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

Standards and datasets for reporting cancers

Dataset for histological reporting of endometrial cancer

February 2014

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Unique document number	G090
Document name	Dataset for histological reporting of endometrial cancer
Version number	4
Produced by	All authors are consultant histopathologists, actively engaged in the diagnosis and multidisciplinary care of patients with gynaecological cancers, and in professional associations that promote research and guideline development on their diagnosis and treatment. All have published widely in the field.
Date active	February 2014
Date for review	February 2015
Comments	In accordance with the College's pre-publications policy, this document was on The Royal College of Pathologists' website for consultation from 18 December 2013 to 22 January 2014. Fifty-six items of feedback were received and the authors considered them and amended the document as appropriate. Please email publications@rcpath.org if you wish to see the responses and comments. This document supersedes the 2010 document, *Dataset for histological reporting of endometrial cancer (3rd edition).* **Dr Suzy Lishman** **Vice-President for Advocacy and Communications**

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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. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

Each dataset contains **core data items** that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 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 are clearly defined to allow the unambiguous recording of data.

The following stakeholder groups have been consulted:

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

Evidence review

The information used to develop this dataset was collected from electronic searches of databases including databases of systematic reviews, journals (PubMed), conference proceedings, Cochrane review, NICE guidance for relevant evidence and systematic reviews up to September 2013. The recommendations are in line with those of other national pathology organisations (College of American Pathologists, The Royal College of Pathologists of Australasia and Canadian Partnership against Cancer) and are detailed in the dataset produced by the International Collaboration on Cancer Reporting (ICCR)[1] at www.rcpa.edu.au/Publications/StructuredReporting/ICCR.htm.

Modified SIGN guidance has been used to grade the evidence (Appendix E) and the grade is indicated in the text. Consensus of evidence in the dataset has been achieved by expert review during the consultation process. Gaps in evidence were identified by Fellows via feedback received from consultation.

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 to 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 sub-specialty adviser to the College, to consider whether or not the dataset needs to be revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Specialty Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken, whereby a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the short notice of

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

The dataset has been reviewed by the Working Group on Cancer Services and was placed on the College website for consultation with the membership from 18 December 2013 to 22 January 2014. All comments received from the Working Group and membership have been addressed by the authors to the satisfaction of the Chair of the Working Group and the Vice-President for Advocacy and Communications.

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

1 Introduction

This dataset includes a brief account of the salient features of the major subtypes of endometrial carcinoma but not a detailed description, for which the reader is referred to standard textbooks. Rare types of endometrial carcinoma, tumours metastatic to the endometrium and endometrial hyperplasia (considered a precursor of endometrioid adenocarcinoma) are not discussed. Mesenchymal tumours of the uterus are covered in a separate College dataset (www.rcpath.org/publications-media/publications/datasets/uterine-sarcomas.htm).

The clinical application of these guidelines is important for the following reasons.

a. Certain features of endometrial carcinoma, such as the type and grade of carcinoma, the presence of cervical involvement, depth of myometrial invasion, serosal breach and lymph node involvement, will determine the type of surgery performed, whether adjuvant therapy will be administered and the choice of adjuvant therapy.

b. The core data items provide accurate pathological information that can be used in conjunction with clinical data to determine prognosis.

c. Accurate typing of endometrial cancers will allow epidemiological information to be collected with regard to cancer subtypes and association with genetic syndromes.

d. The collection of core data items such as histopathological type, tumour stage, etc., are mandatory for enrolment of patients into trials. Use of a structured reporting form allows easy extraction of the necessary information.

Changes since the second edition

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

a. Core and non-core items: vaginal involvement and omental involvement have been added to the microscopic core data items. Peritoneal involvement, peritoneal cytology and cervical surface and gland/crypt involvement have been moved to non-core items on the basis of the FIGO 2009 staging.

b. Staging: specific mention has been made that vascular invasion without tissue invasion does not affect staging.

c. Type of carcinoma: additional information has been provided about endometrioid adenocarcinoma with squamous differentiation, neuroendocrine and undifferentiated carcinomas.

d. Myometrial invasion: it is recognised that assessment of this is difficult and the range of methods of evaluating myoinvasion are discussed.

e. Lymphovascular invasion: artefactual vascular invasion secondary to intrauterine balloon manipulators is discussed.

Target users and health benefits of this guideline

The dataset is primarily intended for use by consultant and trainee pathologists when reporting on resection specimens of endometrial carcinoma. Surgeons and oncologists can refer to the dataset when interpreting histopathology reports. The datasets should be available at the multidisciplinary team meeting (MDTs) for recording of accurate information and to inform discussions. The datasets can be used to assist in clinical trials. Many of the data items are collected for epidemiological analysis by Cancer Registries on behalf of the National Cancer Intelligence Network.

2 Clinical information required on the specimen request form

This should include patient demographic details, clinical presentation, results of previous biopsies and radiological investigations for tumour staging, and details of the surgical procedure especially the type of hysterectomy performed. It is also desirable to include details of any family history of cancer and relevant hormonal therapy. The nature of surgical specimens from multiple sites should be carefully recorded and the specimen pots should be labelled to correspond to the specimen details on the request form and appropriately labelled as to site of origin.

3 Preparation of specimen before dissection

The usual treatment for endometrial cancer is hysterectomy and bilateral salpingo-oophorectomy. 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 in order to facilitate fixation of the tumour and preservation of tumour morphology. Endometrial carcinomas are particularly susceptible to autolysis. Good preservation of tumour morphology is of crucial importance for accurate subtyping and grading of any tumour. If the ovaries and fallopian tubes are normal, they can be allowed to fix intact. In some cases, one or both ovaries may contain tumour (either primary or metastatic). In these cases, the ovaries should be handled in the same way as an ovarian tumour (see www.rcpath.org/publications-media/publications/datasets/ovaries-fallopian-tubes-peritoneum.htm). Slicing of the ovary/ies may facilitate adequate fixation, but this should only be done after careful inspection of the capsule.

4 Specimen handling and block taking

There are several ways of opening the uterus, depending on the preference and experience of the pathologist.[2,3] Some pathologists prefer to open the uterus in the sagittal plane while others open it coronally along the lateral borders and between the cornua. Whatever the manner of opening, it should enable accurate mapping and appropriate sampling of the tumour. A photographic record of the specimen may be useful.

Selection of blocks for histology

- Tumour: at least four blocks of tumour must be sampled. These blocks should include, in more than one block or a big block if necessary, the full thickness of the uterine wall and the serosa at the site of deepest myometrial invasion.

- At least one block of isthmus/lower uterine segment (LUS) should be taken in all cases. Approximately 14% of endometrial carcinomas arise in the LUS/isthmus and these are more frequent in association with mismatch repair gene abnormalities and hereditary non-polyposis colorectal cancer syndrome (HNPCC)/Lynch syndrome.[4,5]

- In cases with biopsy proven carcinoma, but no visible tumour, cornual blocks must be taken, and the entire endometrium may need to be blocked depending on the histological findings in the initial sections.

- Cornual blocks may also be taken to facilitate evaluation of adnexal involvement.

- Parametrial tissue,should be sampled completely. Generally one block on each side will suffice to completely sample the parametrium. However, in those cases where radical hysterectomy has been performed (usually when cervical involvement is suspected preoperatively), more than one block from each side may be needed.

- Two longitudinal blocks, each including a lip of the cervix, should be submitted. Additional blocks may be needed to include the vaginal cuff if present.

- One block each of both ovaries and tubes should be submitted if grossly normal. The tubal blocks should include the fimbria. Sampling of the fimbrial end of the tube is recommended as good practice because this is the site currently believed to be most likely to show any primary pathology, and may rarely be the source of an apparent endometrial primary carcinoma.

- Appropriate numbers of blocks should be taken to sample other abnormalities such as fibroids or adnexal masses. Apart from the tumour details, the presence of any gross abnormalities in any anatomical structure should be documented and sampled, if relevant.

- Omentum: one block, taken from an area of obvious tumour, is adequate in cases where macroscopically visible tumour nodules are present. If the specimen is macroscopically normal, we recommend that four blocks be taken. This number is based on accepted current practice. Omental biopsy in endometrial carcinoma is performed in high-risk cases and the presence of omental involvement, even if microscopic, is an important prognostic factor.

- All resected lymph nodes should be sampled. Every lymph node should be examined histologically in its entirety, unless obviously grossly involved by tumour. Only one block is necessary from any grossly involved node. Nodes greater than 5 mm should be bisected or sliced, while those smaller than 5 mm can be processed intact.

- Peritoneal biopsies: site of origin, dimensions and appearance should be stated.

- Representative blocks should be taken from any other tissues submitted.

[Block taking in endometrial carcinoma – Level of evidence D and GPP.]

5 Core data items to be included in the histopathology report

5.1 Clinical core data items

5.1.1 Type of specimen

Depending on the preoperative diagnosis, results of radiological staging and intraoperative findings, the hysterectomy specimen may be accompanied by lymph nodes and an omental biopsy or omentectomy.

5.1.2 Other clinical details

Clinical working diagnosis, results of previous biopsy, details of previous or current treatment including hormonal treatment, type of surgical procedure and relevant family history should be mentioned.

