the specimen is completely necrotic or non-viable to exclude a small focus of viable tumour. This may be triggered by discordant serum markers. Both NSGCT and seminoma are markedly sensitive to cisplatin-based chemotherapy, but seminoma more so. Thus, post-chemotherapy residual masses are likely to show extensive necrosis without viable germ cell tumour and in the case of NSGCT, post-chemotherapy teratoma.

The minimum distance from tumour to margins should be recorded and sampled. Although a metastatic site, margins remain important as complete resection of viable malignancy in the residual mass has a substantial effect on treatment algorithms.

## 4.4 Block selection

See relevant sections above.

### 4.4.1 Orchidectomy specimens for clinically localised disease

Blocks are selected to represent:

- the cord resection margin and base of cord (further cord blocks depending on macroscopy)
- the relationship of the tumour(s) to the rete testis, TV, hilar soft tissue, epididymis and cord
- the minimum distance of the tumour to the nearest inked resection margin for partial orchidectomies
- all areas of the tumour(s) with different macroscopic appearances (solid, cystic, pale or haemorrhagic). If the tumour is 2 cm or less in size, embed in entirety; if >2 cm, embed ten blocks or a minimum of one to two blocks per centimetre, whichever is greater. In some cases, more extensive sampling is warranted.
- adjacent testis including the tunica albuginea, a common site for vascular invasion
- uninvolved testis to identify presence or absence of GCNIS.

### 4.4.2 Retroperitoneal lymph node dissections and post-chemotherapy residual masses

Blocks are selected to represent:

- all areas of the positive node(s) with different macroscopic appearances (solid, cystic, pale or haemorrhagic) with at least one block per centimetre with more samples taken if there are macroscopically different areas
- the minimum distance of the tumour to the nearest resection margin (which should be inked)
- all macroscopically negative nodes to search for micrometastatic disease

- necrotic areas to identify microscopic viable areas of germ cell tumour.

For post-chemotherapy residual masses, particularly in the absence of a biopsy diagnosis prior to treatment, it is often useful to include areas of necrosis, as ghost outlines of the tumour often remain and allow the distinction between seminoma and non-seminomatous germ cell tumour. It is important to recognise that residual viable malignancy (embryonal carcinoma, yolk sac tumour, seminoma or choriocarcinoma) may trigger further chemotherapy and therefore it is important to report only viable elements and not semi-viable or non-viable tumour. Increasingly, a watchful waiting approach is taken especially if the amount of viable embryonal carcinoma, yolk sac tumour, seminoma or teratoma, post-pubertal type, is limited. Necrosis and post-chemotherapy teratoma, post-pubertal type, would not usually trigger further therapy, unless the clinical situation dictates otherwise.

# 5 Core data items

This is an evidence-based list of items that are essential for prognosis or management.

## 5.1 Clinical data items

Clinical data items include:

- type of specimen and procedure
- anatomic site.

These items are self-explanatory. Ideally, serum makers would be a core data item, however, during the consultation phase for the 3rd version of the dataset many pathologists highlighted the potential difficulty with obtaining these at the time of reporting. There are also occasional testes removed for trauma that have incidental germ cell tumours. This has therefore been removed as a core data item, but knowledge of serum markers is desirable for optimal assessment of a tumour. For example, it is important to inspect closely, and possibly sample more widely, a case that appears macroscopically to be seminoma but in which there is a raised AFP. Identification of an additional non-seminomatous component will influence clinical management.

## 5.2 Macroscopic data items

Macroscopic data items include:

- number (multifocality), location and description of tumour(s)
- maximum tumour dimension
- status of TV.

These items are unchanged from the previous dataset. It is the maximum tumour dimension that seems to have prognostic significance, especially in seminomas.[28] In TNM 8, if tumours are multifocal, it is the maximum tumour dimension that is recorded as the size, although this does not affect the staging within the modified version of UICC TNM 8 used in this dataset. The status of the TV remains unchanged from the 2nd edition of the dataset. Although it is essential for TNM staging, we cannot find evidence that it is a prognostic factor.

## 5.3 Microscopic data items

Different prognostic factors can be important in seminoma and NSGCT. We therefore recommend that core data items that have shown to be significant for seminoma or NSGCT should be regarded as core data items for both groups. This does inflate the number of core data items but avoids the complexity of a ‘split’ system.

### 5.3.1 Classification

Accurate typing of a testicular tumour is of paramount importance and influences clinical decisions far more than pathological stage. The WHO 2016 system[1] is used in virtually every country and should be used for tumour typing. The British Testicular Tumour Panel (BTTP) classification should no longer be used.

### 5.3.2 Tumour types

The WHO 2016 system has redefined the classification of testicular germ cell tumours to divide them into tumours that are derived from GCNIS and those that are unrelated to GCNIS. If tested, tumours in the former group will often show isochromosome of the short arm of chromosome 12 [i(12p)] or other forms of 12p amplification on molecular testing, whereas the latter group will usually lack i(12p). Molecular testing is not needed in the vast majority of cases – the specific situations where it may be helpful are described in section 10.

**Germ cell tumours derived from GCNIS**

- Seminoma.
- Embryonal carcinoma.
- Yolk sac tumour, post-pubertal type.
- Choriocarcinoma.
- Teratoma, post-pubertal type.
- Teratoma with somatic type malignancy.
- Mixed.
- Regressed.

**Germ cell tumours unrelated to GCNIS**

- Spermatocytic tumour.
- Teratoma, pre-pubertal type (usually occurs in children, but can occur in adults):
  - epidermoid cyst
  - dermoid cyst.
- Yolk sac tumour, pre-pubertal type.

Approximately 50–55% of germ cell tumours are 100% seminoma.[29,30] The WHO 2016 classification system has redefined seminoma, such that there is now only one type of seminoma. This was the subtype previously referred to as ‘classical seminoma’. The ‘classical’ prefix should no longer be used with the tumour being referred to as ‘seminoma’. It is now clear that the entity previous designated as ‘spermatocytic seminoma’ is separate from other germ cell tumours on genetic as well as morphological grounds and, for this reason, was renamed as a spermatocytic tumour in the WHO 2016 system.[31]

There is less literature and information available about prognostic factors in seminoma compared with NSGCT, probably owing to the lower rates of recurrence and death, making studies extremely hard to power statistically. Current management practice is for surveillance in the majority of patients with stage I seminoma[32] and has been used in some centres for over 30 years.[33] If adjuvant therapy is the patient’s or oncologist’s preference, then adjuvant carboplatin[8,34] is now generally the treatment of choice rather than radiotherapy, although this is disputed in some countries, notably the USA.[35] Those with relapse are almost invariably salvaged by cisplatin-based chemotherapy. Death from stage I seminoma is extremely rare; a systematic review showed a cause-specific survival of 99.7% in a pooled analysis.[36] Almost all patients with stage I seminoma are cured, regardless of the management strategy

adopted after orchidectomy, and therefore any decisions about the need for adjuvant therapy in stage I seminoma should be made with the aim of reducing morbidity and recurrence risk, rather than mortality. Seminoma often shows later recurrence than non-seminoma.

