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

Standards and datasets for reporting cancers
Dataset for histopathological reporting of uterine sarcomas

September 2018

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Unique document number	G106
Document name	Dataset for histopathological reporting of uterine sarcomas
Version number	4
Produced by	Professor W Glenn McCluggage and Professor Cyril Fisher, on behalf of the Working Group for Cancer Services of The Royal College of Pathologists. The authors are specialist gynaecological and soft tissue pathologists, have published and lectured widely in the fields of gynaecological and soft tissue pathology and have sat on national advisory committees relevant to quality assurance and policy in gynaecological and soft tissue pathology.
Date active	September 2018 **(to be implemented within 3 months)**
Date for review	September 2021
Comments	This document supersedes the December 2014 document, *Dataset for histopathological reporting of uterine sarcomas*. In accordance with the College's pre-publications policy, this dataset was on the College website for consultation with the membership from 8 March to 5 April 2018. Responses and authors' comments are available to view on request. **Dr Bridget Wilkins** **Clinical Director of Clinical Effectiveness**

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Registered charity in England and Wales, no. 261035

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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 D and E) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Dataset) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 90% of reports on cancer resections should record a full set of core data items. Other non-core data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholder organisations have been consulted during the preparation of the dataset:

- British Association of Gynaecological Pathologists (BAGP)
- British Gynaecological Cancer Society (BGCS)
- British Sarcoma Group.

Evidence for the revised dataset was obtained from updates to international tumour grading, staging and classification systems and by electronically searching medical literature databases for relevant research evidence, systematic reviews and national or international publications on uterine sarcomas. The level of evidence for the recommendations has been summarised (Appendix F). Unless otherwise stated, the level of evidence corresponds to 'Good practice point (GPP): Recommended best practice based on the clinical experience of the authors of the writing group'. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in Appendix G.

No major organisational changes or cost implications have been identified that would hinder the implementation of the dataset for the core items.

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 advisor to the College, to consider whether or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken for two weeks for Fellows' attention.

The dataset has been reviewed by the Clinical Effectiveness department, Lay Governance Group and Working Group on Cancer Services. It was placed on the College website for consultation with the membership from 8 March to 5 April 2018. All comments received from the Working Group and the membership were addressed by the authors to the satisfaction of the Chair of the Working Group and the Clinical Director of Clinical Effectiveness.

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

Careful and accurate reporting of uterine sarcomas is important because pathology reports are used to:

- confirm the diagnosis
- inform prognosis
- plan the treatment of individual patients
- audit pathology service
- evaluate the quality of other clinical services (radiology, surgery, oncology)
- collect accurate data for cancer registration and epidemiology
- facilitate high-quality research
- plan service delivery.

This dataset (and the background information that forms part of the dataset) should be used in the context of the multidisciplinary team (MDT) meeting to optimise management decisions. According to NICE's *Improving Outcomes for People with Sarcoma*,[1] all patients with a confirmed diagnosis of sarcoma should have their care supervised by or in conjunction with a sarcoma MDT. Uterine and other gynaecological sarcomas should primarily be discussed at a gynaecological oncology MDT meeting since oncologists managing gynaecological neoplasms generally have more experience with these uncommon tumours. However, there should be close liaison with, and referral to, local sarcoma MDT meetings. The more common uterine sarcomas (leiomyosarcoma, endometrial stromal sarcoma, undifferentiated sarcoma or adenosarcoma) may be included as notations at sarcoma MDT meetings, but close collaboration between sarcoma and gynaecological MDTs is particularly important in the management of extra-uterine gynaecological sarcomas (not discussed in this document), disseminated uterine sarcomas and sarcomas of a morphological type other than the more common gynaecological sarcomas indicated above.

Access to pathologists with expertise in sarcoma pathology is important, and robust local mechanisms must be in place to ensure that the MDT clinical leads and cancer registries are informed of supplementary or revised histology reports that are issued by one or other MDTs as this may affect patient treatment and data collection.

This is a revised dataset for the histological reporting of uterine sarcomas, which are rare neoplasms, accounting for 1% of female genital malignancies and 3–5% of malignant uterine tumours. On the whole, they are characterised by a poor prognosis with a high rate of local recurrence and/or metastasis.[2,3]

In the past, because of their relative rarity, there was no staging system for uterine sarcomas and they were usually staged using the 1988 International Federation of Gynecology and Obstetrics (FIGO) system for carcinomas of the uterine corpus. The utility of this staging system for uterine sarcomas was never established and there was no evidence that this system was of prognostic importance. In fact, the FIGO staging system for carcinomas of the uterine corpus was shown to be of no prognostic value for leiomyosarcomas, the most common uterine sarcoma.[4] In 2009, FIGO introduced two staging systems for uterine sarcomas[5,6] (see Appendix A); the morphological tumour subtype determines which staging system is used.

With regard to the two FIGO staging systems for uterine sarcomas that were introduced in 2009, the same staging system is used for leiomyosarcoma and endometrial stromal sarcoma, and a different system is used for adenosarcoma.[5,6] Tumours such as adenosarcoma, which tend to arise at the endometrial or cervical surface and progressively invade the myometrium or cervical stroma in a similar way to endometrial carcinomas, are staged in a comparable way to endometrial carcinomas. Conversely, tumours such as leiomyosarcoma and endometrial stromal sarcoma that usually arise within the myometrium do not progress in the same way, and are therefore staged according to a different system. It is now accepted that carcinosarcomas (malignant mixed Mullerian tumours) are essentially carcinomas that have undergone sarcomatous metaplasia with the epithelial elements being the 'driving force',[7,8] although a recent study has shown that in stage I uterine carcinosarcomas, the presence of heterologous mesenchymal elements is an adverse prognostic factor.[9] Given this, the recommendation is to stage carcinosarcomas in an identical manner to carcinomas of the uterine corpus[6] and they are not discussed further in this guideline.

The 2009 FIGO staging systems make no mention of undifferentiated uterine sarcomas or pure heterologous sarcomas, such as rhabdomyosarcoma, but we recommend these should be staged in the same way as leiomyosarcomas and endometrial stromal sarcomas. The term 'uterus' includes the uterine corpus and uterine cervix and the 2009 FIGO staging systems are used for all uterine sarcomas, irrespective of whether tumours arise in the corpus or cervix.

Sarcomas also arise at other sites in the female genital tract in addition to the uterus but they are much less common at extra-uterine sites. The morphological subtypes are, in general, similar to those occurring within the uterus. However, there are some notable differences; for example, fibrosarcomas uncommonly occur within the ovary and these are exceptionally rare within the uterus. In addition, pathologists should note that in some circumstances the reporting of extra-uterine sarcomas differs from their uterine or soft tissue counterparts; for example, the diagnostic and prognostic criteria for vulvovaginal leiomyosarcomas differ from what is generally applied to their uterine and soft tissue equivalents. These rare extra-uterine gynaecological sarcomas are outside the remit of this dataset. Because of the rarity of these tumours, they must be reported in compliance with the most current published evidence available in the literature.