5.2 Pathological core data: macroscopic data items

5.2.1 Specimen type

The type of hysterectomy should be documented: simple, radical or other. It is also useful to record the route of hysterectomy: abdominal, vaginal or laparoscopic, as this may influence block selection; for example, parametrial or vaginal tissue may not be present in laparoscopic hysterectomies. This information may also be important for evaluation of certain histological parameters, for example laparoscopic hysterectomy using balloon manipulators can result in artefactual vascular pseudo-invasion, as discussed below.

5.2.2 Attached anatomical structures

The different components of the hysterectomy specimen, uterine corpus, cervix, ovaries and tubes, should be specified, and their dimensions and macroscopic appearance recorded. The uterus is orientated by the comparative heights of the anterior and posterior peritoneal reflections, the attached adnexal structures or both. The presence of a vaginal cuff and its maximum length, and the presence of parametrial tissues should be recorded, in case of radical hysterectomy specimens.

5.2.3 Accompanying specimens

The omentum, if received, should be measured and the presence and dimensions of any gross tumour recorded.

The numbers of lymph nodes recovered from each anatomical site (which should be submitted in separate labelled pots) should be stated. There is some data regarding optimum lymph node yields with regard to detection of metastasis.[6]

The peritoneal biopsies from each submitted anatomical site must be described and measured, and any gross abnormalities recorded.

5.2.4 Tumour details

The gross appearance of the tumour, including its maximum dimension, and the presence or absence of gross myometrial invasion, cervical involvement, parametrial involvement or serosal surface involvement should be recorded. There is evidence that involvement of the isthmus/lower uterine segment (LUS) in early stage endometrial carcinomas is an independent prognostic factor for lymph node involvement, distant recurrence and death, and the presence or absence of this should be recorded.[7,8,9,10]

The location of the tumour within the uterus is important. This should be recorded as LUS/isthmus, body, fundus or cornu. LUS/isthmus is defined as the area between the narrowed distal uterine body and the top of the endocervical canal. The fundus is the part of the uterus above the level of the fallopian tubes. Approximately 14% of endometrial carcinomas arise in the LUS/isthmus and these are more frequent in association with mismatch repair gene abnormalities and hereditary non polyposis colorectal cancer syndrome (HNPCC)/ Lynch syndrome.[4.5]

[Correlation of tumour site with inherited endometrial carcinomas: Level of evidence – C.]

[Correlation of lower uterine segment involvement with prognosis: Level of evidence – C.]

5.3 Pathological core data: microscopic data items

5.3.1 Tumour type

Endometrial carcinomas should be typed according to the 2003 WHO classification[11] (Appendix A). Publication of the revised WHO classification is anticipated in 2014. Accurate typing is necessary in both biopsies and resection specimens. Diagnosis of aggressive tumours such as serous carcinoma, clear cell carcinoma, carcinosarcoma, undifferentiated carcinoma and grade 3 endometrioid carcinoma will usually result in full surgical staging including pelvic and para-aortic lymphadenectomy and omentectomy at a Cancer Centre. Endometrioid carcinomas have, in general, a better prognosis than serous and clear cell carcinomas.[12,13,14] Information about mucinous carcinomas is still relatively limited, but available information suggests that their clinical behaviour is similar to that of endometrioid adenocarcinoma.[15] Serous EIC is the *in-situ* equivalent of uterine serous carcinoma, which has the capacity to metastasise.

It is outside the scope of this document to provide detailed information regarding the histopathological features of endometrial carcinoma subtypes and the reader is referred to specialist textbooks of gynaecological pathology. A few points will, however, be highlighted for clarification. The term ‘endometrioid adenocarcinoma with squamous differentiation’ refers to the entities previously termed ‘adenoacanthoma’ and ‘adenosquamous carcinoma’. Some 30% of endometrioid adenocarcinomas of the endometrium contain squamous elements. It has been shown that the cytomorphology of the squamous elements in such tumours is not a useful prognostic indicator and, accordingly, these tumours are now referred to as ‘endometrioid adenocarcinoma with squamous differentiation’.[11]

‘Mucinous adenocarcinoma’ refers to a subtype of endometrioid adenocarcinoma in which more than 50% of the tumour cells contain intracytoplasmic mucin. Many endometrioid adenocarcinomas contain focal mucinous areas and endometrioid and mucinous adenocarcinomas form part of a spectrum. Carcinosarcomas (malignant mixed Mullerian tumours) are now known to be epithelial neoplasms that have undergone sarcomatous metaplasia,[16,17] the epithelial elements being the ‘driving force’. Undifferentiated carcinoma has recently been highlighted as an aggressive form of uterine carcinoma. It has been defined as ‘‘a tumour composed of medium or large cells with complete absence of squamous or glandular differentiation and with absent or minimal (<10%) neuroendocrine differentiation’’.[18] Undifferentiated carcinoma may occur in pure form or in combination with, and probably as a result of, dedifferentiation in a low-grade (grade 1 or 2) endometrioid adenocarcinoma (dedifferentiated endometrioid adenocarcinoma or mixed endometrioid and undifferentiated adenocarcinoma). Undifferentiated carcinoma is a specific histologic entity and does not imply that the pathologist cannot supply a definitive diagnosis. Although the current WHO classification does not include a separate category of neuroendocrine carcinomas, these may occur within the uterine corpus. Both small-cell and large-cell neuroendocrine carcinomas can arise within the uterine corpus, with or without an endometrioid component.[19,20] Minor foci of neuroendocrine marker positivity (<10%) are allowable in undifferentiated carcinoma.

'Mixed carcinoma' refers to a tumour composed of more than one morphological type. Using the current WHO definition, at least 10% of the tumour must comprise the non-dominant type of differentiation. However, it is recommended that all morphological types are mentioned in the pathology report along with the approximate percentage of each component, even if the minor component comprises less than 10% of the neoplasm. This is of importance in that most oncologists administer treatment for an aggressive tumour type, even if this comprises <10% of the neoplasm.

[Prognostic importance of tumour type: Level of evidence – B.]

5.3.2 Tumour grade

The histologic FIGO grade[11] has been consistently identified as one of the more important prognosticators for women with endometrial carcinoma. The FIGO grading system is a modification of the grading system devised by the Gynecologic Oncology Group, and is primarily based on the architectural arrangement of the neoplastic cells, which characteristically produce glands. Grade 1 is defined as a gland-forming tumour in which <5% of the neoplastic cells form solid sheets, grade 2 as a tumour in which 5–50% of the neoplasm forms solid sheets, and grade 3 as a tumour in which >50% of the neoplasm is formed of solid sheets of neoplastic cells. In tumours showing squamous differentiation, the squamous elements should be excluded from the architectural assessment. A secondary modification resulting in an increase in grade is made for grade 1 or 2 tumours in the presence of notable nuclear atypia, inappropriate for the architectural grade. When the grade of an endometrioid carcinoma is increased because of the high nuclear grade, it is recommended that this is clearly indicated in the report. Although notable nuclear atypia was not defined by FIGO, a subsequent investigation resulted in a simple, pragmatic approach: those tumours in which the **majority** of the neoplasm is composed of cells with highly pleomorphic nuclei and large nucleoli, identifiable at low-power magnification, are associated with a diminished survival rate and should be upgraded by 1 grade.[21] Marked discordance between architectural and nuclear grades occurs uncommonly in endometrioid adenocarcinomas and, if identified, the alternative possibility of an unusual variant of serous or clear cell carcinoma should be considered. It is recommended that serous, clear cell and undifferentiated carcinomas and carcinosarcomas are not graded, but are automatically regarded as grade 3. In other words, FIGO grading should only be undertaken for endometrioid carcinomas including its variants.

The FIGO grading system has demonstrated prognostic utility, but is unfortunately poorly reproducible.[22,23,24] The poor reproducibility of FIGO grading has led to attempts to devise a two-tier grading system that is likely to be more reproducible simply by reducing the number of categories. However, for the time being, it is recommended that histopathologists continue to use the generally accepted, albeit imperfect, FIGO grading system.

[Prognostic importance of tumour grade: Level of evidence – B.]

5.3.3 Myometrial invasion

Deep myometrial invasion by tumour has repeatedly been shown to be an important poor prognostic indicator in endometrial carcinoma. This is the only independent predictor of haematogenous dissemination by endometrial carcinoma and it is therefore an important determinant of adjuvant therapy.[25,26,27] The tumour is FIGO Stage IA if myometrial invasion is absent or confined to less than one half (<50% myoinvasion). The tumour is staged as IB if it invades one half or more of the uterine wall (≥50% myoinvasion). The depth of myometrial invasion (inner or outer half) should be documented as this is required for tumour staging, prognostication and adjuvant therapy.