Historically, the 'anaplastic (classical) seminoma' subtype was reported to have a worse prognosis. However, it is now clear that based on the original criteria,[37,38] such as mitotic rate, this label is not effective in recognising aggressive behaviour and should no longer be used.[39] Often, tumours classified as 'anaplastic seminomas' were likely to be either poorly fixed seminomas, with obscuring of the diagnostic features, or solid pattern embryonal carcinomas. 'Seminoma with atypia' was described based on nuclear pleomorphism and crowding, dense cytoplasm and few lymphocytes.[40] Such tumours were more likely to express CD30 and lose c-kit reactivity; we interpret this as likely early transformation to non-seminoma (embryonal carcinoma). There is widespread agreement from the international urological pathology community that labels such as 'anaplastic' or 'atypical' should not be applied to seminoma.

**Spermatocytic tumour**

Spermatocytic tumour is no longer considered a variant of seminoma. It shows an almost universally excellent prognosis with only the rare scenario of sarcomatous de-differentiation resulting in malignant behaviour. Small case series and individual case reports of an 'anaplastic variant' of spermatocytic tumour have been described where there is a predominance of the intermediate size cells and a high mitotic index. However, this does not seem to correspond to an adverse prognosis in the limited literature available and no patients have shown metastasis.[41–43] Thus, there is no evidence that tumours with this morphology display anything other than the almost invariably excellent prognosis of spermatocytic tumour, and use of this term is not recommended.

**Non-germ cell tumours of the testis**

The assessment of non-germ cell tumours of the testis is highly specialised and challenging even for experts in the field. Most will be Leydig cell tumours and behave in a benign manner and need no follow-up. However, some may be associated with clinical syndromes and rarely behave in a malignant fashion. Features suggestive of malignancy include invasion of other structures, LVI, large size, necrosis and increased mitotic activity. We recommend referral to a national or even international expert if suspicious features are identified. Treatment of malignant cases may include a prophylactic retroperitoneal lymph node dissection.[44] Lymphomas should be referred to a lymphoreticular expert.

### 5.3.3 Percentage of tumour elements in mixed germ cell tumours

The percentage and volume of embryonal carcinoma is a prognostic factor associated with the rate of relapse in stage I NSGCTs, although the use of different dichotomous cut-offs in different studies hampers generalisation of the literature. Many studies have found between 50 and 100% embryonal carcinoma to be predictive of relapse.[45] However, embryonal carcinoma predominance showed no association with metastatic disease in some studies and more frequent local extension in others.[22,46]

In a study of 132 patients, the presence of LVI, embryonal carcinoma and yolk sac tumour were risk factors for relapse.[47] Another study showed that 25 of 85 men who had predominantly embryonal carcinoma histology relapsed (p=0.008).[48] Of 93 men with stage I NSGCTs who were placed in a surveillance study following orchidectomy, 81 men had a predominantly embryonal carcinoma component in their primary tumour and a third of these developed metastases, whereas none of the men lacking an embryonal carcinoma component developed metastases (p=0.05).[49] The absence of yolk sac tumour is an unfavourable prognostic factor.[36,50] Choriocarcinoma in pure or mixed form shows aggressive behaviour.[51,52] It is helpful for clinicians to know the approximate proportions of each tumour subtype present for these reasons.

*[Level of evidence C – it is helpful for clinicians to know the approximate proportions of each tumour subtype present.]*

### 5.3.4 Tumour size

Size of tumour is not a proven predictive factor in NSGCT, but it is a robust risk factor for disease relapse in seminoma in cohort studies. Tumour size was used as a continuous variable in some studies[53,54] and a dichotomous variable in others, with the cut-off variably being 3 cm,[55,56] 4 cm[28] or 6 cm.[55,57]

In a pooled analysis of data from four large cohort studies in seminoma (638 patients), size (tumour size >4 cm) and rete testis invasion were the only two factors independently predictive of recurrence at five years on multivariate analysis.[36] If the tumour was >4 cm, there was a two-fold increased risk of recurrence. Patients with both rete testis invasion and a tumour >4 cm were 3.4-times more likely to relapse than patients with no adverse factors.

Although the AJCC TNM 8 substages seminoma into pT1a and pT1b based on size, this dataset recommends the use of UICC, which does not use this substaging and therefore size does not affect TNM stage.

The tumour size is usually determined macroscopically but may be determined microscopically if it was not possible macroscopically or is more accurately done microscopically, e.g. a small tumour.

*[Level of evidence – C.]*

### 5.3.5 Lymphovascular invasion

Accurate assessment of the presence or absence of LVI in prognostic stage group I NSGCT is essential as this is one of the few areas of testicular germ cell tumour practice where we have strong evidence that a microscopic feature confers adverse prognosis. Most studies show LVI to be prognostic for NSGCT, but in the few studies looking at seminomas the data is not as clear.[28,58,59] Although LVI has been shown to be a statistically significant factor for predicting relapse in occasional small cohort studies in seminoma,[59] it has not proved independently statistically significant in stage I seminoma in large cohort pooled studies.[28,58] The potential reasons for the difference between seminoma and NSGCT include the presence of LVI and adverse events being more common in NSGCT than seminoma and the presence of frequent implantation artefacts in seminoma, which makes assessment difficult and error prone.

Unlike seminomas, LVI is the most powerful prognostic factor for stage I NSGCT. In a study of 102 men with stage I NSGCT, Fosså and colleagues showed that LVI was the most significant risk factor predicting relapse (p=0.0007).[60] In a separate study, LVI was identified as a significant poor prognostic factor, with 62% of men with lymphatic invasion developing distant metastases.[49] This is further confirmed by Colls and colleagues who demonstrated that 46% of men with LVI in their primary tumour experienced relapse.[61] A multivariate analysis of stage I NSGCTs showed that 23 of 88 patients with vascular invasion of the primary tumour had a high risk of relapse (61%; 95% CI: 55–67%). A linked cohort surveillance of 105 men with stage I NSGCTs revealed that 27 of 105 (25.7%) men had disease relapse.[62] All relapses in this group of men occurred within two years of orchidectomy and vascular invasion was identified as one of the significant predictors of relapse during surveillance. Furthermore, in examining the records of 82 patients with stage I NSGCTs following radical orchidectomy, 30 patients did not have vascular invasion in their primary tumour, while 52 did.[63] In the group of men who had vascular invasion, 24 of 52 (46%) experienced relapse, thus indicating that vessel invasion could be used as a prognostic factor in monitoring stage I NSGCTs. The presence of LVI in stage I NSGCT is often used as a trigger for adjuvant chemotherapy rather than surveillance, although patients with LVI are often offered surveillance but counselled as to this higher risk of disease

relapse. In seminoma, determining the presence or absence of LVI is of lesser importance as it would not usually trigger adjuvant therapy.

Categorising vascular invasion as 'uncertain' is unhelpful for the treatment of patients with germ cell tumours. If the pathologist is uncertain but overcalls it as present, this could trigger unnecessary adjuvant chemotherapy in stage I NSGCT. It is recommended that vascular invasion is noted as positive in cases in which the pathologist is certain of its presence and called negative when features are equivocal or uncertain.