Pathologists examining gynaecological specimens may also see sarcomas arising in the vulvovaginal region or in structures outside the female genital tract, for example in the pelvis or abdomen. When handling such cases, internal or external consultation with a pathologist specialising in soft tissue pathology may be important. Pathologists should also refer to the College's *Dataset for histopathological reporting of soft tissue sarcomas*.[10]

This uterine sarcoma dataset has been revised to ensure that all recommendations for histological diagnosis are up to date, terminology and tumour classification comply with recommendations in the 2014 World Health Organization (WHO) classification of tumours of the female reproductive tract,[11] and the guideline conforms to the revised format of the College's cancer dataset series. The most important changes in uterine sarcoma tumour classification and nomenclature in the 2014 revision of the WHO 'Blue book' relate to endometrial stromal sarcomas. The 2003 WHO classification of endometrial stromal sarcomas eliminated the category of high-grade endometrial stromal sarcoma because of the recognition that low-grade endometrial stromal sarcoma and undifferentiated uterine sarcoma were two different and separate neoplastic entities, and that it was not possible to differentiate reliably between high-grade stromal sarcomas and undifferentiated endometrial/uterine sarcomas. Recent molecular and morphological data have emerged that have validated the re-introduction of high-grade endometrial stromal sarcoma, for a specific subset of uterine sarcomas (see section 5.1, Tumour type), as a separate entity in the WHO classification of endometrial stromal sarcoma.[11,12] In the 2014 WHO classification, the

category of undifferentiated endometrial sarcoma was replaced by undifferentiated uterine sarcoma to reflect the fact that an endometrial origin is not proven.

1.1 Target users of the dataset

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

2 Clinical information required on the specimen request form

This should include full patient details, clinical presentation, results of previous biopsies and radiological investigations for tumour staging, and comprehensive details about the surgical procedure. It is also important to provide details of any family history of cancer, history of prior pelvic irradiation and relevant hormonal or other drug therapy. The latter may be particularly important since morphological features that can mimic malignancy may be seen within uterine leiomyomas after treatment with hormones or other drugs, for example progestogens, gonadotropin-releasing hormone agonists and tranexamic acid.[13–15] Note that hormonal treatment may also result in morphological changes in uterine sarcomas. It is beyond the scope of this document to detail these features, but the reader is referred to several other publications.[13,14] Details of non-drug treatment modalities should also be provided, e.g. uterine artery embolisation, which is used to shrink suspected uterine leiomyomas, can result in extensive necrosis of mesenchymal lesions and cause diagnostic problems.[16–18]

[Level of evidence – C.]

The nature of surgical specimens from multiple sites should be carefully recorded and the specimen pots should be labelled to correspond with the specimen details on the request form.

3 Preparation of specimen(s) before dissection

The usual surgical treatment for uterine sarcomas (either confirmed by preoperative biopsy or suspected on imaging) is hysterectomy and bilateral salpingo-oophorectomy. Omentectomy and pelvic and para-aortic lymphadenectomy may also be performed. However, a variety of other procedures, including 'myomectomy' or hysterectomy alone, may be performed if a malignant lesion is not suspected. The specimen should be transported to the laboratory as soon after surgery as possible. Whether received fresh or in formalin, the uterus should be opened as soon after receipt as possible to facilitate fixation of the tumour and preservation of tumour morphology. Good preservation of tumour morphology is of crucial importance for accurate histological diagnosis and tumour subtyping. If the ovaries and fallopian tubes are normal, they can be allowed to fix intact. In occasional cases, one or both ovaries may contain metastatic tumour and slicing will facilitate adequate fixation.

There are several ways of opening the uterus, depending on the preference and experience of the pathologist. Some pathologists prefer to open the uterus in the sagittal plane, while others open it coronally, along the lateral border and between the cornua. Whatever the manner of opening, it should facilitate optimal visualisation and assessment of the tumour, accurate gross description and appropriate tumour sampling.

A photographic record of the specimen is recommended.

4 Specimen handling and block selection

Depending on the preoperative diagnosis, results of radiological imaging and intraoperative findings, the hysterectomy specimen may be accompanied by pelvic and/or para-aortic lymph nodes and an omental biopsy or omentectomy. All of the specimens should be received in separate pots, appropriately labelled as to the site of origin.

4.1 Gross examination and dissection

The different components of the hysterectomy specimen (uterus, ovaries, tubes) should be described and their dimensions and macroscopic appearance recorded. The gross appearance of the tumour, including its maximum dimension, the presence or absence of haemorrhage or necrosis, the nature of the margin (circumscribed or infiltrative), and the presence or absence of gross cervical involvement, serosal involvement or adnexal involvement should be recorded. Many leiomyosarcomas and undifferentiated sarcomas are relatively well circumscribed while most, but not all, low-grade endometrial stromal sarcomas have an irregular margin, sometimes with prominent 'worm-like' infiltration of the myometrium and myometrial vascular channels. Other low-grade endometrial stromal sarcomas are polypoid neoplasms that project into the uterine cavity. Adenosarcomas are usually polypoid neoplasms that project into and often distend the uterine cavity. It is useful to record whether the tumour is located entirely within the myometrium or also involves the endometrium. This may be important when the histological differential diagnosis includes an endometrial carcinoma or a carcinosarcoma, since these neoplasms usually arise from the endometrium. The maximum tumour dimension is important in substaging stage I leiomyosarcomas and endometrial stromal sarcomas: a cut-off of 5 cm distinguishes between stage IA and IB (≤5 cm = stage IA; >5 cm = stage IB).[5,6] Tumour size has been shown to be of prognostic significance in leiomyosarcomas confined to the uterus.[19] A recent large study showed that the five-year survival of stage IA (using the 2009 FIGO system) low-grade endometrial stromal sarcoma is better than that of stage IB (100% versus 93.5%).[20]

[Level of evidence – B.]

Tumour size is also important to guide tumour sampling. Documenting the tumour size will provide evidence to the specialist pathologists responsible for reviewing these uncommon cases that the tumour has been adequately sampled (see section 4.2 below).

Any ovarian or tubal abnormalities should be documented. The omentum, if received, should be measured and the presence of any obvious tumour must be noted. The number of lymph nodes retrieved from each site and the presence of macroscopic tumour involvement should be noted.

4.2 Block selection

Some pathologists block the uterus in the transverse plane. An alternative method involves blocking the uterus in the sagittal plane as this preserves the continuity of the endocervical canal with the endometrial cavity and allows easier mapping of the tumour and more accurate evaluation of cervical involvement by the tumour. Whichever method is chosen for blocking the uterus, the pathologist should ensure that the tumour is sampled in such a way as to ensure accurate staging.