Various methods of determining the extent of myometrial invasion have been evaluated in predicting regional lymph node metastasis. These have included the absolute depth of invasion from the endomyometrial junction to the deepest focus of invasive carcinoma, the

distance from the uterine serosa to the deepest focus of invasive carcinoma, and the percentage of myometrium involved, defined by the depth of myometrial invasion from the endomyometrial junction to the deepest focus of invasive carcinoma in comparison with the overall myometrial thickness.[28,29] In a recent study, all three of these methods predicted pelvic lymph node metastasis in univariate analysis, but the absolute depth of myometrial invasion outperformed the distance from the serosa and the percentage of myometrium involved in multivariate analysis.[30]

In most cases, determining the depth of myometrial invasion is not difficult. However, in some instances, this may be problematic.[25] The irregularity of the endomyometrial junction may make it difficult to determine the exact superficial reference point for measuring the depth of myometrial invasion. When the tumour involves adenomyosis in the outer half of the myometrium, without myometrial involvement outside the confines of the adenomyosis, this is still classified as FIGO Stage IA and this does not seem to affect the outcome, although the number of studies is small.[31] Morphologic features of the myoinvasive tumour such as a minimal deviation pattern, a microcystic elongated and fragmented (MELF) pattern and associated smooth muscle metaplasia in polypoid neoplasms may result in problems in the assessment of myoinvasion and the extent of this.[32,33] Tumours within lymphatics or blood vessels in the myometrium should not be used in the assessment of depth of invasion. For example, if there is tumour within lymphovascular channels in the outer half of the myometrium but the tumour is otherwise confined to the inner half of the myometrium, it is FIGO stage IA.

Maximum depth of tumour invasion is best assessed in a well-orientated, full thickness block of the uterine wall from the site of deepest tumour infiltration. In practice, measuring the distance from the deepest focus of invasive carcinoma to the serosal surface and using this measurement to determine the depth of invasion by comparison with the thickness of uninvolved myometrium is an easy way to determine whether the carcinoma infiltrates the inner or outer half. The uterine wall in the cornual region is thin and therefore blocks from the cornual region should not be used for evaluation of depth of invasion unless the tumour is located wholly in this region or it reaches/breaches the serosa only in this region. In cases where percentage depth of myometrial invasion cannot be ascertained, myometrial infiltration that reaches the arcuate vascular plexus of the uterus usually indicates >50% myometrial invasion.[26]

[Prognostic value of depth of myometrial invasion: Level of evidence – C.]

5.3.4 Tumour-free distance to serosa

This is a measure of the distance in millimetres from the deepest point of the myoinvasive tumour to the serosal surface. Several studies have evaluated the predictive value of this parameter.[30,34-37] Unlike the difficulties in assessing the depth of myometrial invasion or percentage of myometrial infiltrated by carcinoma outlined above, this is a simple, objective and reproducible measurement that was included in the previous version of this dataset, but has not featured in those from other countries nor in the list of core (required) dataset items of the ICCR. All studies have shown this to be a significant predictive factor, though its performance relative to myometrial depth of invasion and percentage of infiltration has varied. Its ease and reproducibility of measurement, in comparison with other measures of myoinvasive depth, justifies its inclusion in a synoptic report. Various cut-off measures have been put forward as being predictive of outcome but their evaluation requires larger prospective studies.

[Prognostic importance of tumour-free distance to the serosa: Level of evidence – C.]

5.3.5 Lymphovascular invasion

Lymphovascular invasion within the myometrium has been demonstrated in repeated studies to be an independent prognostic factor in endometrial adenocarcinomas.[38-44]

Lymphovascular invasion is typically most easily seen at the invasive front of the tumour, and a perivascular lymphocytic infiltrate, including lymphoid aggregates, should raise the possibility of vessel involvement. Lymphovascular invasion is a relatively uncommon finding in endometrioid carcinoma in which it generally correlates with deep myometrial invasion and other poor prognostic factors. It is a much more common finding in uterine serous carcinoma, where it may be present in superficially myoinvasive or even non-myoinvasive tumours. It is important to note that the presence of lymphovascular invasion, whether within the uterus or outside it, does **not** upstage the tumour.

Lymphovascular invasion should be distinguished from retraction artefact, which is not uncommonly seen in endometrial carcinomas. This distinction may be difficult, but retraction artefact is often more widespread than true lymphovascular invasion and is characterised by a smooth round contour. With true vascular invasion, the spaces typically have a more slit-like or angulated contour and are lined by endothelial cells.[45] Immunohistochemistry for markers such as CD31 (which stains all vascular channels) and D2-40 (which stains lymphatic channels) may assist in identifying vascular invasion.

True lymphovascular invasion should also be distinguished from artefactual vascular involvement, which is particularly common when there is marked tumour autolysis. Artefactual vascular invasion secondary to autolysis is characterised by 'smearing artefact' or the so-called 'toothpaste effect'. The vascular invasion may be disproportionate to the stage and grade of the tumour and often the vessels involved are predominantly in the outer myometrium, where tumour may also be seen smeared on the serosa.

The phenomenon of artefactual vascular pseudo-invasion in total laparoscopic hysterectomy specimens using an intrauterine balloon manipulator has recently been highlighted.[46] It has been suggested that this artefact, where both benign and malignant endometrial tissues are displaced into vascular spaces, is the result of a closed positive-pressure system created by the inflation of an intrauterine balloon after occlusion of the fallopian tubes.[47] It is also suggested that this may be due to mechanical displacement of friable intraluminal tumour by the balloon. There are several clues that this is an artefact: the discrepancy between the low stage and grade of the tumour and the high volume of vascular invasion, the preferential involvement of large, thick-walled muscular blood vessels in the outer myometrium, the presence of both benign and malignant tissues within blood vessels, the presence of stromal tissues accompanying glands and the lack of tumour adherence to the vessel lining. Other features that may be seen in association with intrauterine balloon manipulators are disruption of the endometrial lining, the presence of fragments of endometrium and tumour within endomyometrial clefts, intratubal contaminants, nuclear crush artefact and the presence of inflammatory debris within vascular lumina. Correlation with the method of hysterectomy is, of course, essential.

[Prognostic relevance of lymphovascular invasion: Level of evidence – B.]

[Artefactual displacement of tumour cells by intraoperative manipulation: Level of evidence – C.]

5.3.6 Cervical stromal invasion

Cervical involvement by endometrial carcinoma is associated with an overall worse prognosis than carcinoma confined to the uterine corpus. However, tumours involving the cervix tend to have other known poor prognostic factors such as aggressive morphology, deeper myometrial invasion and a higher rate of lymphovascular invasion and nodal spread than tumours that are confined to the corpus.[48,49,50] For this reason, the true significance of cervical involvement has been difficult to determine and more recent studies have cast some doubt on cervical stromal invasion as an independent prognosticator. The presence of cervical stromal involvement is an indication for most oncologists to administer adjuvant brachytherapy and reporting of this parameter is therefore mandatory.

The 2009 revision of FIGO staging[51] includes only cervical stromal invasion as stage II; tumours showing only cervical epithelial or crypt involvement, which would have been stage IIA in the 1988 staging system, remain within stage I. Assessment of cervical involvement is often difficult and has been shown to have low reproducibility even amongst specialised gynaecological pathologists.[52] In particular, the junction between the upper endocervix and LUS is not strictly defined and criteria for distinguishing stromal invasion from glandular involvement alone have not been defined. At the two ends of the spectrum, large confluent infiltrative masses of tumour with a desmoplastic reaction, and partial replacement of benign surface or crypt epithelium can both be confidently identified as stromal and epithelial-only involvement respectively. More problematically, many endometrial cancers involving the cervix have an architectural arrangement only slightly different from that of benign endocervical crypts and lack confluent back-to-back arrangement of glands or a desmoplastic stromal reaction. Rarely, a subtle 'burrowing' or 'adenoma malignum-like' pattern of stromal infiltration is present.[53] The preservation or loss of the normal architectural arrangement of the neoplastic glands compared with that of adjacent benign endocervical glands is probably the most reliable feature in assessment of cervical stromal invasion.

[Prognostic importance of cervical stromal invasion: Level of evidence – B.]

5.3.7 Vaginal involvement

Vaginal involvement may be identified as a distinct nodule and submitted separately by the gynaecologist at the time of operation. Radical hysterectomy is not usually undertaken for endometrial cancer unless cervical involvement is suspected pre-operatively. Identification of vaginal involvement in randomly submitted sections is unusual. Vaginal involvement signifies FIGO stage IIIB disease.

The reported five-year survival for women with isolated vaginal metastasis is only about 25% and the median survival is less than 2 years.[54] Reporting of vaginal involvement thus provides prognostic information that is critical to appropriate management and it is considered a core data item.

[Vaginal involvement is an indicator of poor prognosis: Level of evidence – C.]

5.3.8 Uterine serosal involvement

The uterine serosa is considered to be involved when tumour is seen to penetrate through the serosal layer. It most commonly occurs secondary to full thickness myometrial invasion, but occasionally represents discontinuous tumour involvement, possibly secondary to transtubal spread. For staging purposes, serosal lymphovascular involvement, unaccompanied by tissue infiltration, is not considered as representing serosal involvement. Uterine serosal involvement with or without adnexal involvement is noted to be an independent marker of high recurrence risk and signifies FIGO Stage IIIA disease.[55,56]

[Serosal involvement is an indicator of higher risk of recurrence: Level of evidence – C.]

5.3.9 Parametrial involvement

The majority of endometrial carcinomas are surgically managed by a simple hysterectomy. Surgically dissected parametrium is not part of a simple hysterectomy specimen. Radical hysterectomy or modified radical hysterectomy is sometimes performed for endometrial carcinoma when cervical involvement is suspected pre-operatively. In these cases, the entire parametrium should be submitted for microscopic examination.[57,58] For staging purposes and in common with lymphovascular space invasion at other sites, parametrial lymphovascular involvement unaccompanied by tissue infiltration is not considered as representing parametrial involvement. Parametrial involvement signifies FIGO stage IIIB disease.