Most studies in the literature do not discriminate between lymphatic and blood vessel invasion. Some studies have specifically found that lymphatic but not blood vessel invasion was associated with prognosis.[64] Conversely, others have found that blood vessel but not lymphatic invasion was prognostic.[65] It is not necessary to separate lymphatic from blood vessel invasion and either can be referred to as LVI.

Immunohistochemistry does not need to be routinely performed as typically the problem is not whether tumour is in a vessel or not, but whether it is an artefactually displaced tumour or genuine. There is currently no evidence for the introduction of the routine use of immunohistochemistry, such as D2-40 against podoplanin (identification of lymphatic endothelium)[66] or CD34 (vascular endothelium), to assist in identifying lymphatic or vascular invasion, although this may help in individual cases. CD34 is present in normal testicular stroma[67] and lines seminiferous tubules, and thus is often more useful. Immunohistochemistry may help in selected cases, but it is not mandatory.

LVI may be seen in the spermatic cord vessels or the parenchyma of the testis. Some of the best places to look for genuine LVI are at the periphery of the tumour and in the tunica albuginea. All warrant a category of pT2. Based on current evidence and TNM 8, its presence in spermatic cord vessels does not warrant a stage of pT3 and this should be staged as pT2. However, further literature is emerging in small studies suggesting that LVI in NSGCT in the cord, as opposed to LVI limited to the testis, is associated with advanced clinical stage but not disease progression.[68] Furthermore, it is comparable to direct cord invasion in terms of clinical stage, disease recurrence and survival.[69] However, larger studies and further discussion are needed before considering any changes to staging systems.

If there is invasion of the tumour out of the vessels into the cord soft tissue, this is now regarded as pM1 (see spermatic cord section above) since this represents a soft tissue deposit of tumour. LVI assessment is often difficult and a supraregional review is undertaken by a central laboratory pathologist who regularly sees high volumes of germ cell tumour cases. In theory this should increase reproducibility. In one study, 27% of cases on review at a central pathology laboratory were reclassified as LVI and 19% were reclassified as no LVI, with only the central pathology LVI correlated with node metastases.[70]

Pitfalls in identifying LVI include histiocytes in cord vessels. LVI tends to be over diagnosed in seminoma owing to implantation artefact in the adjacent non-tumoural parenchyma. Features thought to be representative of true LVI are listed below and representative images of genuine and non-genuine LVI can be found in the ISUP paper.[3] LVI can be intra-parenchymal, in the cord or in the tunica; all count as pT2.

The morphological features of true LVI include:

- tumour occupies a lymphovascular structure lined by flattened endothelial cells
- cluster may not conform to the exact shape of the vascular lumina
- associated fibrinous thrombosis and/or mural attachment and re-endothelialisation
- lack of obvious background artefactual deposition of germ cell tumour cells on the tunical surface

- cluster is more cohesive and has a rounded smooth edge
- cluster looks markedly different in its architecture from surrounding tumour
- LVI may be peripheral, in the cord or intratumoural.

In one survey,[71] 60% of pathologists reported that they did not specify the type of tumour involved in LVI in mixed NSGCT and there is no evidence on this issue. However, it is considered good practice in a mixed germ cell tumour to specify the tumour type showing LVI since it can affect treatment decisions. For example, if it were embryonal carcinoma, this may trigger adjuvant therapy, whereas this would not be the case if it were a seminoma element showing the LVI.

*[Level of evidence C – the presence or absence of LVI in NSGCT has significant prognostic value in stage I NSGCT.]*

*[Level of evidence D – the presence or absence of LVI in seminoma is an inconsistent risk factor across the literature for disease relapse in stage I seminoma.]*

*[Level of evidence GPP – it is considered good practice in a mixed germ cell tumour to specify the tumour type showing LVI.]*

### 5.3.6 Invasion of hilar soft tissue and epididymis

Invasion of hilar soft tissues and epididymis is an area of difference between the UICC and AJCC TNM 8th editions. In the AJCC TNM 8th edition, hilar soft tissue invasion and epididymis invasion have been adopted as pT2, which represents a change from the 7th edition and reflects the outcome of expert consensus conference discussion.[2,3] In the UICC TNM 8th edition, hilar soft tissue and epididymis invasion remain pT1 in the absence of LVI, TV invasion, or scrotal or cord invasion. In an RCPath appendix to the UICC TNM 8th edition published in 2017, it was clarified that although hilar soft tissue invasion is not specifically mentioned in UICC TNM 8, it should be interpreted as pT2. Epididymal invasion in the absence of hilar soft tissue or vascular invasion is very unusual. In these circumstances, extension into the epididymis is likely to represent occult hilar soft tissue extension/vascular invasion and should be recorded as pT2.

The hilar soft tissue and rete testis together comprise the hilum of the testis. The hilar soft tissue is a zone of adipose tissue and vessels beyond the rete testis but before the base of the cord is reached and is adjacent to the head of the epididymis. Hilar soft tissue invasion is the most common site of extratesticular extension in both seminomas and NSGCT.[20,72] In a study of 447 orchidectomies, tumour extension into hilar soft tissues was found in 25% (113 of 447) cases.[73] In 81% of those cases, extratesticular extension into hilar soft tissues occurred via direct invasion of the rete testis due to close anatomic proximity. The study underscores the significance of adequate sampling of the testicular hilum at the time of gross dissection.[73] Studies on the importance of hilar soft tissue invasion as an adverse factor are relatively few and focus on metastasis at presentation rather than later disease relapse. In one study, on multivariate analysis, both rete testis and hilar soft tissue invasion were strong independent predictors of metastasis at presentation.[22] Despite evidence of potential significance as an adverse factor, there has not been up until now clear guidance on how to categorise these cases. Since the hilum lacks TV, in cases with no LVI, this type of hilar spread prior to this clarification represented a potential understaging pitfall.

Although evidence is limited, epididymis invasion probably represents relatively aggressive disease on the basis of expert consensus opinion. It is infrequently seen and usually in the context of an otherwise locally infiltrative tumour. Furthermore, since one can usually only see epididymal invasion following hilar soft tissue invasion, and the latter was considered pT2 (as detailed above), it was agreed that the pT2 category is an appropriate designation for epididymal invasion.[11]

*[Level of evidence C – hilar soft tissue invasion is a predictor of metastasis at presentation.]*

*[Level of evidence GPP – epididymis invasion probably represents relatively aggressive disease.]*

### 5.3.7 Invasion of the rete testis

Although still not included in the TNM staging system, in a pooled analysis of data from four large cohort studies, rete testis invasion in seminoma was independently predictive of recurrence at five years on multivariate analysis, conferring an increased risk of recurrence by a factor of 1.7 (95% CI: 1.1–2.6).[28] This was confirmed by a further large cohort analysis of 425 patients.[58] Rete testis invasion was defined in the pooled analysis as extension of the tumour into the testicular mediastinum without necessarily involving the tubular lumens (i.e. rete testis stroma invasion only was counted and not pagetoid spread into the rete epithelium). The evidence is not consistent, however, and smaller recent series have not confirmed that rete testis invasion is an independent predictor of progression.[74]

In NSGCT, the evidence for rete testis stroma invasion as a prognostic factor is limited. In one study of 148 orchidectomy specimens of NSGCT, rete testis stroma invasion was identified in 52% (72 of 138 evaluable cases) and exclusive pagetoid spread was found in 17% (23 of 138 evaluable cases). The study found significant statistical correlation between direct rete testis stroma invasion and advanced clinical stage at presentation but no such correlation existed between pagetoid spread of neoplastic germ cells into the rete epithelium.[22]

There is no evidence that pagetoid spread alone is a prognostic factor and many of these cases probably represent extension of GCNIS into the rete testis epithelium. We recognise that rete testis invasion and tumour size are probably closely related, and further work may show which is superior in multivariate analysis. Currently, both are used by many clinicians to determine adjuvant chemotherapy in seminoma and are part of existing clinical guidelines.[75,76] The failure to discriminate between rete testis stroma invasion and pagetoid spread in some studies can make it difficult to draw meaningful conclusions and clearly more evidence with control of such factors is needed.