Uterine sarcomas should be extensively sampled since the morphological appearance may vary from area to area. At least one block per centimetre of maximum tumour dimension should be taken,[21] and depending on the morphological features in the original sections, additional sampling may be necessary. Tumours <2 cm in diameter should be blocked in

their entirety. Thorough sampling is particularly important in problematic smooth muscle tumours where some sections are diagnostic of leiomyosarcoma while others are not. This may also be important in identifying areas of carcinoma and thereby confirming a diagnosis of carcinosarcoma. The specific type of high-grade endometrial stromal sarcoma associated with *YWHAE-FAM22* genetic fusion (see section 5.1, Tumour type) may be associated with a component of low-grade endometrial stromal sarcoma, which may be revealed by judicious sampling. With any undifferentiated sarcoma or pure heterologous sarcoma such as rhabdomyosarcoma, extensive sampling must be undertaken to exclude a carcinosarcoma. If possible, some tumour blocks should include the full thickness of the uterine wall. Where the uterine wall is too thick to fit into one cassette, the block should be divided into two or more parts and the cassettes appropriately labelled. At least some of the blocks should be taken to demonstrate the interface of the tumour with the adjacent uninvolved myometrium. Blocks must also be taken to show serosal involvement or the closest area of tumour to the serosa. At least one block of background endometrium should be sampled if possible.

If there is obvious gross cervical involvement, blocks should be taken to demonstrate this. At least two blocks of grossly unremarkable cervix should be taken, one from the anterior and one from the posterior lip. Parametrial connective tissue, where present, should be blocked in its entirety. If the ovaries are macroscopically normal, one or two blocks should be taken depending on their size. If the fallopian tubes are macroscopically normal, one to two sections should be taken of each tube. In addition, any grossly abnormal areas should be sampled.

Where an omentectomy specimen is submitted, this should be subjected to careful macroscopic examination. One block of obvious tumour is adequate in cases where macroscopically visible tumour nodules are present. If the specimen is macroscopically normal, two to four blocks should be taken.

All resected lymph nodes must be sampled for histological examination. Only one block of any grossly involved node is necessary.

The origin/designation of all tissue blocks should be recorded and every block should be individually labelled so that its origin is readily identifiable. This is particularly important should the need for internal or specialist external review arise. The reviewer needs to be clear about the origin of each block to provide an informed specialist opinion. It may be helpful to record the position of tissue blocks on a photograph of the uterus. Recording the origin/designation of tissue blocks also facilitates retrieval of blocks, for example for further immunohistochemical or molecular analysis, research studies or clinical trials.

5 Core data items

5.1 Tumour type

The most common sarcomas occurring in the uterus are leiomyosarcoma, endometrial stromal sarcoma, adenosarcoma and undifferentiated uterine sarcoma.[2,3] A variety of uncommon pure heterologous sarcomas (with no associated epithelial component) also occur, the most common of which is rhabdomyosarcoma. Embryonal rhabdomyosarcoma in the uterus most commonly involves the cervix in women in their 20s and 30s,[22–24] while pleomorphic rhabdomyosarcomas are most common in the corpus in postmenopausal females.[25,26]

It is vitally important to type uterine sarcomas accurately since the behaviour, management and patient outcome differ markedly between the different tumour types. For example, leiomyosarcomas, undifferentiated sarcomas and heterologous sarcomas are, in general, highly aggressive neoplasms with a marked propensity for extra-uterine spread and systemic metastasis. By contrast, low-grade endometrial stromal sarcomas are indolent neoplasms,

which are compatible with long-term survival despite the tendency for late recurrences or metastatic tumour. Adenosarcomas are mixed tumours of low malignant potential containing a benign epithelial and a malignant stromal component, usually of low grade. They are usually polypoid neoplasms that project into the uterine cavity and have a favourable prognosis unless associated with sarcomatous overgrowth or deep myometrial invasion.[27–30]

[Level of evidence – B.]

Uterine sarcomas should be typed according to the 2014 WHO classification[11] (see Appendix B).

It is beyond the scope of this document to provide detailed information regarding the histopathological features of the various uterine sarcomas and the reader is referred to specialist textbooks of gynaecological pathology. A few points are, however, highlighted here for clarification.

In the 2003 WHO classification of endometrial stromal sarcoma, only two subcategories of this tumour were recognised:[31]

- low-grade endometrial stromal sarcoma
- undifferentiated endometrial/uterine sarcoma.

Low-grade endometrial stromal sarcoma is a morphologically low-grade sarcoma, the constituent cells of which generally resemble normal proliferative-type endometrial stromal cells, although a wide range of morphological variations is occasionally found.[32] A network of small arteriole-like vascular channels is a characteristic histological feature. Such neoplasms are usually, but not always, mitotically quite inactive. Low-grade endometrial stromal sarcomas are distinguished from endometrial stromal nodules by having an infiltrative edge and/or exhibiting vascular invasion; they often exhibit widespread myometrial infiltration with a 'tongue-like' pattern and commonly show conspicuous lymphovascular permeation. Many low-grade endometrial stromal sarcomas harbour t(7:17)(p21;q15), which results in fusion between *JAZF1* and *SUZ12(JJAZ1).*[33–35]

[Level of evidence – B.]

The WHO definition of an undifferentiated uterine sarcoma is a tumour arising within the endometrium or myometrium, lacking any resemblance to proliferative-phase endometrial stroma, with high-grade cytological features and no specific differentiation.[11] According to the 2014 WHO 'Blue book', undifferentiated endometrial sarcoma is a synonym for undifferentiated uterine sarcoma but its use is not recommended.[11] Undifferentiated uterine sarcomas usually exhibit marked nuclear pleomorphism, a high mitotic rate and contain areas of necrosis.

More recently, some tumours previously considered to be undifferentiated uterine sarcomas have been shown to be of endometrial stromal derivation (often associated with a component of low-grade endometrial stromal neoplasm)[36,37] and are designated high-grade endometrial stromal sarcomas in the 2014 WHO 'Blue book'.[11] These tumours present as intracavitary polypoid and/or intramural mass(es) and often show extra-uterine extension at the time of diagnosis. Although low-power examination may reveal a similar pattern of infiltrative growth and vasculature to low-grade endometrial stromal sarcoma, these tumours typically have a confluent, permeative and destructive growth pattern with deep myoinvasion;[38] there is usually brisk mitotic activity and necrosis. A subset of these tumours displays specific morphological features and genetic abnormalities. There are usually two morphologically distinctive components that are juxtaposed. A (usually predominant) high-grade, round cell tumour component is present in association with a low-grade spindle cell component with fibromyxoid features; the low-grade component is not present in all cases. The high-grade round cell component may be non-cohesive or may have a nested, pseudopapillary or

pseudoglandular appearance, or a rhabdoid morphology. These tumours harbour the *YWHAE-FAM22* genetic fusion as a result of t(10;17)(q22;p13).[38,39] It is very important to identify these tumours and distinguish them from low-grade endometrial stromal sarcomas because patients have earlier and more frequent recurrences, usually within a year, and are less likely to survive. It is also important to distinguish these from undifferentiated uterine sarcomas.

[Level of evidence – C.]