[Parametrial involvement is an indicator of poor prognosis: Level of evidence – C.]

5.3.10 Adnexal involvement

Adnexal involvement has been identified as an independent poor prognostic factor for both recurrence-free and overall survival, and signifies FIGO stage IIIA disease.[59] Adnexal involvement, however, is frequently associated with other poor prognostic factors and other sites of metastatic disease.

Adnexal involvement by endometrial carcinoma should be distinguished from synchronous independent carcinomas involving the uterus and one or both ovaries or fallopian tubes.[60] The most common scenario is simultaneous involvement of the uterus and one or both ovaries by an adenocarcinoma. Most commonly, these adenocarcinomas are endometrioid in type.[61,62,63] When early-stage, low- grade endometrioid adenocarcinomas involve the uterus and one or both ovaries, they most likely represent synchronous independent primary neoplasms. Adjacent endometrial hyperplasia (in the case of the uterine tumour) and endometriosis or a component of benign or borderline endometrioid adenofibroma (in the case of the ovarian neoplasm) are pointers towards an origin in these organs. With a deeply myoinvasive endometrial tumour exhibiting prominent lymphovascular invasion and nodular cortical and surface ovarian tumour, a uterine primary with ovarian metastasis is likely.

With a serous carcinoma involving the uterus and one or both ovaries, the situation is different. Uterine serous carcinoma has a marked propensity for extra-uterine spread, which may occur even with a small primary tumour apparently confined to the endometrium. In such cases, it is important to distinguish between a primary uterine serous carcinoma with metastasis to the adnexa, a primary adnexal serous carcinoma with spread to the endometrium and independent primaries. Most ovarian and tubal serous carcinomas exhibit diffuse strong nuclear positivity with WT1. In contrast, uterine serous carcinoma is usually negative, although some cases are positive.[64,65] Currently it is considered that with a serous carcinoma in more than one location, these are much more likely to represent metastasis from one site to the other rather than synchronous independent neoplasms.

[Adnexal involvement as a poor prognostic indicator: Level of evidence – C.]

5.3.11 Omental involvement

Omental involvement by endometrial carcinoma is associated with an adverse outcome with a decreased overall survival and is categorised as FIGO Stage IVB.[66] Omental involvement correlates with deep myometrial invasion, high tumour grade, non-endometrioid histology, lymph node metastasis and adnexal involvement.

[Prognostic value of omental involvement: Level of evidence – C.]

5.3.12 Lymph node involvement

Patients with lymph node metastasis have significantly lower survival than those without, and the incidence of nodal spread increases with tumour grade and depth of myometrial invasion. It is very uncommon for positive para-aortic lymph nodes to be present in the absence of positive pelvic nodes, but it does occur occasionally. In the 2009 revision of the FIGO staging system, stage IIIC is divided into Stage IIIC 1 (positive pelvic nodes) and Stage IIIC 2 (positive para-aortic nodes with or without positive pelvic nodes).[52,67,68] The prognostic implications of this change will become clearer as data are collected on the basis of this new staging system.

The probability of detecting nodal metastasis, and therefore of accurately staging a carcinoma, increases with greater nodal counts. As at other anatomical sites, it is considered useful to record the number of lymph nodes retrieved from each site as well as

the number involved by tumour. This information is recorded in most pathology departments.

[Relationship between lymph node count and identification of metastasis: Level of evidence – C.]

[Prognostic importance of lymph node involvement: Level of evidence – C.]

5.3.13 Provisional FIGO stage

Two staging systems are in widespread use for gynaecological cancers: the FIGO system, which is specific for gynaecological cancers, and TNM,[69] which is applicable to all tumour sites. A survey undertaken in the United Kingdom showed that most gynaecological pathologists report gynaecological cancers using FIGO staging systems and most gynaecological oncologists and other specialists dealing with patients with gynaecological malignancies likewise use FIGO.[70] Worldwide, most clinical trials and retrospective and prospective studies use FIGO rather than TNM. There is evidence that FIGO staging provides risk stratification for patients[72] and FIGO staging is therefore recommended as a core data item.

The 2009 provisional FIGO stage[51] (provisional on the basis of the material submitted for pathologic examination) of all endometrial carcinomas should be documented in the pathology report. The final FIGO stage should be assigned at the multidisciplinary team meeting. TNM staging is considered a non-core element.

[Prognostic importance of FIGO staging: Level of evidence – C.]

5.3.14 Summary of core data items

- Clinical core data items:
  - type of specimen
  - other clinical details.
- Pathological core data: macroscopic:
  - specimen type
  - attached anatomical structures
  - accompanying specimens
  - maximum dimension of tumour
- Pathological core data: microscopic:
  - tumour type
  - tumour grade
  - myometrial invasion
  - tumour free distance to serosa
  - lymphovascular invasion
  - cervical stromal invasion
  - vaginal involvement
  - uterine serosal involvement
  - parametrial involvement

- adnexal involvement
- lymph node involvement
- omental involvement
- provisional FIGO stage.

6 Non-core data items

These are data items that are of uncertain prognostic or therapeutic relevance and are not required for staging. They may provide supplementary information that contributes to the management in individual cases. They are generally based on Level D evidence or Good Practice Point. They may be included in the report depending on the preference of individual laboratories, individual groups of pathologists or to assist clinical research. These include the following.

6.1 Macroscopic non-core data items

6.1.1 Specimen weight and measurements

Many pathologists routinely weigh and measure all solid organs. The variability in dimensions and weight of the uterus relative to age, parity, phase of the menstrual cycle and associated benign abnormalities such as fibroids or adenomyosis mean that these parameters have no significance in relation to the cancer prognosis or management and are therefore not included in the core data items.[1]

6.2 Microscopic non-core data items

6.2.1 Percentages of different components of mixed carcinomas

It is recommended that all components of an endometrial carcinoma be recorded in the pathology report, even if the minor component comprises <10% of the neoplasm. The most common combinations are an admixture of endometrioid adenocarcinoma and another component such as serous, clear cell, or undifferentiated carcinoma. The published data regarding the amount of a morphologically 'high-grade' component that influences the outcome are inconsistent. As the exact amount of an aggressive component that would influence outcome is not known, it is recommended that the percentages of the various components should be recorded so that this information is available for future studies. Many oncologists would administer adjuvant therapy based on only a small component of an aggressive tumour type, for example serous.

6.2.2 Morphological components of carcinosarcomas

Evidence regarding the prognostic importance of the differentiation of the mesenchymal component in uterine carcinosarcomas is variable. Those tumours with heterologous elements have a worse prognosis than those where the mesenchymal component is homologous.[73,74,75] A recent study has suggested that in stage I uterine carcinosarcomas, the presence of a heterologous mesenchymal component is a powerful adverse prognostic indicator.[76] Given this, it is recommended that with a carcinosarcoma, the percentages of the epithelial and mesenchymal components be included in the report along with the morphologic subtypes within the epithelial and mesenchymal components. However, at present, the level of evidence is not sufficient to include this as a core item.

6.2.3 Cervical surface and gland (crypt) involvement

With the introduction of the 2009 FIGO staging system,[51] involvement of the cervical surface epithelium or glands (crypts) without stromal invasion represents Stage I rather than Stage IIA (as in FIGO 1988). Various studies have provided conflicting data regarding

survival and recurrence rates when comparing between cervical epithelial and stromal invasion. It is therefore advisable to document the presence or absence of cervical surface epithelial or crypt involvement, especially since some oncologists administer adjuvant brachytherapy when this is present. Tumours that unequivocally fall into this category are those in which the disease is limited to only partial replacement of the surface or underlying benign cervical glandular epithelium by neoplastic cells.

6.2.4 Distance of tumour from cervical (or vaginal) margin

General oncological principles indicate that the margin of excision of tumours dictates their management. In those tumours with cervical (or vaginal) involvement, it may be useful to record information regarding the distance from the margins prospectively so that the likelihood of recurrence related to distance from the margin may be quantified in the future.

6.2.5 Percentage of myometrium involved by tumour

Myometrial involvement can be recorded in several ways, all of which have been shown to correlate with other prognostic factors and outcome. The percentage of myometrium involved may be recorded if this is a local preference.

6.2.6 Background endometrium

With regard to adjuvant treatment or prognosis in a woman with endometrial carcinoma, the histologic findings in the background endometrium carry little, if any, significance. However, the features may provide useful information regarding tumour pathogenesis. For this reason, the presence of hyperplasia, atrophy and polyps should be recorded.

6.2.7 Peritoneal involvement

Peritoneal involvement, defined as involvement of the peritoneum by endometrial carcinoma, is more common with non-endometrioid carcinomas, especially of serous type. Peritoneal involvement, apart from uterine serosa, is not specifically referred to in the 2009 FIGO staging system[52] but should be documented if present. The site of the peritoneal involvement should also be documented. Occasionally, keratin granulomas are identified in the peritoneum, on the ovarian surface, or uterine serosa in association with a uterine endometrioid adenocarcinoma exhibiting squamous differentiation. In the absence of tumour cells, this should not result in upstaging of the tumour.[76]

6.2.8 Peritoneal cytology

The significance of positive peritoneal cytology as an independent prognostic factor is controversial and it is for this reason that the 2009 FIGO staging does not take account of the results of peritoneal cytology. However, if peritoneal fluid is submitted, the results should be recorded in the pathology report. Advanced-stage disease (Stage III or IV) is associated with positive peritoneal cytology in approximately 25% of cases.