Rete testis invasion should be specified as stromal invasion (core data item) or pagetoid spread into the epithelium of the rete (non-core data item).

*[Level of evidence C – rete testis invasion in seminoma is predictive of recurrence in stage 1 seminoma in some large cohort studies, but not all studies.]*

*[Level of evidence D – in NSGCT, there is an association in some studies between rete testis stroma invasion and advanced clinical stage at presentation.]*

### 5.3.8 Direct invasion of the cord (spermatic cord invasion)

This is regarded as a core data item as it is required for TNM staging, but evidence on its prognostic significance in seminoma and NSGCT is limited.[22,77] In a large cohort study of stage I seminoma, spermatic cord invasion was not found to be independently prognostic for recurrence.[58] In a review of 326 testicular germ cell tumours, of which 79 had tumour in the spermatic cord, 72% of cases were thought to be due to contamination compared with 19% cases of true involvement, with 8.9% showing both contamination and true involvement. Spermatic cord contamination was most frequently seen with seminomas.[17] Because of the extremely friable nature of seminoma, careful specimen handling and interpretation is required. The definition of cord invasion has been discussed in macroscopic assessment. If the tumour surrounds or invades the vas deferens microscopically, this is also conclusive evidence of spermatic cord invasion and warrants a pT3 category.

*[Level of evidence – GPP.]*

### 5.3.9 Tunica vaginalis invasion

This is a rare route of extratesticular extension (only 2% cases in one study) and therefore of dubious significance.[73] The value of TV invasion as a prognostic factor shows very little support in the literature. Because it is a staging point in TNM 8, it is good practice to mention involvement. As mentioned above, involvement of either the visceral or parietal layer constitutes involvement of the TV and is regarded as pT2 in TNM 8. If TV involvement is identified microscopically only, there must be at least penetration of the visceral TV mesothelial layer.

*[Level of evidence – GPP.]*

### 5.3.10 Scrotal invasion

This is rarely seen and is required for TNM staging, resulting in a pT4 category. Evidence as to whether it is an adverse prognostic factor in NSGCT is limited.[70]

*[Level of evidence – D.]*

### 5.3.11 Margin status

The margin status in a partial orchidectomy will determine whether the tumour may remain in the testis and a positive margin may trigger radical orchidectomy. The margin must therefore be carefully assessed and its status (positive or negative) should be commented upon where possible. In rare circumstances, distortion or fragmentation may make it non-assessable.

In a radical orchidectomy, there is little evidence that surgical margin status has been studied as an independent prognostic factor.[4] It is, however, considered good practice to comment on the cord margin. Vascular invasion at the cord margin does not represent a positive margin.

*[Level of evidence – GPP.]*

### 5.3.12 Somatic transformation

Rarely, a teratoma can show malignant overgrowth of either sarcoma, carcinoma or primitive neuroectodermal tumour. Although an evidence base for defining overgrowth is lacking, it is usually considered as involvement of one low-power (x4) field in primitive neuroectodermal tumour and sarcoma. Overgrowth by somatic carcinoma is characterised by invasive growth.

## 5.4 Lymph node excisions/retroperitoneal lymph node dissection surgery

The role of pathology in metastatic disease is to confirm the diagnosis of a germ cell tumour if there is clinical uncertainty. However, prognosis and treatment decisions are then largely based on the International Consensus Classification.[9] Serum markers and imaging are used to assess response to chemotherapy. Residual masses may persist after completion of treatment. Patients with seminoma do not generally require resection of a persistent mass, as the presence of residual viable seminoma and the development of recurrence are rare. On the other hand, two-thirds of resections in patients with NSGCT contain viable disease, and it is not always possible to identify preoperatively those with fibrosis or necrosis only. It is only viable and not semi-viable or non-viable tumour elements that are clinically important. In some cases, it is not entirely straightforward to determine if tumour elements are viable or semi/non-viable. Features that might suggest the tumour is semi/non-viable are pyknotic nuclei, loss of cytoplasm and a degenerate appearance. The presence of germ cell elements other than teratoma (seen in 20–30% of cases) and incomplete resection are independent risk factors for progression.[78] The presence of embryonal carcinoma has been identified as the single most significant risk factor for progression in patients with complete resections.[79,80] If the amount of residual viable non-teratoma malignancy is limited, then further chemotherapy may not be required[80] and the patient can be offered surveillance.

Transformation to other types of tumour is extremely difficult to assess and, where there is doubt, referral to an expert in the area is recommended. Determination of whether there is extranodal spread of the tumour should be stated, as this is required for nodal staging.

The careful microscopic analysis and reporting of retroperitoneal lymph node dissections is important for prognostic and therapeutic reasons. There are three main features to observe: residual, viable, non-teratomatous germ cell tumour; teratoma; and scar/necrosis. These findings may be alone or in combination. The presence of any amount of viable non-teratomatous germ cell tumour is an adverse prognostic factor and may mandate additional systemic therapy. Scars/necrosis and teratoma on their own, regardless of the level of immaturity or degree of cytologic atypia, have a favourable prognosis.[81] If, however, the teratoma is associated with a non-germ cell somatic malignancy, the outcome is generally adverse.[82] Additionally, in the rare situation where a cystic trophoblastic tumour has been identified, this is associated with a favourable prognosis.[83]

The prognostic significance of the number of positive lymph nodes, fraction of positive lymph nodes and the presence of extranodal extension is unclear from the literature currently available. However, it is considered good practice to report them to give an indication of burden of disease and feedback on quality of resection to the surgeon.[27,84]

The retroperitoneal lymph node dissection report should clearly identify the presence or absence of viable non-teratomatous germ cell tumour and scar/necrosis. The number of positive lymph nodes, fraction of positive lymph nodes and the presence of extranodal extension should be reported recognising that the prognostic significance of these observations is unclear.

### 5.4.1 Microscopic core data items for orchidectomy specimens

These data items include:

- tumour subtype(s)
- percentage of all tumour elements for mixed tumours
- maximum tumour dimension (if not assessed macroscopically). This has no impact on stage.
- invasion of the rete testis stroma (no change to stage)
- invasion of the hilar soft tissue (pT2)
- invasion of the epididymis (pT2)
- invasion of the TV (pT2)
- direct invasion of the spermatic cord (pT3)
- LVI and in mixed tumours, which tumour element shows LVI (pT2). If equivocal, regard as not present.
- invasion of the scrotum where assessment is possible (pT4)
- surgical margin status (partial orchidectomies)
- cord margin status (radical orchidectomies)
- presence or absence of GCNIS where possible
- primary tumour categories (pT stage).