Uterine tumours resembling ovarian sex cord tumour (UTROSCT)[40] are now included in the WHO classification of 'Endometrial stromal and related tumours'. WHO defines them as 'neoplasms that resemble ovarian sex cord tumours, without a component of recognizable endometrial stroma'. The location of the tumours may be intramural, submucosal or take the form of a polypoid mass that projects into the uterine cavity. Although most tumours are relatively well circumscribed, the incorporation of smooth muscle at their periphery may impart a pseudo-infiltrative tumour border. The tumour cells usually show minimal cytological atypia and have a variable corded, trabecular, nested, sheet-like or sertoliform tubular architecture. Most of the tumour cells are small to medium-sized with scanty cytoplasm, but cells with moderate amounts of eosinophilic or foamy cytoplasm may also be seen.[41] Most UTROSCTs behave in a benign fashion, although very rarely metastasis occurs.[42]

Most uterine smooth muscle neoplasms are obviously benign or malignant. According to WHO, uterine tumours exhibiting smooth muscle differentiation are diagnosed as leiomyosarcoma based on the presence of at least two of the following three histological features: diffuse, moderate to severe nuclear atypia; mitotic count ≥10 per 10 high power fields (HPFs); and tumour cell necrosis.[24] These criteria do not apply to smooth muscle neoplasms of epithelioid or myxoid type, where the criteria for malignancy differ.[43,44] There are occasional neoplasms where it is difficult or impossible to differentiate with confidence between a benign and a malignant smooth muscle lesion. Such tumours can be referred to as 'smooth muscle tumour of uncertain malignant potential (STUMP)'.[45] The WHO definition of a STUMP is 'a smooth muscle tumour with features that preclude an unequivocal diagnosis of leiomyosarcoma, but that do not fulfil the criteria for leiomyoma or its variants, and raise concern that the neoplasm may behave in a malignant fashion'.[11] This category of smooth muscle neoplasm should be diagnosed sparingly and is reserved for smooth muscle neoplasms whose appearance is ambiguous for some reason. For example, in some cases, it may be difficult to determine whether necrosis is of hyaline (infarct) type or coagulative tumour cell type. The category of 'STUMP' should not be used as a 'wastebasket' term for variants of benign smooth muscle neoplasm such as cellular leiomyoma, mitotically active leiomyoma or leiomyoma with bizarre nuclei.

[Level of evidence – C.]

Although some authors have suggested mitotic activity in the stromal component in excess of 1/10 HPFs (i.e. two or more mitoses per 10 HPFs) is required for a diagnosis of adenosarcoma[28,29] and others use a cut-off of 4/10 HPFs,[30] the 2014 WHO 'Blue book' states that even a minimal degree of mitotic activity in the stromal component in the presence of cellularity and typical architectural features warrants a diagnosis of adenosarcoma.[11] This pragmatic approach recognises that there are problems associated with identifying and counting mitotic figures and that the number of mitoses may be variable from area to area. In practice, therefore, if the characteristic leaf-like architecture of adenosarcoma is present with periglandular cuffing resulting in a cambium layer, a diagnosis of adenosarcoma is made with mitotic counts <2 per 10 HPFs or even in the absence of mitotic figures.[29,46] Sarcomatous overgrowth in adenosarcoma is defined as the presence of pure sarcoma, usually high grade and without an epithelial component, occupying at least 25% of the tumour,[47] and which may include heterologous elements.

As stated in the introduction, carcinosarcomas (malignant mixed Mullerian tumours) are now known to be epithelial neoplasms that have undergone sarcomatous metaplasia, the epithelial elements being the driving force.[7,8] Accordingly, they are a subtype of high-grade endometrial carcinoma. Undifferentiated carcinoma has recently been highlighted as an aggressive form of uterine carcinoma that may be associated with a more differentiated endometrioid component, as part of a mixed carcinoma (mixed endometrioid and undifferentiated carcinoma or dedifferentiated endometrioid carcinoma).[48] If undifferentiated carcinoma occurs in pure form, there may be problems in distinguishing it from undifferentiated sarcoma.[48]

5.2 Mitotic count

A single study investigating the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system (see 'Non-core data items' below) for uterine sarcomas found mitotic count to be a prognostic indicator in leiomyosarcomas.[49] The prognostic impact of mitotic count in early stage uterine leiomyosarcomas has also been consistently shown in other studies.[2,50–54]

[Level of evidence – B.]

We recommend that the mitotic count per 10 HPF, as evaluated using the criteria in Appendix C, should be given for all uterine sarcomas, although in the absence of deep myometrial involvement or sarcomatous overgrowth, this does not seem to be of prognostic significance or of value in predicting recurrence in adenosarcoma. Consistent documentation of this parameter may facilitate future studies investigating the prognostic value of mitotic counts in uterine sarcomas.

5.3 Depth of myometrial invasion

The depth of myometrial invasion is important in the substaging of stage I adenosarcomas (tumour confined to the uterus) and is a risk factor for recurrence.[11] Stage IA tumours are limited to the endometrium or endocervix with no myometrial involvement, stage IB equates to less than or half of myometrial invasion and stage IC equates to more than one half myometrial invasion. This staging system is similar to the 1988 FIGO staging system for carcinomas of the uterine corpus. Since low-grade endometrial stromal sarcomas, leiomyosarcomas and most other uterine sarcomas are predominantly myometrial-based lesions, myometrial invasion per se is not used in the staging of these neoplasms.

[Level of evidence – C.]

5.4 Serosal involvement

The presence or absence of uterine serosal involvement should be documented. One study showed serosal involvement to be of adverse prognostic significance in uterine leiomyosarcomas.[4]

[Level of evidence – C.]

5.5 Tumour-free distance to uterine serosa

This term refers to the distance between the deepest point of tumour within the myometrium and the nearest serosal surface.

[Level of evidence – GPP.]

5.6 Sarcomatous overgrowth

The presence or absence of sarcomatous overgrowth in adenosarcoma (as defined previously) should be documented. Metastatic disease is usually associated with tumours in which there is sarcomatous overgrowth.[55]

[Level of evidence – B.]

5.7 Cervical involvement

If the origin of a uterine leiomyosarcoma is equivocal and it is difficult to establish whether the tumour has arisen from the cervix or the uterine isthmus, deference should be given to a corpus origin.[56] Although cervical involvement is not included in the 2009 FIGO staging systems for uterine sarcomas, the presence or absence of this should be recorded. A recent study showed that the five-year survival of stage I undifferentiated sarcoma is worse in patients with than without cervical involvement (49.6% versus 24.4%)[20] and cervical involvement by leiomyosarcoma has an adverse influence on prognosis. Cervical involvement is used in the normogram of the prognostic model developed by the Memorial Sloan-Kettering Cancer Center to predict five-year overall survival for patients with uterine leiomyosarcoma.[57,58]

[Level of evidence – B.]

5.8 Parametrial involvement

The presence or absence of parametrial involvement should be documented.

[Level of evidence – GPP.]

5.9 Lymphovascular invasion

The presence or absence of lymphovascular invasion should be documented. Extensive involvement of lymphovascular channels is often a feature of low-grade endometrial stromal sarcoma and sometimes of leiomyosarcoma and undifferentiated sarcoma. Adenosarcomas rarely exhibit lymphovascular invasion unless associated with deep myometrial invasion or sarcomatous overgrowth. Lymphovascular invasion has been shown to be of adverse prognostic significance in early stage uterine leiomyosarcoma.[53]

[Level of evidence – C.]