6.2.9 Distant metastases

Distant spread refers to metastasis beyond the pelvic cavity and signifies stage IV disease. Common sites of distant spread are the omentum and the lungs. Less common sites are the liver, brain and bone. Omental status is included in core data items; the remaining sites of dissemination are usually not sampled for histological examination.

6.2.10 Extracapsular spread of lymph node metastases

Extracapsular spread has not been investigated as a prognostic factor in endometrial cancer. It is felt that it would be useful to record this information in the pathology report for future analysis.

6.2.11 Ancillary investigations

Ancillary investigations, especially immunohistochemistry but also increasingly molecular tests, may play a diagnostic, predictive, and/or prognostic role in the evaluation of endometrial cancers. Single antibodies, in general, lack specificity and a combination of antibodies is usually required to make a diagnosis. Hormone receptor (oestrogen and progesterone receptor) status may be useful in the management of recalcitrant or recurrent disease or in the management of low-grade adenocarcinomas where surgery is contraindicated, for example due to comorbidities or desirability to preserve fertility.

6.2.12 Provisional TNM stage

The updated version of the TNM classification for endometrial carcinoma[71] mirrors most of the changes in the 2009 FIGO staging system and may be recorded as a non-core data item. The TNM system includes individual parameters which should be recorded, as well as a final stage grouping (both should be recorded, see Appendix B).

6.2.13 Block key

The origin/designation of all tissue blocks should be recorded and documented in the final pathology report. This is particularly important should the need for internal or external review arise.

6.2.14 Summary of non-core data items

- Pathological data: macroscopic
  - specimen weight and measurements.

- Pathological data: microscopic
  - percentages of different components of mixed carcinomas
  - morphological components of carcinosarcomas
  - cervical surface and gland (crypt) involvement
  - distance of tumour from cervical (or vaginal) margin
  - percentage of myometrium involved by tumour
  - background endometrium
  - peritoneal involvement
  - peritoneal cytology
  - distant metastases
  - extracapsular spread of lymph node metastases
  - ancillary investigations
  - block key
  - provisional TNM stage.

7 Diagnostic coding and staging

Primary endometrial carcinomas should be subtyped according to the WHO classification[11] (Appendix A) and coded using SNOMED codes (Appendix B).

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 (Appendix B).

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

Tumours should be staged using the 2009 FIGO staging system (Appendix C), with the option to include 7th edition of TNM staging (Appendix C).

8 Reporting of small biopsy specimens

Most endometrial carcinomas are diagnosed on biopsies that are obtained by either an outpatient sampling procedure or by endometrial curettage under anaesthesia. The outpatient sample is a blind procedure and samples less of the endometrium. There is evidence that its reliability is similar to the curettage in generalised endometrial disorders.[77] However, in some cases formal curettage may be required to obtain sufficient tissue for tumour diagnosis, typing and grading.

When handling endometrial biopsy specimens, a sieve or mesh basket may be useful to ensure that all the material is retrieved. All of the submitted tissue should be processed. Where the biopsy confirms malignancy, the report should clearly specify the subtype of tumour present and the FIGO grade. It is recognised that there may be disparity in tumour grade between the endometrial biopsy and the subsequent hysterectomy specimen but correlation for tumour type is good.[78,79]

Unequivocal distinction between atypical hyperplasia and grade 1 endometrioid adenocarcinoma can be difficult on small biopsies. Discussion of the morphological features useful in differentiation between the entities is outside the scope of this document and the reader is referred to specialist gynaecological pathology textbooks. In a significant proportion of cases diagnosed as atypical hyperplasia on endometrial biopsy, the resected uterus contains endometrioid adenocarcinoma. Patients with a diagnosis of atypical endometrial hyperplasia may benefit from discussion at the gynaecological oncology multidisciplinary team meeting and their management should be based on the results of clinical, pathological and imaging findings.[80]

9 Reporting of frozen sections

In most institutions in the United Kingdom, intra-operative frozen sections are rarely performed in patients with endometrial carcinoma.[81] Frozen sections may be performed occasionally to confirm endometrial carcinoma when there is no preoperative diagnosis, determine the nature of unexpected and clinically suspicious extra-uterine lesions at surgery for endometrial carcinoma, evaluate depth of myometrial invasion and look for metastasis in suspicious lymph nodes. It is important that clinicians who request frozen sections are cautioned about the potential limitations of the technique.

10 Immunohistochemistry of endometrial carcinomas

In general, endometrial carcinomas express pan-cytokeratins, EMA, CA125, Ber-EP4, B72.3, CK7, ER, PR and vimentin, whereas they are usually negative for CK20 and lack diffuse, strong cytoplasmic expression of carcinoembryonic antigen (CEA). There are some specific situations where immunohistochemistry is of importance in the diagnosis of endometrial carcinomas.

Immunohistochemistry to distinguish between an endometrial and a cervical adenocarcinoma is more often necessary in biopsies than in resection specimens. Generally, endometrioid endometrial carcinomas are strongly and diffusely positive for vimentin, ER, and PR and are largely negative for CEA.[82] The converse profile is usual in cervical adenocarcinomas. Vimentin expression in endometrioid adenocarcinomas is usually strong and expressed on the lateral membranes, but endometrial carcinomas with mucinous differentiation express vimentin less frequently.[83,84] CEA expression in cervical adenocarcinomas

of the usual type is characteristically, although not always, diffuse with cytoplasmic and luminal border reactivity, whereas endometrioid adenocarcinomas of the uterus may exhibit weak, luminal CEA positivity. Squamous elements in endometrioid carcinomas often show strong positivity with CEA. p16 staining may be useful in the distinction between an endometrioid adenocarcinoma of the uterine corpus and a usual cervical adenocarcinoma; the former is usually patchily positive and the latter diffusely immunoreactive.

Grade 3 endometrioid adenocarcinomas show clinical behaviour similar to serous carcinomas.[85,86] Grade 3 endometrioid carcinomas generally show a greater incidence of expression of ER and PR, whilst expression of p53 and p16 is commoner is serous carcinomas. However, there is considerable immunophenotypic overlap and markers may not be of value in an individual case. Serous carcinomas almost always exhibit aberrant p53 staining (intense nuclear staining of almost all nuclei or totally negative staining.)[87]

Immunohistochemistry may be helpful in distinguishing clear cell carcinomas from endometrioid adenocarcinomas with clear cells. Both carcinoma types show similar expression of CK7, EMA, CA125, Ber-EP4, B72.3 and CEA. More recently, HNF-1β has been shown to be expressed in endometrial clear cell carcinomas in contrast to endometrioid carcinomas.[88]

Serous carcinoma of the endometrium can be difficult to distinguish from clear cell carcinoma, the latter being extremely uncommon within the uterus. Aberrant p53 expression (diffuse and strong or totally absent) and diffuse p16 expression favours the diagnosis of serous carcinoma.

Gynaecological malignancies occur commonly in women with Lynch syndrome. Among these, endometrial carcinoma is the most frequent. Pathological features of endometrial carcinomas associated with Lynch syndrome are not well studied but lower uterine segment location, undifferentiated areas and abundant tumour infiltrating lymphocytes may be a feature. Loss of expression of mismatch repair proteins (MLH1/PMS2 or MSH2/MSH6 usually occurs.)[89.90]On the basis of the immunohistochemical results, additional testing may follow to determine if the patient has a germline mutation diagnostic of Lynch syndrome.

11 Criteria for audit of dataset

The core data items in this dataset can be used as a standard for audits in gynaecological pathology. Examples of audits include completeness of recording of all core data items in histopathology reports, audits of numbers of lymph nodes retrieved and of variation between tumour characteristics in diagnostic biopsies and final reports on hysterectomy specimens.

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

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

  Standard: 95% of reports must contain structured data.

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

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

References

1. McCluggage WG, Colgan T, Duggan M, Hacker NF, Mulvany N, Otis C *et al*. Dataset for reporting of endometrial carcinomas: recommendations from the International Collaboration on Cancer Reporting (ICCR) between United Kingdom, United States, Canada, and Australasia. *Int J Gynecol Pathol* 2013;32:45–65.

2. Rosai J. *Rosai and Ackerman's Surgical Pathology (10th edition).* Edinburgh: Mosby, 2011.

3. Kurman RF, Hedrick Ellenson L, Ronnett BM. Gross description, processing, and reporting of gynaecologic and obstetric specimens. In: *Blaustein's Pathology of the Female Genital Tract (6th edition)*. New York: Springer, 2011.

4. Westin SN, Lacour RA, Urbauer DL, Luthra R, Bodurka DC, Lu KH *et al*. Carcinoma of the lower uterine segment: a newly described association with Lynch syndrome. *J Clin Oncol* 2008;26:5965–5971.

5. Garg K, Soslow RA. Lynch syndrome (hereditary non-polyposis colorectal cancer) and endometrial carcinoma. *J Clin Pathol* 2009;62:679–684.

6. Chan JK, Urban R, Cheung MK, Shin JY, Husain A, Teng NN *et al*. Lymphadenectomy in endometrioid uterine cancer staging. How many nodes are enough? A study of 11,443 patients. *Cancer* 2007;109:2454–2460.