### 5.4.2 Microscopic core data items for lymphadenectomies or resections of residual masses

These data items include:

- tumour subtype(s) and percentages
- viability of the tumour(s)
- margin status
- extranodal spread of tumour
- number of positive nodes and fraction of positive nodes.

## 6 Non-core data items

These data items include:

- pagetoid spread of GCNIS into the rete testis epithelium
- presence of normal spermatogenesis
- invasion of the tunica albuginea.

### 6.1 Other experimental factors

The following have been studied to identify patients at risk of recurrence or metastasis: DNA ploidy status; mitotic rate; DNA S phase percentage; gene expression analysis of genes such as DRD1 or FAM71F2; the presence of syncytiotrophoblastic giant cells; the degree of lymphocytic infiltrate in the tumour; expression of βhCG, low-molecular-weight keratins, p53, Ki67, CD30 or loss of CD117 expression on immunohistochemical analysis; spontaneous regression; or necrosis. However, significant evidence on any of these as a predictor of recurrence/metastasis is currently either limited or absent.[57,85–87] There is increasing interest in the use of image analysis in pathology, but only a limited number of studies have been performed in testicular germ cell tumours. However, these have shown promise. For example, one small study showed a relationship between low tumour infiltrating lymphocytes, the presence of metastatic disease at presentation and disease relapse.[88] Some studies have mapped the exomic landscape in testicular tumours, but such sequencing remains in the research domain for the moment.[89] A number of studies have tried to investigate other factors of poor prognosis in NSGCTs, but none have been clinically validated.[90–93]

## 7 Diagnostic coding and staging

### 7.1 TNM classification

The UICC 8th edition of TNM should be used with Appendix A.[6]

### 7.2 Diagnostic coding

Coding is recommended and is important for data retrieval, workload measurement and audit. The site, histological diagnosis and procedure should be coded using SNOMED CT (Appendix B).

It is noted, however, that SNOMED is now in a practical transition phase, as part of the intended full implementation by the NHS and Public Health England (PHE) of SNOMED CT. SNOMED ceased to be licensed by the International Health Terminology Standards Development Organisation from 26 April 2017.

A list of applicable T and M SNOMED and SNOMED CT codes is provided in Appendix B. Mapping SNOMED CT terminology is provided.

Procedure codes (P) are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure. Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions (Appendix B).

## 8 Reporting of biopsy specimens

Biopsy specimens are rarely received from testes in the setting of a suspected germ cell tumour as radical (or as a minimum partial) orchidectomy is standard management. There should be a very low threshold for performing additional immunohistochemical studies on testicular biopsies taken for suspected malignancy or if there is a history of, for example, maldescent. OCT3/4 staining is invaluable in highlighting subtle GCNIS or intertubular seminoma.

## 9 Reporting of frozen sections

Frozen sections for testicular neoplasms are difficult and produce a number of challenges. We believe that there is no role for testicular frozen sections when a total orchidectomy has already been planned or when tumour markers strongly suggest a germ cell neoplasm. There are selected cases for which intraoperative consultation using frozen section may be useful: paratesticular lesions, epidermoid cysts, bilateral lesions, a solitary testis, pre-pubertal patients and where testis-sparing surgery may be considered suitable. The main questions from the surgeon are what the lesion is and whether the margin is clear. A sex cord stromal tumour may be identified and prevent the need for a radical orchidectomy. Similarly, confirmation of a germ cell tumour may lead to a change to total orchidectomy.[94,95] There are numerous potential pitfalls in the assessment of frozen section material in testicular neoplasms and for most pathology departments it is an unnecessary procedure, especially given the rarity of testicular tumours.[96] Not least, a benign epidermoid cyst may be almost impossible to separate from a teratoma, post-pubertal type, on frozen section. Testis-sparing surgery is usually only suitable for small testicular masses, <2 cm. In a recent study of 2,681 patients with surgically excised testicular lesions, 81 had lesions with a diameter of <10 mm. The majority of these lesions (69%) were benign, with 42% being sex cord stromal tumours without malignant features.[97] In lesions with a diameter of <5 mm, 100% were benign.[97] Therefore, testis-sparing surgery may represent a safe procedure with optimal results in terms of functional and oncologic end points, where the majority of lesions <10 mm are benign and many are sex cord stromal tumours without malignant features on final diagnosis.[98,99]

## 10 Use of immunohistochemistry/molecular tests

Immunohistochemistry can be used as an adjunct in confirmation of tumour types/subtypes, but it is not necessary in most cases. It is particularly useful in settings such as confirming a tumour to be a germ cell tumour rather than another type of tumour (e.g. lymphoma or sex cord stromal tumour), confirming a germ cell tumour subtype (e.g. seminoma versus solid pattern embryonal carcinoma or spermatocytic tumour) or confirming the various elements present within a mixed germ cell tumour (e.g. yolk sac tumour versus embryonal carcinoma). The use of immunohistochemistry is not discussed in this document as ISUP have published an excellent summary.[100]

Some centres are able to offer isochromosome i(12p) fluorescence in situ hybridisation (FISH) testing. The indications for i(12p) testing by FISH or other appropriate molecular

assays are distinction of pre-pubertal type teratomas from malignant teratomas in a post-pubertal male and in some cases to determine in an extra-testicular site whether a carcinoma or sarcoma is a somatic-type malignancy arising in a malignant germ cell tumour. Post-pubertal type teratoma often has an isochromosome of the short arm of chromosome 12 – i(12p) – or other forms of 12p amplification on FISH testing, but these determinations should prove negative in pre-pubertal type teratoma, pre-pubertal type yolk sac tumour and spermatocytic tumour. Spermatocytic tumours show gains of chromosome 9 and less frequent gains of chromosomes 1 and 20 with partial loss of chromosome 22.[101] i(12p) status may be diagnostically helpful in select cases when these tumours need to be confirmed or ruled out. There are no predictive or prognostic markers in testicular germ cell tumours that are applicable in routine clinical practice.

## 11 Criteria for audit

The following are recommended by the RCPath as key performance indicators (see *Key Performance Indicators – Proposals for implementation*, July 2013 at https://www.rcpath.org/profession/guidelines/kpis-for-laboratory-services.html):

- 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 were required to implement the structured recording of core pathology data in the COSD by January 2016 and to update their systems in line with subsequent COSD updates.
  - standard: 95% of reports must contain structured data
- histopathology cases must be 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.

## 12 References


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## Appendix A TNM pathological staging (UICC TNM 8)

This update to Appendix A provides information on staging using UICC TNM 8, which should be used for all tumours diagnosed no later than 1 January 2018.

The classification applies only to germ cell tumours of the testis. The assessment of the serum tumour markers alpha-fetoprotein (AFP), human chorionic gonadotropin (βhCG) and lactate dehydrogenase (LDH) contributes to the clinical, but not pathological, staging. Although pathologists may not be aware of specific levels to allow stage grouping, the details are provided here for information.