5.10 Adnexal involvement

The presence or absence of ovarian or fallopian tube involvement should be documented. Adnexal involvement affects the tumour stage (FIGO stage IIA) and may occur as a result of direct extension or metastatic spread of tumour. Tumour stage remains the most powerful prognostic factor for uterine sarcomas.[11]

5.11 Tumour circumscription

The nature of the tumour interface with the surrounding myometrium should be documented and correlated with the gross features. Many low-grade endometrial stromal sarcomas exhibit a diffusely infiltrative pattern of myometrial invasion. In early stage uterine leiomyosarcomas, well-circumscribed tumours have been shown to have a better prognosis than those in which the tumour margins are poorly circumscribed.[53]

[Level of evidence – C.]

5.12 Peritoneal washings

The identification of malignant cells in peritoneal washings does not influence the FIGO staging of uterine sarcomas, but the presence or absence of tumour cells should be documented if washings have been performed. The significance of positive peritoneal washings in an individual case should be discussed at the gynaecological oncology MDT meeting. One study found negative peritoneal cytology to be associated with higher survival rates in uterine sarcomas.[59]

[Level of evidence – C.]

5.13 Lymph nodes

Pelvic or para-aortic lymph node involvement upstages uterine sarcomas to stage IIIC. The number of nodes retrieved from each site and the number of lymph nodes containing metastatic tumour must be recorded. It is useful to document the presence of extranodal spread, although this is not of proven prognostic significance. Lymph node metastasis was identified in 6.6% and 11% of two series of patients with uterine leiomyosarcoma who underwent lymphadenectomy.[60,61] In the study by Kapp *et al*, the five-year survival was 26% in patients who had positive nodes, compared to 64% with negative nodes.[61]

[Level of evidence – B.]

5.14 Involvement of pelvic tissues (other than the uterus and adnexa)

Other sites of pelvic tumour involvement should be documented since this equates to FIGO stage IIB.

5.15 Involvement of omentum and other abdominal tissues

This should be documented. FIGO stage IIIA equates to one site of abdominal involvement and IIIB to more than one site.

5.16 Staging and SNOMED coding

Tumours should be staged according to the 2009 FIGO staging systems (Appendix A).[5,6] Although the provisional tumour stage should be included in the pathology report, the final definitive stage must be determined at the MDT meeting, taking into account all clinical, radiological and pathological findings. All tumours should be assigned appropriate SNOMED codes (Appendix B).

5.17 Summary of core data items

The following core data items should be included:

- macroscopic size of tumour
- tumour circumscription
- tumour type
- depth of myometrial invasion (for adenosarcoma)
- sarcomatous overgrowth (for adenosarcoma)
- mitotic count per 10 HPF
- serosal involvement
- tumour-free distance to uterine serosa

- cervical involvement
- parametrial involvement
- lymphovascular invasion
- adnexal involvement
- peritoneal washings (whether taken or not, positive or negative for tumour cells)
- lymph nodes (whether sampled or not, number retrieved from each site [pelvic and para-aortic] and number involved by tumour)
- other pelvic tissues (whether involved or not)
- omentum and other abdominal tissues (whether sampled or not, presence or absence of metastasis)
- tumour stage.

6 Non-core data items

These are data items that are of uncertain prognostic or therapeutic relevance and that are not used for staging. They may be included as a comment in the dataset or within an accompanying text report. They might include:

- uterine weight
- amount of tumour necrosis (none, <50%, >50%)
- presence of extranodal spread
- weight of the omentum
- tumour grading.

One of the most contentious areas in the pathological reporting of uterine sarcomas is the grading of leiomyosarcomas. There is no formal grading system for uterine leiomyosarcomas but oncologists often ask for a grade. The choice of adjuvant therapy may depend on whether the neoplasm is 'high' or 'low' grade. For example, some oncologists administer adjuvant radiotherapy for 'low-grade' leiomyosarcomas confined to the uterus and adjuvant chemotherapy for 'high-grade' leiomyosarcomas, although there is little or no evidence base for this. The FNCLCC has developed a prognostic grading system that has been validated for soft tissue sarcomas (Appendix C);[62,63] this grading system has been adopted by the WHO[64] and is used in the College's dataset on soft tissue sarcomas.[10] At present, there is no evidence that this grading system is of prognostic significance in uterine leiomyosarcomas; only a single study has evaluated this grading system in uterine sarcomas and it found that this system could not be used as a prognostic indicator.[49] In this study, stage and mitotic count were the only factors that had an influence on survival and relapse of uterine leiomyosarcomas.[49] We believe that there is an urgent need for large-scale studies evaluating the prognostic significance of this, and other grading systems, in uterine leiomyosarcomas. If, however, a clinician requests formal grading of a uterine leiomyosarcoma, in the absence of any validated system of grading, we suggest that the FNCLCC system can be used, if locally agreed. A note should be included in the pathology report that this is intended only as a general guide to management and is not evidence-based. This system uses three criteria – tumour differentiation, mitotic count and tumour necrosis – and an overall score is arrived at based on the summation of the three individual scores, as detailed in Appendix C. Mitoses should be counted in the most mitotically active areas in ten successive HPFs using a x40 objective and a standard x10 eyepiece.

Low-grade endometrial stromal sarcomas are by definition low grade, and similarly high-grade endometrial stromal sarcomas and undifferentiated sarcomas are high grade.

7 WHO classification of uterine sarcomas and SNOMED coding

Primary uterine sarcomas should be subtyped according to the 2014 WHO classification[11] and coded using SNOMED codes (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 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.

8 Reporting of small biopsy specimens

Some uterine sarcomas are diagnosed on endometrial biopsy obtained using an outpatient endometrial sampling procedure or by cervical dilatation and endometrial curettage under general anaesthesia. However, since these are often myometrial-based masses, biopsies may not yield diagnostic material. In some cases, image-guided needle core biopsies are undertaken on suspected uterine sarcomas. In other cases, no preoperative biopsy will have been undertaken, and the sarcoma is diagnosed in a hysterectomy, or occasionally myomectomy, specimen for presumed uterine fibroids.

When handling endometrial biopsy specimens, a sieve or mesh basket may be useful to ensure that all the material is retrieved. It may be useful to weigh the submitted tissue. All the submitted tissue should be processed for histology. The presence of a grossly obvious tumour should be recorded, as should the presence of obvious necrosis.

Where the biopsy shows features of a sarcoma, the report should clearly specify the subtype of tumour present. Particularly when only a small amount of tissue is present, it is possible that the sarcomatous component in the biopsy may represent the mesenchymal component of a carcinosarcoma, especially if this comprises undifferentiated sarcoma or rhabdomyosarcoma. However, it is relatively uncommon for only the sarcomatous component of a carcinosarcoma to be represented in biopsy material.

It is virtually impossible on an endometrial biopsy specimen to distinguish between an endometrial stromal nodule and a low-grade endometrial stromal sarcoma since this depends on assessment of the interface with the surrounding myometrium. In such cases, the term endometrial stromal neoplasm should be used with a notation that the differential diagnosis is between an endometrial stromal nodule and a low-grade endometrial stromal sarcoma.