7. Dilek S, Dede M, Gezginç K, Yenen MC, Göktolga U, Ulutin HC *et al*. Does the localization of tumour at stage I endometrial endometrioid adenocarcinoma have an impact on invasion of the tumour and individualisation of the surgical procedure? *Eur J Gynaecol Oncol* 2008;29:138–140.

8. Kizer NT, Gao F, Guntupalli S, Thaker PH, Powell MA, Goodfellow PJ *et al*. Lower uterine segment involvement is associated with poor outcomes in early stage endometrioid endometrial carcinoma. *Ann Surg Oncol* 2011;18:1419–1424.

9. Gemer O, Gdalevich M, Voldarsky M, Barak F, Ben Arie A, Schneider D *et al*. Lower uterine segment involvement is associated with adverse outcome in patients with stage I endometrioid endometrial cancer: results of a multicenter study. *Eur J Surg Oncol* 2009; 35:865–869.

10. Madom LM, Brown AK, Lui F, Moore RG, Granai CO, Disilvestro PA. Lower uterine segment involvement as a predictor for lymph node spread in endometrial carcinoma. *Gynecol Oncol* 2007;107:75–78.

11. Tavassoli FA, Devilee P (eds). *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs*. Lyon: IARC Press, 2003.

12. Prat J. Prognostic parameters of endometrial carcinoma. *Hum Pathol* 2004;35:649−662.

13. Hendrickson M, Ross J, Eifel P, Martinez A, Kempson R. Uterine papillary serous carcinoma: a highly malignant form of endometrial adenocarcinoma. *Am J Surg Pathol* 1982;6:93−108.

14. Sherman ME, Bitterman P, Rosenshein NB, Delgado G, Kurman RJ. Uterine serous carcinoma. A morphologically diverse neoplasm with unifying clinicopathologic features. *Am J Surg Pathol* 1992;16:600−610.

15. Melhem MF, Tobon H. Mucinous adenocarcinoma of the endometrium: a clinico-pathological review of 18 cases. *Int J Gynecol Pathol* 1987;6:347−355.

16. McCluggage WG. Uterine carcinosarcomas (malignant mixed Mullerian tumours) are metaplastic carcinomas. *Int J Gynecol Cancer* 2002;12:687–690.

17. McCluggage WG. Malignant biphasic uterine tumours: carcinosarcomas or metaplastic carcinomas? *J Clin Pathol* 2002;55:321–325.

18. Silva EG, Deavers MT, Malpica A. Undifferentiated carcinoma of the endometrium: a review. *Pathology* 2007;39:134–138.

19. Melgoza F, Brewster WR, Wilczynski S, Rutgers J. p16 – Positive small cell neuroendocrine carcinoma of the endometrium. *Int J Gynecol Pathol* 2006;25:252–256.

20. Mulvany NJ, Allen DG. Combined large cell neuroendocrine and endometrioid carcinoma of the endometrium. *Int J Gynecol Pathol* 2008;27:49–57.

21. Zaino RJ, Kurman RJ, Diana KL, Morrow CP. The utility of the revised International Federation of Gynecology and Obstetrics histologic grading of endometrial adenocarcinoma using a defined nuclear grading system. *Cancer* 1995;75:81–86.

22. Scholten AN, Smit VT, Beerman H, van Putten WL, Creutzberg CL. Prognostic significance and interobserver variability of histologic grading systems for endometrial carcinoma. *Cancer* 2004;100:764−772.

23. Taylor RR, Zeller J, Lieberman RW, O'Connor DM. An analysis of two versus three grades for endometrial carcinoma. *Gynecol Oncol* 1999;74:3−6.

24. Lax SF, Kurman RJ, Pizer ES, Wu L, Ronnett BM. A binary architectural grading system for uterine endometrial endometrioid carcinoma has superior reproducibility compared with FIGO grading and identifies subsets of advance-stage tumours with favorable and unfavorable prognosis. *Am J Surg Pathol* 2000;24:1201−1208.

25. Ali A, Black D, Soslow RA. Difficulties in assessing the depth of myometrial invasion in endometrial carcinoma. *Int J Gynecol Pathol* 2007;26:115−123.

26. Williams JW, Hirschowitz L. Assessment of uterine wall thickness and position of the vascular plexus in the deep myometrium: implications for the measurement of depth of myometrial invasion of endometrial carcinomas. *Int J Gynecol Pathol* 2006;25:59−64.

27. Kaku T, Tsuruchi N, Tsukamoto N, Hirakawa T, Kamura T, Nakano H. Reassessment of myometrial invasion in endometrial carcinoma. *Obstet Gynecol* 1994;84:979−982.

28. Lampe B, Kurzl R, Hantschmann P. Prognostic factors that predict pelvic lymph node metastasis from endometrial carcinoma. *Cancer* 1994;74:2502–2508.

29. Tang X, Tanemura K, Ye W, Ohmi K, Tsunematsu R, Yamada T *et al*. Clinicopathological factors predicting retroperitoneal lymph node metastasis and survival in endometrial cancer. *Jpn J Clin Oncol* 1998;28:673–678.

30. Kondalsamy-Chennakesavan S, van Vugt S, Sanday K, Nicklin J, Land R, Perrin L *et al*. Evaluation of tumour-free distance and depth of myometrial invasion as prognostic factors for lymph node metastases in endometrial cancer. *Int J Gynecol Cancer* 2010;20:1217–1221.

31. Hanley KZ, Dustin SM, Stoler MH, Atkins KA. The significance of tumour involved adenomyosis in otherwise low-stage endometrioid adenocarcinoma. *Int J Gynecol Pathol* 2010;29:445–451.

32. Kalyanasundaram K, Ganesan R, Perunovic B, McCluggage WG. Diffusely infiltrating endometrial carcinomas with no stromal response: report of a series, including cases with cervical and ovarian involvement and emphasis on the potential for misdiagnosis. *Int J Surg Pathol*. 2010;18:138–143.

33. Pavlakis K, Messini I, Vrekoussis T, Panoskaltsis T, Chrysanthakis D, Yiannou P *et al*. MELF invasion in endometrial cancer as a risk factor for lymph node metastasis. *Histopathology*. 2011;58:966–973.

34. Geels YP, Pijnenborg JM, van den Berg-van Erp SH, Snijders MP, Bulten J, Massuger LF. Absolute depth of myometrial invasion in endometrial cancer is superior to the currently used cut-off value of 50%. *Gynecol Oncol*. 2013;129:285–291.

35. Chattopadhyay S, Galaal KA, Patel A, Fisher A, Nayar A, Cross P *et al.* Tumour-free distance from serosa is a better prognostic indicator than depth of invasion and percentage myometrial invasion in endometrioid endometrial cancer. *BJOG* 2012;119:1162–1170.

36. Schwab KV, O'Malley DM, Fowler JM, Copeland LJ, Cohn DE. Prospective evaluation of prognostic significance of the tumour-free distance from uterine serosa in surgically staged endometrial adenocarcinoma. *Gynecol Oncol*. 2009;112:146–149.

37. Lindauer J, Fowler JM, Manolitsas TP, Copeland LJ, Eaton LA, Ramirez NC *et al*. Is there a prognostic difference between depth of myometrial invasion and the tumour-free distance from the uterine serosa in endometrial cancer? *Gynecol Oncol* 2003;91:547–551.

38. Stefansson IM, Salvesen HB, Immervoll H, Akslen LA. Prognostic impact of histological grade and vascular invasion compared with tumour cell proliferation in endometrial carcinoma of endometrioid type. *Histopathology* 2004;44:472–479.

39. Gal D, Recio FO, Zamurovic D, Tancer ML. Lymphovascular space involvement—a prognostic indicator in endometrial adenocarcinoma. *Gynecol Oncol* 1991;42:142–145.

40. Hanson MB, van Nagell JR Jr, Powell DE, Donaldson ES, Gallion H, Merhige M *et al*. The prognostic significance of lymph-vascular space invasion in stage I endometrial cancer. *Cancer* 1985;55:1753–1757.

41. Inoue Y, Obata K, Abe K, Ohmura G, Doh K, Yoshioka T *et al*. The prognostic significance of vascular invasion by endometrial carcinoma. *Cancer* 1996;78:1447–1451.

42. Yamazawa K, Seki K, Matsui H, Sekiya S. Significance of perivascular lymphocytic infiltrates in endometrial carcinoma. *Cancer* 2001;91:1777–1784.

43. McKenney JK, Kong CS, Longacre TA. Endometrial adenocarcinoma associated with subtle lymphovascular space invasion and lymph node metastasis: a histologic pattern mimicking intravascular and sinusoidal histiocytes. *Int J Gynecol Pathol* 2005;24:73–78.

44. McCluggage WG. Ten problematical issues identified by pathology review for multidisciplinary gynaecological oncology meetings. *J Clin Pathol* 2012;65:293–301.

45. Krizova A, Clarke BA, Bernardini MQ, James S, Kalloger SE, Boerner SL *et al*. Histologic artifacts in abdominal, vaginal, laparoscopic, and robotic hysterectomy specimens: a blinded, retrospective review. *Am J Surg Pathol* 2011;35:115–126.

46. Logani S, Herdman AV, Little JV, Moller KA. Vascular ‘‘pseudo-invasion’’ in laparoscopic hysterectomy specimens: a diagnostic pitfall. *Am J Surg Pathol* 2008;32:560–565.