**pT Primary tumour**

pTx Primary tumour cannot be assessed (used if no radical orchidectomy has been performed, except for pTis and pT4, where radical orchidectomy is not always necessary for classification purposes)

pT0 No evidence of primary tumour (e.g. histological scar in testis)

pTis Germ cell neoplasia in situ (GCNIS)

pT1* Tumour limited to testis and epididymis** without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis

pT2* Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis

pT3 Tumour invades spermatic cord with or without vascular/lymphatic invasion

pT4 Tumour invades scrotum with or without vascular/lymphatic invasion

Notes
*Hilar soft tissue invasion is not specifically mentioned in UICC TNM 8, but it should be interpreted as pT2.

**Epididymal invasion in the absence of hilar soft tissue or vascular invasion is very unusual. In these circumstances, extension into the epididymis is likely to represent occult hilar soft tissue extension/vascular invasion and should be recorded as pT2.

In the case of multiple tumours, the tumour with the highest T category should be classified and the multiplicity or number of tumours should be indicated in parentheses, e.g. pT2 (m) or pT2 (5).

**pN Regional lymph nodes**

The regional lymph nodes are the abdominal para-aortic (periaortic), preaortic, interaortocaval, precaval, paracaval, retrocaval and retroaortic nodes. Nodes along the spermatic vein should be considered regional.

Laterality does not affect the N classification.

The intrapelvic and the inguinal nodes are considered regional after scrotal or inguinal surgery.

pNx Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 Metastasis with a lymph node mass 2 cm or less in greatest dimension and five or fewer positive nodes, none more than 2 cm in greatest dimension

pN2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than five nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour

pN3 Metastasis with a lymph node mass more than 5 cm in greatest dimension

**pM Distant metastasis**

Categories pMx and pM0 were removed in the 7th edition of TNM. M0 can only be assigned as a clinical stage, not a pathological stage.

pM1 Distant metastasis

- pM1a Non-regional lymph node(s) or lung
- pM1b Other sites

**S Serum tumour markers**

SX Serum marker studies not available or not performed

S0 Serum marker study levels within normal limits

| | **LDH** | | **βhCG (mIU/ml)** | | **AFP (ng/ml)** |
|---|---|---|---|---|---|
| S1 | <1.5 x N | and | <5,000 | and | <1,000 |
| S2 | 1.5–10 x N | or | 5,000–50,000 | or | 1,000–10,000 |
| S3 | >10 x N | or | >50,000 | or | >10,000 |

N indicates the upper limit of normal for the LDH assay.

**Stage grouping**

| | | | | |
|---|---|---|---|---|
| Stage 0 | pTis | N0 | M0 | S0, SX |
| Stage I | pT1–4 | N0 | M0 | SX |
| Stage IA | pT1 | N0 | M0 | S0 |
| Stage IB | pT2 | N0 | M0 | S0 |
| | pT3 | N0 | M0 | S0 |
| | pT4 | N0 | M0 | S0 |
| Stage IS | Any pT/TX | N0 | M0 | S1–3 |
| Stage II | Any pT/TX | N1–3 | M0 | SX |
| Stage IIA | Any pT/TX | N1 | M0 | S0 |
| | Any pT/TX | N1 | M0 | S1 |
| Stage IIB | Any pT/TX | N2 | M0 | S0 |
| | Any pT/TX | N2 | M0 | S1 |
| Stage IIC | Any pT/TX | N3 | M0 | S0 |
| | Any pT/TX | N3 | M0 | S1 |
| Stage III | Any pT/TX | Any N | M1, M1a | SX |
| Stage IIIA | Any pT/TX | Any N | M1, M1a | S0 |
| | Any pT/TX | Any N | M1, M1a | S1 |
| Stage IIIB | Any pT/TX | N1–3 | M0 | S2 |
| | Any pT/TX | Any N | M1, M1a | S2 |
| Stage IIIC | Any pT/TX | N1–3 | M0 | S3 |
| | Any pT/TX | Any N | M1, M1a | S3 |
| | Any pT/TX | Any N | M1b | Any S |

## Appendix B SNOMED coding of testicular tumours

**Table 1: A comparison of SNOMED 2 or 3 with SNOMED CT codes (topography codes)**

| Topographical codes | SNOMED 2 or 3 | SNOMED CT terminology | SNOMED CT code |
|---|---|---|---|
| Right testis | T94010 (SNOMED 3)<br>T78010 (SNOMED 2) | Structure of right testis (body structure) | 15598003 |
| Left testis | T94020 (SNOMED 3)<br>T78020 (SNOMED 2) | Structure of left testis (body structure) | 6329009 |
| Testis, side unknown | T94000 (SNOMED 3)<br>T78000 (SNOMED 2) | Testis structure (body structure) | 40689003 |
| Right epididymis | T95010 (SNOMED 3)<br>T79110 (SNOMED 2) | Structure of right epididymis (body structure) | 74475002 |
| Left epididymis | T95020 (SNOMED 3)<br>T79120 (SNOMED 2) | Structure of left epididymis (body structure) | 86244002 |
| Epididymis, side unknown | T95000 (SNOMED 3)<br>T79100 (SNOMED 2) | Epididymis structure (body structure) | 87644002 |
| Spermatic cord | T97000 (SNOMED 3)<br>T79300 (SNOMED 2) | Spermatic cord structure (body structure) | 49957000 |

**Table 2: A comparison of SNOMED 2 or 3 with SNOMED CT codes (morphology codes)**

| Morphological codes | SNOMED 2 or 3 | SNOMED CT terminology | SNOMED CT code |
|---|---|---|---|
| Seminoma, classical | M90613 | Seminoma, no ICD-O subtype (morphologic abnormality) | 36741007 |
| Spermatocytic seminoma | M90633 | Spermatocytic seminoma (morphologic abnormality) | 9294008 |
| Embryonal carcinoma | M90703 | Embryonal carcinoma (morphologic abnormality) | 28047004 |
| Germ cell tumour, non-seminomatous | M90653 | Germ cell tumour, non-seminomatous (morphologic abnormality) | 128766005 |
| Teratoma | M90803 | Teratoma, malignant, no ICD-O subtype (morphologic abnormality) | 19467007 |
| Choriocarcinoma | M91003 | Choriocarcinoma, no ICD-O subtype (morphologic abnormality) | 44769000 |
| Yolk sac tumour | M90713 | Endodermal sinus tumour (morphologic abnormality) | 74409009 |
| Mixed embryonal carcinoma and teratoma | M90813 | Teratocarcinoma (morphologic abnormality) | 67830002 |

| Morphological codes | SNOMED 2 or 3 | SNOMED CT terminology | SNOMED CT code |
|---|---|---|---|
| Mixed teratoma and seminoma | M90853 | Mixed germ cell tumour (morphologic abnormality) | 32844007 |
| Leydig cell tumour | M86501 | Leydig cell tumour, no ICD-O subtype (morphologic abnormality) | 45002009 |
| Malignant Leydig cell tumour | M86503 | Leydig cell tumour, malignant (morphologic abnormality) | 77870005 |
| Sertoli cell tumour | M86401 | Sertoli cell tumour, no ICD-O subtype (morphologic abnormality) | 128857001 |
| Malignant Sertoli cell tumour | M86403 | Sertoli cell carcinoma (morphologic abnormality) | 80091008 |
| Sex cord stromal tumour | M85901 | Sex cord-stromal tumour, no ICD-O subtype (morphologic abnormality) | 71440001 |

**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 Reporting proforma for testicular cancer (orchidectomy)

Surname……..… Forenames…… Date of birth……..… Sex…..