In some cases, the morphological appearances in a biopsy may be considered suspicious but not diagnostic of a sarcoma. For example, the tissue represented may be extremely scanty or necrotic or include material from an obvious smooth muscle neoplasm with atypical features that are not diagnostic of malignancy. This should be clearly stated on the pathology report. In such cases, repeat biopsy may be useful to obtain further diagnostic tissue. Radiological examination may also assist in determining whether the lesion is likely to be benign or malignant.

9 Reporting of frozen sections

The use of frozen sections varies considerably among different centres in the United Kingdom.[65] Intraoperative frozen sections may be performed in patients with suspected uterine sarcoma to determine the nature of a clinically or radiologically suspicious uterine mass. This may be of value in dictating the need for full surgical staging. Frozen sections

may also be used to evaluate suspicious lymph nodes or suspected extra-uterine tumour deposits.

It is important that clinicians who request frozen sections are cautioned about the potential limitations of the procedure. For example, given the problems with assessment of cytological atypia and mitotic activity in frozen sections, it may be impossible to determine whether a smooth muscle neoplasm is benign or malignant, or to ascertain the morphological type of a high-grade sarcoma. When the morphological appearances in the sections examined by frozen section suggest an undifferentiated sarcoma or a rhabdomyosarcoma, the possibility of the tumour representing the sarcomatous component of a carcinosarcoma should be borne in mind.

10 Specific aspects of individual tumours not covered elsewhere

Immunohistochemistry can be of use in certain situations in the evaluation of uterine sarcomas. It is beyond the scope of this document to discuss in detail the uses of immunohistochemistry in the evaluation of uterine mesenchymal lesions and the reader is referred to several reviews.[66–69] The results of immunohistochemistry should always be interpreted in conjunction with the clinical features, gross and microscopic findings.

Leiomyosarcomas usually express smooth muscle markers desmin, smooth muscle actin and h-caldesmon. This may be useful in diagnosis and in distinguishing leiomyosarcomas from other neoplasms such as undifferentiated sarcoma. However, smooth muscle actin immuno-reactivity in a high-grade uterine sarcoma is not diagnostic of a leiomyosarcoma and immunopositivity with this marker may occur in undifferentiated sarcoma. Additionally, some 'high-grade' leiomyosarcomas may be only focally positive, or even negative, with desmin and h-caldesmon, as may rare types of leiomyosarcoma such as epithelioid and myxoid leiomyosarcoma.

Immunohistochemistry plays a limited role in the distinction between a benign and malignant uterine smooth muscle neoplasm, this being based on standard histopathological criteria. Several studies have investigated the value of cell cycle-related markers, including p53, MIB1 and p16, in the distinction between a benign and a malignant uterine smooth muscle neoplasm.[70–73] While leiomyosarcomas overall exhibit a much higher MIB1 proliferation index than leiomyomas and are more likely to be diffusely positive with p53 and p16, these markers may not be of value in an individual case, especially in a problematic smooth muscle neoplasm that exhibits intermediate morphology between a typical benign leiomyoma and an obvious leiomyosarcoma. It has been suggested that diffuse p16 immunoreactivity in a STUMP may be a worrisome feature and a predictor of possible adverse behaviour, but this needs to be substantiated by larger studies.[73,74] The cell cycle-related markers listed may also be useful in the distinction between a leiomyoma with bizarre nuclei (formerly termed symplastic, bizarre, pleomorphic or atypical leiomyoma) and diffuse severe nuclear atypia and a 'high-grade' leiomyosarcoma.[73,74] The former exhibits a low MIB1 proliferation index and negative or focal immunoreactivity with p16, while the latter typically exhibits a high MIB1 proliferation index and often diffuse positivity with p16. p53 may be diffusely positive in both. Uterine leiomyosarcomas expressing low levels of MIB1, p53 and p16 and high levels of Bcl-2 are less likely to recur and have a better outcome than those that highly express the former three markers and which are Bcl-2 negative.[75]

[Level of evidence – C.]

Hormone receptor (oestrogen receptor [ER] and progesterone receptor [PR]) expression may be of value in the distinction between benign and malignant uterine smooth muscle neoplasms, since the former are usually positive and the latter are often negative.[76,77] However, again this is unlikely to be of value in problematic cases with intermediate morphology and a significant percentage of uterine leiomyosarcomas are hormone receptor

positive, at least focally.[76,77] Studies suggest that uterine leiomyosarcomas exhibiting greater than 10% hormone receptor expression are associated with an improved prognosis.[78]

In the newly described subset of high-grade endometrial stromal sarcoma with *YWHAE-FAM22* genetic fusion, the high-grade component is typically CD10, ER and PR negative, and shows variable, but often high, expression of cyclin D1.[79] The high-grade component is also sometimes CD99 and CD117 (c-Kit) positive but DOG1 negative. The associated low-grade component is usually, but not always, CD10, ER and PR positive, CD99 and CD117 negative and exhibits low expression of cyclin D1.

Most, but not all, low-grade endometrial stromal sarcomas are diffusely positive for CD10 and this may be useful in diagnosis when used as part of a panel,[80–82] although CD10 is a rather non-specific marker that is positive in a wide range of neoplasms.[83] It may be difficult, especially on a biopsy specimen, to distinguish between an endometrial stromal neoplasm and a cellular or highly cellular leiomyoma. In this distinction, CD10 may be of value, although some cellular leiomyomatous neoplasms are positive. Desmin and h-caldesmon may also be useful, since most cellular leiomyomatous neoplasms are positive while most endometrial stromal neoplasms are negative, although occasional cases are positive. ER and PR are positive in most low-grade endometrial stromal sarcomas and this may be useful therapeutically as progestogens, aromatase inhibitors or gonadotropin-releasing hormone agonists are sometimes used as adjuvant therapy.[84] Bcl-2 is positive in many endometrial stromal neoplasms, while CD34 is usually negative.[85] Cytokeratins are positive in a significant percentage of low-grade endometrial stromal sarcomas, often with a punctate cytoplasmic pattern of immunoreactivity.[86] Sex cord-like elements within endometrial stromal neoplasms exhibit a variable immunophenotype. They may be positive with epithelial and smooth muscle markers and, in some cases, exhibit immunoreactivity, usually focal, with markers of ovarian sex cord neoplasms, including inhibin, calretinin and CD56.

UTROSCT typically exhibits a polyphenotypic immunophenotype and may express epithelial, smooth muscle and sex cord markers (calretinin, inhibin, CD99 and Melan-A), as well as WT1 and hormone receptors.[41,87]

Undifferentiated uterine sarcomas composed of epithelioid cells may exhibit considerable morphological overlap with undifferentiated carcinomas. Recent studies have shown that undifferentiated endometrial carcinomas are not uncommon. It is often focally, but intensely, positive for EMA and cytokeratins, especially cytokeratin 18, and this may be useful in the distinction from undifferentiated sarcomas.[48] p53 is reported to be important in the pathogenesis of undifferentiated uterine sarcomas and is often highly expressed in these neoplasms.[88] This is in contrast to low-grade endometrial stromal sarcomas, which exhibit 'wild-type' p53 expression and do not generally harbour *TP53* mutations or other abnormalities.[88]

In most adenosarcomas with a low-grade stromal component without sarcomatous overgrowth, the stromal element expresses ER, PR, CD10 and WT1, p53 is 'wild type' and there is a low MIB1 proliferation index.[28–30] Thus, the immunophenotype resembles that of low-grade endometrial stromal sarcoma. Smooth muscle actin and desmin may also be positive. In areas of high-grade sarcoma and of sarcomatous overgrowth, the mesenchymal component exhibits a higher MIB1 proliferation index and may be diffusely p53 positive. There is usually loss of expression of the cell differentiation markers ER, PR and CD10, the immunophenotype being similar to that of an undifferentiated sarcoma. Rhabdomyosarcomatous elements in adenosarcomas express desmin and there is nuclear staining, which is usually focal, with the skeletal muscle markers myogenin and myoD1. Sex cord-like elements may express inhibin and calretinin.