47. Kitahara S, Walsh C, Frumovitz M, Malpica A, Silva EG. Vascular pseudoinvasion in laparoscopic hysterectomy specimens for endometrial carcinoma: a grossing artifact? *Am J Surg Pathol* 2009;33:298–303.

48. Morrow CP, Bundy BN, Kurman RJ, Creasman WT, Heller P, Homesley HD *et al*. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. *Gynecol Oncol* 1991;40: 55–65.

49. Pitson G, Colgan T, Levin W, Lockwood G, Manchul L, Milosevic M *et al*. Stage II endometrial carcinoma: prognostic factors and risk classification in 170 patients. *Int J Radiat Oncol Biol Phys* 2002;53:862–867.

50. Zaino R, Zhu J, Abendroth C, Yemelyanova A, Oliva E, Lim D. Stage II endometrial carcinoma: endocervical gland spread is not reproducibly distinguished from endocervical stromal invasion. *Mod Pathol* 2011;24(suppl 224A).

51. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynecol Obstet* 2009;105:103–104.

52. McCluggage WG, Hirschowitz L, Wilson GE, Oliva E, Soslow RA, Zaino RJ. Significant variation in the assessment of cervical involvement in endometrial carcinoma: an interobserver variation study. *Am J Surg Pathol* 2011;35:289–294.

53. Tambouret R, Clement PB, Young RH. Endometrial endometrioid adenocarcinoma with a deceptive pattern of spread to the uterine cervix: a manifestation of stage IIb endometrial carcinoma liable to be misinterpreted as an independent carcinoma or a benign lesion. *Am J Surg Pathol* 2003;27:1080–1088.

54. Nicklin JL, Petersen RW. Stage 3B adenocarcinoma of the endometrium: a clinicopathologic study. *Gynecol Oncol* 2000;78:203–207.

55. Jobsen JJ, Naudin Ten Cate L, Lybeert ML, Scholten A, van der Steen-Banasik EM, van der Palen J *et al*. Outcome of endometrial cancer stage IIIA with adnexa or serosal involvement only. *Obstet Gynecol Int* 2011;2011:962518.

56. Hétu V, Petignat P, Wu Y, Drouin P, Sauthier P, Provencher D *et al*. Positive adnexal or uterine serosal involvement in stage IIIC endometrial cancer is an adverse factor for recurrence. *Gynecol Obstet Invest* 2009;67:173–177.

57. Yura Y, Tauchi K, Koshiyama M, Konishi I, Yura S, Mori T *et al*. Parametrial involvement in endometrial carcinomas: its incidence and correlation with other histological parameters. *Gynecol Oncol* 1996;63:114–119.

58. Sato R, Jobo T, Kuramato H. Parametrial spread is a prognostic factor in endometrial carcinoma. *Eur J Gynaecol Oncol* 2003;24:241–245.

59. Connell PP, Rotmensch J, Waggoner S, Mundt AJ. The significance of adnexal involvement in endometrial carcinoma. *Gynecol Oncol* 1999;74:74–79.

60. Culton LK, Deavers MT, Silva EG, Liu J, Malpica A. Endometrioid carcinoma simultaneously involving the uterus and the fallopian tube: a clinicopathologic study of 13 cases. *Am J Surg Pathol* 2006;30:844–849.

61. Zaino RJ, Unger ER, Whitney C. Synchronous carcinomas of the uterine corpus and ovary. *Gynecol Oncol* 1984;19:329–335.

62. Ayhan A, Yalçin OT, Tuncer ZS, Gürgan T, Küçükali T. Synchronous primary malignancies of the female genital tract. *Eur J Obstet Gynecol Reprod Biol* 1992;45:63–66.

63. Singh N. Synchronous tumours of the female genital tract. *Histopathology* 2010;56:277–285.

64. McCluggage WG. WT1 is of value in ascertaining the site of origin of serous carcinomas within the female genital tract. *Int J Gynecol Pathol* 2004;23:97–99.

65. Hirschowitz L, Ganesan R, McCluggage WG. WT1, p53 and hormone receptor expression in uterine serous carcinoma. *Histopathology* 2009;55:478–482.

66. Fujiwara H, Saga Y, Takahashi K, Ohwada M, Enomoto A, Konno R *et al*. Omental metastases in clinical stage I endometrioid adenocarcinoma. *Int J Gynecol Cancer* 2008;18:165–167.

67. Boren T, Lea J, Kehoe S, Miller DS, Richardson D. Lymph node metastasis in endometrioid adenocarcinomas of the uterine corpus with occult cervical involvement. *Gynecol Oncol*. 2012;127:43–46.

68. Okazawa M, Ueda Y, Enomoto T, Yoshino K, Kono K, Mabuchi S *et al*. A retrospective analysis of endometrial carcinoma cases surgically treated with or without para-aortic lymph node dissection followed by adjuvant chemotherapy. *Eur J Gynaecol Oncol*. 2012;33:620–624.

69. Sobin L, Gospodarowicz M, Wittekind C (eds). *International Union Against Cancer, TNM Classification of Malignant Tumours (7th edition)*. Chichester: Wiley-Blackwell, 2009.

70. McCluggage WG, Hirschowitz L, Ganesan R, Kehoe S, Nordin A. Which staging system to use for gynaecological cancers: recommendations for practice in the United Kingdom. *J Clin Pathol* 2010;63:768–770.

71. Pacaut C, Bourmaud A, Rivoirard R, Moriceau G, Guy JB, Collard O *et al*. Uterine and ovary carcinosarcomas: outcome, prognosis factors, and adjuvant therapy. *Am J Clin Oncol*, in press. doi: 10.1097/COC.0b013e3182979b27.

72. Werner HM, Trovik J, Marcickiewicz J, Tingulstad S, Staff AC, Amant F,Salvesen HB; MoMaTEC study group. Revision of FIGO surgical staging in 2009 for endometrial cancer validates to improve risk stratification. *Gynecol Oncol* 2012;125:103–108.

73. Horn LC, Dallacker M, Bilek K. [Carcinosarcomas (malignant mixed Mullerian tumours) of the uterus. Morphology, pathogenetic aspects and prognostic factors]. *Pathologe* 2009; 30:292–301.

74. Silverberg SG, Major FJ, Blessing JA, Fetter B, Askin FB, Liao SY *et al*. Carcinosarcoma (malignant mixed mesodermal tumour) of the uterus. A Gynecologic Oncology Group pathologic study of 203 cases. *Int J Gynecol Pathol* 1990;9:1–19.

75. Ferguson SE, Tornos C, Hummer A, Barakat RR, Soslow RA. Prognostic features of surgical stage I uterine carcinosarcoma. *Am J Surg Pathol* 2007;31:1653–1661.

76. Van der Horst C, Evans AJ. Peritoneal keratin granulomas complicating endometrial carcinoma: a report of two cases and review of the literature. *Int J Gynecol Cancer* 2008;18:549–553.

77. Demirkiran F, Yavuz E, Erenel H, Bese T, Arvas M, Sanioglu C. Which is the best technique for endometrial sampling? Aspiration (pipelle) versus dilatation and curettage (D&C). *Arch Gynecol Obstet* 2012;286:1277–1282.

78. Sany O, Singh K, Jha S. Correlation between preoperative endometrial sampling and final endometrial cancer histology. *Eur J Gynaecol Oncol* 2012;33:142–144.

79. Mitchard J, Hirschowitz L. Concordance of FIGO grade of endometrial adenocarcinomas in biopsy and hysterectomy specimens. *Histopathology* 2003;42(4):372–378.

80. Mittal K, Sebenik M, Irwin C, Yan Z, Popiolek D, Curtin J *et al*. Presence of endometrial adenocarcinoma in situ in complex atypical endometrial hyperplasia is associated with increased incidence of endometrial carcinoma in subsequent hysterectomy. *Mod Pathol* 2009;22:37–42.

81. Ganesan R, Brown LJ, Kehoe S, McCluggage WG, El-Bahrawy MA. The role of frozen sections in gynaecological oncology: survey of practice in the United Kingdom. *Eur J Obstet Gynecol Reprod Biol* 2013;166:204–208.

82. Alkushi A, Irving J, Hsu F, Dupuis B, Liu CL, Rijn M *et al*. Immunoprofile of cervical and endometrial adenocarcinomas using a tissue microarray. *Virchows Arch* 2003;442:271–277.

83. Castrillon DH, Lee KR, Nucci MR. Distinction between endometrial and endocervical adenocarcinoma: an immunohistochemical study. *Int J Gynecol Pathol*. 2002;21:4–10.

84. McCluggage WG, Sumathi VP, McBride HA, Patterson A. A panel of immunohistochemical stains, including carcinoembryonic antigen, vimentin, and estrogen receptor, aids the distinction between primary endometrial and endocervical adenocarcinomas. *Int J Gynecol Pathol* 2002;21:11–15.

85. Voss MA, Ganesan R, Ludeman L, McCarthy K, Gornall R, Schaller G *et al*. Should grade 3 endometrioid endometrial carcinoma be considered a type 2 cancer – a clinical and pathological evaluation. *Gynecol Oncol* 2012;124:15–20.

86. Zannoni GF, Vellone VG, Arena V, Prisco MG, Scambia G, Carbone A *et al*. Does high-grade endometrioid carcinoma (grade 3 FIGO) belong to type I or type II endometrial cancer? A clinical-pathological and immunohistochemical study. *Virchows Arch* 2010;457:27–34.