Hospital……..……..… Hospital no……..... NHS/CHI no……...

Date of surgery……..… Date of report authorisation……. Report number……....

Date of receipt……. Pathologist……..... Surgeon……

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### Nature of specimen/procedure and core macroscopic items

Biopsy □ Radical orchidectomy □ Partial orchidectomy □

Laterality: Right □ Left □

Tumour location ……..……..

Tumour description …….....

Macroscopic tunica vaginalis invasion: Present □ Not identified □ Cannot be assessed □

Cord invasion: Present □ Not identified □ Cannot be assessed □

Tumour focality:† Multifocal □ Unifocal □ Indeterminate □

Cannot be assessed □

Maximum tumour size if assessable: ..…… (mm)

### Core microscopic items

#### 1. Tumour typing – state percentage of each tumour element present†

| Tumour type(s) (one or more) | **Germ cell tumour** | % | **Other** | % |
|---|---|---|---|---|
| | Seminoma | | Leydig cell tumour | |
| | Embryonal carcinoma | | Sertoli cell tumour | |
| | Yolk sac tumour, post-pubertal type | | Spermatocytic tumour | |
| | Choriocarcinoma | | Teratoma, pre-pubertal type | |
| | Teratoma, post-pubertal type | | Teratoma, pre-pubertal type (dermoid cyst) | |
| | Scar/necrosis/non-viable germ cell tumour | | Teratoma, pre-pubertal type (epidermoid cyst) | |
| | Regressed germ cell tumour | | Yolk sac tumour, pre-pubertal type | |
| | Teratoma with somatic type malignancy | | | |

**2. Tumour parameters**

Maximum tumour dimension (if not assessed macroscopically): ..... mm

†Lymphovascular invasion (score equivocal foci as negative, i.e. not identified):

Present □ Not identified □ Cannot be assessed □

If lymphovascular invasion present, state which element is showing lymphovascular invasion:

Embryonal carcinoma □ Yolk sac tumour □ Choriocarcinoma □

Teratoma □ Seminoma □ Cannot be assessed □

†‡Rete testis stroma invasion:

Present □ Not identified □ Cannot be assessed □

†Hilar soft tissue invasion (pT2):

Present □ Not identified □ Cannot be assessed □

†Direct spermatic cord invasion (pT3):

Present □ Not identified □ Cannot be assessed □

Separate soft tissue deposit in the spermatic cord:

Present □ Not identified □ Cannot be assessed □

†Microscopic tunica vaginalis invasion:

Present □ Not identified □ Cannot be assessed □

†Epididymis invasion:

Present □ Not identified □ Cannot be assessed □

†GCNIS identified:

Present □ Not identified □ Cannot be assessed □

†Spermatic cord margin status (radical orchidectomy only)

Involved □ Not involved □ Uncertain □ Not applicable □

†Margin status (partial orchidectomy only):

Involved □ Not involved □ Uncertain □ Not applicable □

If not involved, distance to margin .....mm

†Tumour viability (post-chemotherapy only):

Viable □ Non- or semi-viable □

pT stage: ..... (TNM 8)

SNOMED codes: T…….. M…….

T…….. M…….

**Signature of pathologist …… Date ……..……**

†Data items that are used in version 1.0 of the ICCR Neoplasia of the Testis – Orchidectomy dataset.

‡Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 9.

## Appendix D Reporting proforma for testicular cancer (retroperitoneal lymph node dissections, other lymph node excisions or resections of metastatic deposits)

Surname……..… Forenames…… Date of birth……..… Sex…..

Hospital……..……..… Hospital no……..... NHS/CHI no……...

Date of surgery……..… Date of report authorisation…… Report number……....

Date of receipt……. Pathologist……..... Surgeon……

### Clinical information required

History of chemotherapy (if known) ……

### Nature of specimen/procedure and core macroscopic items

Retroperitoneal lymph node dissection □ Other □ Please specify……

Size of specimen (three dimensions): ..... x ..... x ....… mm

Size of any lymph node masses present: …..... mm

### Core microscopic items

#### 1. Tumour typing – state percentage of each viable tumour element present

| Tumour type(s) (one or more) | **Germ cell tumour** | % | **Non-germ cell tumour** | % |
|---|---|---|---|---|
| | Seminoma | | Please specify | |
| | Embryonal carcinoma | | | |
| | Yolk sac tumour, post-pubertal type | | | |
| | Choriocarcinoma | | | |
| | Teratoma, post-pubertal type | | | |
| | Semi-viable tumour, non-viable tumour, necrosis or fibrosis only (no viable tumour) | | | |
| | Other | | | |
| | Please specify:…… | | | |

#### 2. Tumour parameters

Maximum tumour dimension (if not assessed macroscopically): ..... mm

Number of positive lymph nodes: ……..

Total number of lymph nodes: ……..

Margin status:

Involved □ Not involved □ Uncertain □ Not applicable □

If not involved, distance to margin .....mm

Tumour viability (post-chemotherapy specimens):

Viable □ Non- or semi-viable □

Extranodal spread of tumour (retroperitoneal lymph node dissection or other lymph node excision only):

Present □ Not identified □ Cannot be assessed □

pT stage: .....(TNM 8)

SNOMED codes:

T…….. M…….

T…….. M…….

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**Signature of pathologist …… Date ……..……..**

## Appendix E Reporting proforma for testicular cancer (orchidectomy) in list format

| Element name | Values | Implementation comments |
|---|---|---|
| Nature of specimen/procedure | Single selection value list:<br>• Biopsy<br>• Radical orchidectomy<br>• Partial orchidectomy | |
| Laterality | Single selection value list:<br>• Right<br>• Left | |
| Tumour location | Free text | |
| Tumour description | Free text | |
| Macroscopic tunica vaginalis invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Cord invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Tumour focality | Single selection value list:<br>• Multifocal<br>• Unifocal<br>• Indeterminate<br>• Cannot be assessed | |
| Maximum tumour size | Size in mm | |
| Percentage of tumour element present, Seminoma | Integer | |
| Percentage of tumour element present, Embryonal carcinoma | Integer | |
| Percentage of tumour element present, Yolk sac tumour, post-pubertal type | Integer | |
| Percentage of tumour element present, Choriocarcinoma | Integer | |
| Percentage of tumour element present, Teratoma, post-pubertal type | Integer | |
| Percentage of tumour element present, Scar/necrosis/non-viable germ cell tumour | Integer | |