Specific skeletal muscle markers, such as myogenin and myoD1, may assist in confirming a rhabdomyosarcoma or rhabdomyosarcomatous elements in an adenosarcoma or carcinosarcoma. Desmin is a pan-muscle marker that does not assist in differentiating between a

smooth muscle and a skeletal muscle neoplasm. A variety of other benign and malignant mesenchymal neoplasms rarely occur in the uterus. The immunophenotype of these is identical to when they occur at more usual sites. Rare mesenchymal tumours that have been reported in the uterus and may be mistaken for a smooth muscle neoplasm include inflammatory myofibroblastic tumours, which are usually ALK-1 positive,[89] gastrointestinal stromal tumours, which are usually CD117 (c-kit), DOG-1 and CD34 positive,[90,91] and perivascular epithelioid cell tumours (PEComa), which express HMB45 as well as smooth muscle markers.[92]

Increasingly, molecular studies are proving to be of value in the diagnosis of uterine sarcomas and these are becoming routinely available in specialist centres. Many, but not all, of the techniques can be performed on formalin-fixed, paraffin-processed tissue. A recurrent t(7;17)(p15;q21) translocation resulting in a JAZF1-JJAZ1 gene fusion has been demonstrated in over 60% of endometrial stromal tumours, including its variants.[34,35,93] A group of high-grade endometrial stromal sarcomas harbour the *YWHAE-FAM22* genetic fusion as a result of t(10;17)(q22;p13).[38,39] Molecular studies may also be useful in confirming diagnosis in problematic cases. Other sarcomas that occasionally occur in the uterine corpus or cervix or at other sites in the female genital tract harbour consistent molecular abnormalities, for example alveolar rhabdomyosarcoma, desmoplastic small round cell tumour and neoplasms in the Ewing family of tumours.

11 Criteria for audit

The following criteria may be assessed in periodic reviews of histological reports on uterine sarcomas:

- completeness of histopathology reports, expressed as the average proportion of core data items recorded or as proportion of reports that include 100% of the core data items
  - standard: all reports contain 100% of the items
- size distribution of leiomyosarcomas, mitotic counts and grading for correlation with clinical outcome
- percentage of leiomyosarcomas and undifferentiated sarcomas with cervical, lymph node and/or omental involvement and correlation with clinical outcome.

Audits recommended by RCPath as key performance indicators (KPIs) (see *Key Performance Indicators – Proposals for implementation*, July 2013, on www.rcpath.org/clinical-effectiveness/kpi) are as follows:

- 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 the College cancer datasets. English Trusts are required to implement the structured recording of core pathology data in the COSD.
  - 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
- monitoring of delayed reports: a published report on the number and percentage cases reported after 20 days must be provided. (KPI 6.5 for monitoring delayed cellular pathology reports requires there to be a documented system in place to identify, manage and report cases remaining unreported longer than is anticipated. Exception reporting

must be undertaken of all cases [including decalcified cases] remaining unreported after 20 calendar days.)

- standard: 100% compliance.

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Appendix A 2009 FIGO staging systems for uterine sarcomas

Uterine leiomyosarcoma and endometrial stromal sarcoma

Stage I	Tumour limited to uterus
IA	≤5 cm
IB	>5 cm
Stage II	Tumour extends beyond the uterus, within the pelvis
IIA	Adnexal involvement
IIB	Involvement of other pelvic tissues
Stage III	Tumour invades abdominal tissues (not just protruding into the abdomen)
IIIA	One site
IIIB	More than one site
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IV	
IVA	Tumour invades bladder and/or rectum
IVB	Distant metastasis

Uterine adenosarcoma

Stage I	Tumour limited to uterus
IA	Tumour limited to endometrium/endocervix with no myometrial invasion
IB	Less than or equal to half myometrial invasion
IC	More than half myometrial invasion
Stage II	Tumour extends beyond the uterus, within the pelvis
IIA	Adnexal involvement
IIB	Involvement of other pelvic tissues
Stage III	Tumour invades abdominal tissues (not just protruding into the abdomen)
IIIA	One site
IIIB	More than one site
IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IV	
IVA	Tumour invades bladder and/or rectum
IVB	Distant metastasis

Appendix B WHO classification of malignant or potentially malignant uterine mesenchymal tumours and SNOMED codes

Morphological codes	SNOMED code	SNOMED CT terminology	SNOMED CT code
Smooth muscle tumours			
Smooth muscle tumour of uncertain malignant potential	M-88971	Smooth muscle tumour (morphologic abnormality	75109009
Leiomyosarcoma	M-88903	Leiomyosarcoma, no subtype (morphologic abnormality)	51549004
• Epithelioid leiomyosarcoma	M-88913	Epithelioid leiomyosarcoma (morphologic abnormality)	42392001
• Myxoid leiomyosarcoma	M-88963	Myxoid leiomyosarcoma (morphologic abnormality)	16090008
Endometrial stromal and related tumours			
Low-grade endometrial stromal sarcoma	M-89313	Endometrial stromal sarcoma, low grade (morphologic abnormality)	128726006
High-grade endometrial stromal sarcoma	M-89303	Endometrial stromal sarcoma, high grade (morphologic abnormality)	70555003
Undifferentiated uterine sarcoma	M-88053	Undifferentiated sarcoma (morphologic abnormality)	128734000
Uterine tumour resembling ovarian sex cord tumour (UTROSCT)	M-85901	Sex cord-stromal tumour, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	71440001
Miscellaneous mesenchymal tumours			
Rhabdomyosarcoma	M-89003	Rhabdomyosarcoma, no subtype (morphologic abnormality)	30924005
Perivascular epithelioid cell tumour			
• Benign	M-87140	Perivascular epithelioid tumor, benign (morphologic abnormality)	703604002
• Malignant	M-87143	Perivascular epithelioid tumor, malignant (morphologic abnormality)	703605001
Mixed epithelial and mesenchymal tumours			
Adenosarcoma	M-89333	Adenosarcoma (morphologic abnormality)	31470003

SNOMED P (Procedure) codes

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 French Federation of Cancer Centres (FNCLCC) grading of soft tissue sarcomas

Tumour differentiation

Score	1	
	2	
	3	

Mitosis count (1 HPF = 0.1734 sq mm)

Score	1	0–9/10 HPF
	2	10–19/10 HPF
	3	≥20/10 HPF

Microscopic tumour necrosis

Score	0	No necrosis
	1	<50% tumour necrosis
	2	>50% tumour necrosis

Histological grade

Grade 1	Total score 2 or 3
Grade 2	Total score 4 or 5
Grade 3	Total score 6, 7 or 8

Appendix D Reporting proforma for uterine sarcomas in hysterectomy specimens

Surname: ..... Forenames: .....Date of birth: .....