87. McCluggage WG, Soslow RA, Gilks CB. Patterns of p53 immunoreactivity in endometrial carcinomas: 'all or nothing' staining is of importance. *Histopathology* 2011;59:786–788.

88. Yamamoto S, Tsuda H, Aida S, Shimazaki H, Tamai S, Matsubara O. Immunohistochemical detection of hepatocyte nuclear factor 1beta in ovarian and endometrial clear-cell adenocarcinomas and nonneoplastic endometrium. *Hum Pathol* 2007;38:1074–1080.

89. Lynch HT, Lynch PM, Lanspa SJ, Snyder CL, Lynch JF, Boland CR. Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. *Clin Genet* 2009;76:1–18.

90. Resnick KE, Hampel H, Fishel R, Cohn DE. Current and emerging trends in Lynch syndrome identification in women with endometrial cancer. *Gynecol Onco.* 2009;114:128–134.

Appendix A WHO classification of endometrial carcinomas

- Adenocarcinoma
  - Endometrioid
    - Variant with squamous differentiation
    - Villoglandular variant
    - Secretory variant
    - Ciliated cell variant
  - Mucinous
  - Serous
  - Clear cell
  - Mixed cell carcinoma

- Squamous cell carcinomas
- Transitional carcinomas
- Small cell carcinoma
- Undifferentiated carcinoma
- Carcinosarcoma

Appendix B SNOMED T and M codes and SNOMED CT codes for endometrial tumours

Topographical codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Uterus	T83000 (SNOMED3.5) T82000 (SNOMED2)	Uterine structure (body structure)	35039007
Endometrium	T83400 (SNOMED3.5) T84000 (SNOMED2)	Endometrial structure (body structure)	2739003

Morphological codes	SNOMED 2 or 3	SNOMED CT terminology	SNOMED CT code
Endometrioid adenocarcinoma	M83803	Endometrioid carcinoma (morphologic abnormality)	30289006
Endometrioid adenocarcinoma variant with squamous differentiation	M85703	Adenocarcinoma with squamous metaplasia (morphologic abnormality)	15176003
Endometrioid adenocarcinoma, villoglandular variant	M82623	Villous adenocarcinoma (morphologic abnormality)	28558000
Endometrioid adenocarcinoma, secretory variant	M83823	Endometrioid adenocarcinoma, secretory variant (morphologic abnormality)	128680006
Endometrioid adenocarcinoma, ciliated cell variant	M83833	Endometrioid adenocarcinoma, ciliated cell variant (morphologic abnormality)	128681005
Mucinous adenocarcinoma	M84803	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Serous adenocarcinoma	M84413	Serous cystadenocarcinoma (morphologic abnormality)	90725004
Clear cell adenocarcinoma	M83103	Clear cell adenocarcinoma (morphologic abnormality)	30546008
Mixed cell adenocarcinoma	M83233	Mixed cell adenocarcinoma (morphologic abnormality)	38958001
Squamous cell carcinoma	M80703	Squamous cell carcinoma, no ICD-O subtype (morphologic abnormality)	28899001

Morphological codes (continued)	SNOMED 2 or 3	SNOMED CT terminology	SNOMED CT code
Transitional carcinoma	M81203	Transitional cell carcinoma (morphologic abnormality)	27090000
Small cell carcinoma	M80413	Small cell carcinoma (morphologic abnormality)	74364000
Undifferentiated carcinoma	M80203	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Carcinosarcoma	M89803	Carcinosarcoma (morphologic abnormality)	63264007

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 FIGO and TNM staging of endometrial tumours

FIGO stage (2009)

IA Tumour confined to the uterus, no or < half myometrial invasion

IB Tumour confined to the uterus, ≥ half myometrial invasion

II Tumour involves the uterus and the cervical stroma

IIIA Tumour invades serosa or adnexa

IIIB Vaginal and/or parametrial involvement

IIIC1 Pelvic lymph node involvement

IIIC2 Para-aortic lymph node involvement, with or without pelvic node involvement

IVA Tumour invasion bladder mucosa and/or bowel mucosa

IVB Distant metastases including abdominal metastases and/or inguinal lymph nodes

TNM classification (7th edition)

Primary tumour (T)

Tx Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma *in situ* (preinvasive carcinoma)

T1 Carcinoma confined to corpus uteri

T1a Tumour limited to endometrium or invades less than one half of the myometrium

T1b Tumour invades one half or more of the myometrium

T2 Tumour invades stromal connective tissue of the cervix but does not extend beyond the uterus

T3a Tumour involves serosa and/or adnexa (direct extension or metastases)

T3b Vaginal or parametrial involvement (direct extension or metastases)

T4 Tumour invades bladder mucosa and/or bowel mucosa (bullous oedema is not enough to classify a tumour as T4)

Regional lymph nodes (N)

NX Regional nodes cannot be assessed

N0 No regional lymph node metastases

N1 Regional lymph node metastases to pelvic lymph nodes

N2 Regional lymph node metastasis to para-aortic nodes, with or without positive pelvic lymph nodes

Distant metastases (M)

M0 No distant metastases

M1 Distant metastases (includes metastases to inguinal lymph nodes, intraperitoneal disease, or lung, liver, or bone metastases; it excludes metastases to para-aortic lymph nodes, vagina, serosa or adnexa)

Positive peritoneal cytology has to be reported without altering stage.

Stage grouping

Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1,T2,T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Appendix D Histology reporting proforma for endometrial tumours

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

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

Date of receipt……. Report no……..... Surgeon……..…

Core clinical items

Hysterectomy type: Abdominal ☐ Vaginal ☐ Laparoscopic ☐ Not known ☐

Core macroscopic items

Specimen type: Simple hysterectomy ☐ Radical hysterectomy ☐
Other (specify): …….

Attached structures: Adnexa ☐ Vaginal cuff ☐ Parametrium ☐
Other (specify): ….....

Accompanying specimens: Omentum ☐

Lymph nodes: ☐ Pelvic ☐ Para-aortic ☐

Other ☐ (specify) ……..……..

Site of tumour: Fundus ☐ Body ☐ Isthmus ☐ Cornu ☐

Maximum dimension of tumour: ….....mm

Core microscopic items

Tumour type: Endometrioid ☐ Mucinous ☐ Serous ☐
Clear cell ☐ Carcinosarcoma ☐
Undifferentiated ☐ Other (specify)……

FIGO grade: 1 ☐ 2 ☐ 3 ☐

Myometrial invasion: None or < 50% ☐ ≥ 50% ☐

Tumour-free distance to serosa (mm): ….

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

Microscopic involvement of:

Cervical stroma	Yes ☐	No ☐	Not assessable ☐
Vagina	Yes ☐	No ☐	Not assessable ☐
Adnexa	Yes ☐	No ☐	Not assessable ☐
Uterine serosa	Yes ☐	No ☐	Not assessable ☐
Parametrium	Yes ☐	No ☐	Not assessable ☐

Lymph nodes: Not sampled ☐ Sampled ☐

Right pelvic lymph nodes (number positive/total number): ……/……

Left pelvic lymph nodes (number positive/total number): ……/……

Para-aortic lymph nodes (number positive/total number): ……/……

Omentum: Not sampled ☐

If sampled: Involved by tumour ☐ Not involved by tumour ☐

Comments:

Provisional FIGO stage:

Provisional TNM stage:

SNOMED code/s T …… M……

Reporting pathologist .....…….. Date……...../……...../……..

Appendix E Summary table – explanation of levels of evidence

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

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

Appendix F AGREE compliance monitoring sheet

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

AGREE standard	Section of dataset
SCOPE AND PURPOSE	
1. The overall objective(s) of the guideline is (are) specifically described	Foreword
2. The clinical question(s) covered by the guidelines is (are) specifically described	Introduction
3. The patients to whom the guideline is meant to apply are specifically described	Foreword
STAKEHOLDER INVOLVEMENT	
4. The guideline development group includes individuals from all the relevant professional groups	Foreword
5. The patients' views and preferences have been sought	N/A
6. The target users of the guideline are clearly defined	Introduction
7. The guideline has been piloted among target users	Introduction
RIGOUR OF DEVELOPMENT	
8. Systematic methods were used to search for evidence	Foreword
9. The criteria for selecting the evidence are clearly described	Foreword
10. The methods used for formulating the recommendations are clearly described	Foreword
11. The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword and Introduction
12. There is an explicit link between the recommendations and the supporting evidence	All sections
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	All sections
16. The different options for management of the condition are clearly presented	All sections
17. Key recommendations are easily identifiable	5 and 6
18. The guideline is supported with tools for application	Appendices
APPLICABILITY	
19. The potential organisational barriers in applying the recommendations have been discussed	Foreword
20. The potential cost implications of applying the recommendations have been considered	Foreword
21. The guideline presents key review criteria for monitoring and/audit purposes	11
EDITORIAL INDEPENDENCE	
22. The guideline is editorially independent from the funding body	Foreword
23. Conflicts of interest of guideline development members have been recorded	Foreword

* The Lay Advisory Committee (LAC) of The Royal College of Pathologists advised the Director of Communications that there is no reason to consult directly with patients or the public regarding this dataset because it is technical in nature and intended to guide pathologists in their practice. The authors will refer to the LAC for further advice if necessary.