| Element name | Values | Implementation comments |
|---|---|---|
| Percentage of tumour element present, Regressed germ cell tumour | Integer | |
| Percentage of tumour element present, Teratoma with somatic type malignancy | Integer | |
| Percentage of tumour element present, Leydig cell tumour | Integer | |
| Percentage of tumour element present, Sertoli cell tumour | Integer | |
| Percentage of tumour element present, Spermatocytic tumour | Integer | |
| Percentage of tumour element present, Teratoma, pre-pubertal type | Integer | |
| Percentage of tumour element present, Teratoma, pre-pubertal type (dermoid cyst) | Integer | |
| Percentage of tumour element present, teratoma pre-pubertal type (epidermoid cyst) | Integer | |
| Percentage of tumour element present, Yolk sac tumour, pre-pubertal type | Integer | |
| Maximum tumour dimension | Size in mm | |
| Lymphovascular invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Lymphovascular invasion present, element involved | Multiple selection value list:<br>• Embryonal carcinoma<br>• Yolk sac tumour<br>• Choriocarcinoma<br>• Teratoma<br>• Seminoma<br>• Cannot be assessed | Only applicable if 'Lymphovascular invasion, Present' is selected. |
| Rete testis stroma invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Hilar soft tissue invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |

| Element name | Values | Implementation comments |
|---|---|---|
| Direct spermatic cord invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Separate soft tissue deposit in the spermatic cord | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Microscopic tunica vaginalis invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Epididymis invasion | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| GCNIS identified | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| Spermatic cord margin status | Single selection value list:<br>• Involved<br>• Not involved<br>• Uncertain<br>• Not applicable | Only applicable if 'Nature of specimen/procedure, Radical orchidectomy' is selected. |
| Margin status | Single selection value list:<br>• Involved<br>• Not involved<br>• Uncertain<br>• Not applicable | Only applicable if 'Nature of specimen/procedure, Partial orchidectomy' is selected. |
| Distance to margin | Size in mm | Only applicable if 'Margin status, Not involved' is selected. |
| Tumour viability (post-chemotherapy only) | Single selection value list:<br>• Viable<br>• Non- or semi-viable | |

| Element name | Values | Implementation comments |
|---|---|---|
| pT category | Single selection value list:<br>• X<br>• 0<br>• is<br>• 1<br>• 2<br>• 3<br>• 4 | |
| TNM version | 8 | 8 automatically selected. |
| SNOMED Topography code | May have multiple codes. Look up from SNOMED tables. | |
| SNOMED Morphology code | May have multiple codes. Look up from SNOMED tables. | |

## Appendix F Reporting proforma for testicular cancer (retroperitoneal lymph node dissections, other lymph node excisions or resections of metastatic) in list format

| Element name | Values | Implementation comments |
|---|---|---|
| History of chemotherapy (if known) | Free text | |
| Nature of specimen/procedure | Single selection value list:<br>• Retroperitoneal lymph node dissection<br>• Other | |
| Nature of specimen/procedure, other, specify | Free text | Only applicable if 'Nature of specimen/procedure, Other' is selected. |
| Dimension of specimen, Length | Size in mm | |
| Dimension of specimen, Breadth | Size in mm | |
| Dimension of specimen, Depth | Size in mm | |
| Size of lymph node masses present, lymph node n | Size in mm | Repeating data item.<br>n value increases as required. |
| Percentage of viable tumour element present, Seminoma | Integer | |
| Percentage of viable tumour element present, Embryonal carcinoma | Integer | |
| Percentage of viable tumour element present, Yolk sac tumour, post-pubertal type | Integer | |
| Percentage of viable tumour element present, Choriocarcinoma | Integer | |
| Percentage of viable tumour element present, Teratoma, post-pubertal type | Integer | |
| Percentage of viable tumour element present, Semi-viable tumour, non-viable tumour, necrosis or fibrosis only (no viable tumour) | Integer | |
| Percentage of viable tumour element present, Other | Integer | |
| Percentage of viable tumour element present, Other, specify | Free text | Only applicable if 'Percentage of viable tumour element present, Other' is selected. |

| Element name | Values | Implementation comments |
|---|---|---|
| Percentage of viable tumour element present, Non-germ cell tumour | Integer | |
| Percentage of viable tumour element present, Non-germ cell tumour, specify | Free text | Only applicable if 'Percentage of viable tumour element present, Non-germ cell tumour' is selected. |
| Maximum tumour dimension | Size in mm | |
| Number of positive lymph nodes | Integer | |
| Total number of lymph nodes | Integer | |
| Margin status | Single selection value list:<br>• Involved<br>• Not involved<br>• Uncertain<br>• Not applicable | |
| Distance to margin in mm | Integer | Only applicable if 'Margin status, Not involved' is selected. |
| Tumour viability (post-chemotherapy only) | Single selection value list:<br>• Viable<br>• Non- or semi-viable | |
| Extranodal spread of tumour (retroperitoneal lymph node dissection or other lymph node excision only) | Single selection value list:<br>• Present<br>• Not identified<br>• Cannot be assessed | |
| pT category | Single selection value list:<br>• X<br>• 0<br>• is<br>• 1<br>• 2<br>• 3<br>• 4 | |
| TNM version | 8 | 8 automatically selected. |
| SNOMED Topography code | May have multiple codes. Look up from SNOMED tables. | |
| SNOMED Morphology code | May have multiple codes. Look up from SNOMED tables. | |

## Appendix G 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<br>or<br>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<br>or<br>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<br>or<br>Extrapolation evidence from studies described in B. |
| Level D | Non-analytic studies such as case reports, case series or expert opinion<br>Or<br>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 H AGREE II compliance monitoring sheet

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

| AGREE standard | Section of guideline |
|---|---|
| **Scope and purpose** | |
| 1 The overall objective(s) of the guideline is (are) specifically described | Introduction |
| 2 The health question(s) covered by the guideline is (are) specifically described | Introduction |
| 3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described | Foreword |
| **Stakeholder involvement** | |
| 4 The guideline development group includes individuals from all the relevant professional groups | Foreword |
| 5 The views and preferences of the target population (patients, public, etc.) have been sought | Foreword |
| 6 The target users of the guideline are clearly defined | Introduction |
| **Rigour of development** | |
| 7 Systematic methods were used to search for evidence | Foreword |
| 8 The criteria for selecting the evidence are clearly described | Foreword |
| 9 The strengths and limitations of the body of evidence are clearly described | Foreword |
| 10 The methods for formulating the recommendations are clearly described | Foreword |
| 11 The health benefits, side effects and risks have been considered in formulating the recommendations | Foreword and Introduction |
| 12 There is an explicit link between the recommendations and the supporting evidence | 2–10 |
| 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 | 2–10 |
| 16 The different options for management of the condition or health issue are clearly presented | 2–10 |
| 17 Key recommendations are easily identifiable | 2–10 |
| **Applicability** | |
| 18 The guideline describes facilitators and barriers to its application | Foreword |
| 19 The guideline provides advice and/or tools on how the recommendations can be put into practice | Appendices A–F |
| 20 The potential resource implications of applying the recommendations have been considered | Foreword |
| 21 The guideline presents monitoring and/or auditing criteria | 11 |
| **Editorial independence** | |
| 22 The views of the funding body have not influenced the content of the guideline | Foreword |
| 23 Competing interest of guideline development group members have been recorded and addressed | Foreword |