Patient identifier (CHI/NHS no): ..... Hospital: .....Hospital no: .....

Date of receipt: ..... Date of reporting: .....Report no: .....

Pathologist: ..... Surgeon: .....

Gross description

Specimen type†: Hysterectomy ☐ Myomectomy ☐ Other (specify).....

Dimensions of uterus: Length:……mm Transverse……..mm Antero-posterior…….mm

Adnexa: Received ☐ Not received ☐ Normal ☐

Abnormal ☐ (if abnormal, specify.....)

Maximum dimension of tumour†:…….....mm Tumour circumscribed: Yes ☐ No ☐

Cervical involvement: Yes ☐ No ☐ Serosal involvement: Yes ☐ No ☐

Myometrial invasion (adenosarcoma only): Present ☐ Not identified ☐

Omentum: Received ☐ Not received ☐ Normal ☐

Abnormal ☐ (if abnormal, specify.....)

Lymph nodes: Received ☐ Not received ☐

Histology

Tumour type†: Leiomyosarcoma ☐ Low-grade endometrial stromal sarcoma ☐

Undifferentiated uterine sarcoma ☐ High-grade endometrial stromal sarcoma ☐

Adenosarcoma ☐ Pure heterologous sarcoma ☐

Other ☐ (specify…….…….....) (specify subtype……..…….....)

For adenosarcoma

Depth of myometrial invasion†: None ☐ ≤50% ☐ >50% ☐

Sarcomatous overgrowth: Present ☐ Not identified ☐

For all sarcomas

Mitotic count/10 HPF: 0–9 ☐ 10–19 ☐ ≥20 ☐

Serosal involvement†: Present ☐ Not identified ☐ Cannot be assessed ☐

Tumour-free distance to uterine serosa†: ….....mm

Cervical involvement†: Present ☐ Not identified ☐ Cannot be assessed ☐

Parametrial involvement†: Present ☐ Not identified ☐ Cannot be assessed ☐

Lymphovascular invasion†: Present ☐ Not identified ☐ Cannot be assessed ☐

Adnexal involvement: Present ☐ Not identified ☐ Cannot be assessed ☐

Peritoneal washings†: Positive ☐ Negative ☐ Not submitted ☐

Pelvic lymph nodes†: Total no. nodes …… No. positive nodes ……

Para-aortic nodes†: Total no. nodes …… No. positive nodes ……

Omentum (if received) †: Not involved ☐ Involved by tumour ☐

Other pelvic or abdominal tissues: Not involved ☐ Involved by tumour ☐ (if yes, specify.....)

Provisional FIGO stage† ……..……

SNOMED codes†: T……..… M……..…...

Pathologist: .....…… Date: ……...../……../……..

Note:

†Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 8.

Appendix E Reporting proforma for uterine sarcomas in hysterectomy specimens in list format

Element name	Values	Implementation notes
Specimen type	Single selection value list: • Hysterectomy • Myomectomy • Other	
Specimen type, specify	Free text	Only applicable if 'Specimen type, Other' is selected.
Length of uterus	Size in mm	
Transverse dimension of uterus	Size in mm	
Antero-posterior dimension of uterus	Size in mm	
Adnexa received	Single selection value list: • Received • Not received	
Adnexal abnormality	Single selection value list: • Normal • Abnormal	Only applicable if 'Adnexa, Received' is selected.
Adnexal abnormality, specify	Free text	Only applicable if 'Adnexa, Abnormal' is selected.
Maximum dimension of tumour	Size in mm	
Tumour circumscribed	Single selection value list: • Yes • No	
Cervical involvement, macroscopic	Single selection value list: • Yes • No	
Serosal involvement, macroscopic	Single selection value list: • Yes • No	
Myometrial invasion	Single selection value list: • Present • Not identified	
Omentum received	Single selection value list: • Received • Not received	
Omental abnormality	Single selection value list: • Normal • Abnormal	Only applicable if 'Omentum, Received' is selected.

Omental abnormality, specify	Free text	Only applicable if 'Omentum, Abnormal' is selected.
Lymph nodes received	Single selection value list: • Received • Not received	
Tumour type	Single selection value list: • Leiomyosarcoma • Low-grade endometrial stromal sarcoma • Undifferentiated uterine sarcoma • High-grade endometrial stromal sarcoma • Adenosarcoma • Pure heterologous sarcoma • Other	
Pure heterologous sarcoma, specify	Free text	Only applicable if 'Tumour type, Pure heterologous sarcoma' is selected.
Other specify	Free text	Only applicable if 'Tumour type, Other' is selected.
Depth of myometrial invasion	Single selection value list: • None • ≤50% • >50%	Only applicable if 'Tumour type Adenosarcoma' is selected.
Sarcomatous overgrowth	Single selection value list: • Present • Not identified	Only applicable if 'Tumour type, Adenosarcoma' is selected.
Mitotic count/10 HPF	Single selection value list: • 0–9 • 10–19 • ≥20	
Serosal involvement, microscopic	Single selection value list: • Present • Not identified • Cannot be assessed	
Tumour-free distance to uterine serosa	Size in mm	

Cervical involvement, microscopic	Single selection value list: • Present • Not identified • Cannot be assessed	
Parametrial involvement	Single selection value list: • Present • Not identified • Cannot be assessed	
Lymphovascular invasion	Single selection value list: • Present • Not identified • Cannot be assessed	
Adnexal involvement, microscopic	Single selection value list: • Present • Not identified • Cannot be assessed	
Peritoneal washings	Single selection value list: • Positive • Negative • Not submitted	
Pelvic nodes, total	Numeric	
Pelvic nodes, positive	Numeric	
Para-aortic, total	Numeric	
Para-aortic, positive	Numeric	
Omentum (if received)	Single selection value list: • Not involved • Involved by tumour • Not applicable	Not applicable if 'Omentum, Not received' is selected.
Other pelvic or abdominal tissues	Single selection value list: • Not involved • Involved by tumour	
Other pelvic or abdominal tissues, specify	Free text	Only applicable if 'Other pelvic or abdominal tissues, Involved by tumour' is selected.

Provisional FIGO stage	Single selection value list: • IA • IB • IC • IIA • IIB • IIIA • IIIB • IIIC • IVA • IVB	
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 Summary table – Explanation of levels of evidence

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

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

Appendix G 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. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard		Section of dataset
Scope and purpose		
1	The overall objective(s) of the guideline is (are) specifically described	1
2	The health question(s) covered by the guideline is (are) specifically described	1
3	The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword, 1
Stakeholder involvement		
4	The guideline development group includes individuals from all the relevant professional groups	1
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	1
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 used for formulating the recommendations are clearly described	Foreword
11	The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword
12	There is an explicit link between the recommendations and the supporting evidence	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	5–6
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–E
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