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

Standards and datasets for reporting cancers

Dataset for histological reporting of endometrial cancer

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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 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 in the production of this 5th edition of the dataset:

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

The information used to develop this dataset was collected from electronic searches of databases including databases of systematic reviews, journals (PubMed), conference proceedings, Cochrane reviews, NICE guidance for relevant evidence and systematic reviews up to December 2015. 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] (www.iccr-cancer.org/datasets).

Modified SIGN guidance has been used to grade the evidence (Appendix H) and the grade is indicated in the text.

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

The International Society of Gynecological Pathologists (ISGyP) is undertaking a major working group exercise regarding many aspects of endometrial carcinomas. This work is likely to be published in 2017/2018 and may result in a further revision of this dataset earlier than the three-year cycle.

The dataset has been reviewed by the Clinical Effectiveness department, Working Group on Cancer Services and Lay Governance Group. It was placed on the College website for consultation with the membership from 13 February to 13 March 2017. All comments received be addressed by the authors to the satisfaction of the Chair of the Working Group and the Director of Publishing and Engagement.

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

This document details core (or required) and non-core (or recommended) data items to be included in histopathology reports on endometrial carcinoma. Core data items are identified as items that are required by the National Cancer Outcomes and Services Dataset (COSD) for the staging and grading of cancers and that published evidence indicates are required for optimal patient management and prognosis. Items that fall outside the core definition are included as non-core items. Such items are included to provide a comprehensive report or to meet local clinical or research requirements.[2]

This dataset includes a brief account of the major subtypes of endometrial cancer included in the 2014 World Health Organization (WHO) classification,[3] namely endometrioid adenocarcinoma, mucinous, serous, clear cell, mixed, undifferentiated and dedifferentiated carcinomas, neuroendocrine carcinomas and carcinosarcoma (malignant mixed Mullerian/mesodermal tumour). The latter is included in the category of mixed epithelial and mesenchymal neoplasms in WHO 2014 but is discussed here since it is in essence a malignancy of epithelial origin and is staged in the same manner as other endometrial carcinomas; this is stated in the FIGO 2009 staging system for endometrial cancers.[4] Serous endometrial intraepithelial carcinoma (serous EIC) is considered a precursor of uterine serous carcinoma and coded as such by the IARC/WHO committee for ICD-O, but is listed within the endometrial carcinomas in the new WHO 2014 classification. There are variants of endometrioid carcinoma that are not listed here.

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

- certain features, such as type and grade of carcinoma, cervical involvement, depth of myometrial invasion, serosal involvement and lymph node metastasis will determine the type of surgery performed, whether adjuvant therapy will be administered and the choice of adjuvant therapy
- the features noted as core data items provide sufficiently accurate pathological information that can be used together with clinical data for the patient to be given a prognosis
- accurate typing of endometrial cancers can allow epidemiological information to emerge especially with regard to occurrence in genetic syndromes
- to facilitate patient enrolment in trials, the collection of necessary information (key elements) as to histopathological type, baseline staging, etc. is mandatory. Use of a structured reporting format allows easy extraction of the necessary information.

1.1 Changes since the 4th edition

The revised dataset is largely modelled on the previous edition but has undergone major revision. The main items that have been added or altered are as follows:

- discussion of new entities in WHO 2014[3] classification of endometrial carcinoma

- serous EIC
- neuroendocrine carcinomas
- undifferentiated and dedifferentiated carcinoma
- quantifying components of mixed carcinoma
- upgrading of tumour on basis of nuclear grade
- specific mention that vascular invasion without tissue involvement does not affect staging
- assessment of myometrial invasion including discussion of methods used
- peritoneal involvement and distant metastases moved from non-core to core items of dataset
- measurement of tumour free distance to serosa and site of tumour moved from core to non-core item of dataset
- inclusion of absolute depth of myometrial invasion and percentage of myometrium involved in non-core items
- update on molecular pathology to include genomic characterisation of endometrial carcinoma and molecular evidence in understanding of synchronous endometrial and ovarian carcinoma
- updated section on immunohistochemistry.

No major organisational changes have been identified that would hinder the implementation of the dataset, which is fully integrated with the COSD, and there are no major financial implications arising from implementation of this guidance.

The core items are summarised as a proforma, which may be used as the main reporting format but preferably with free text.

1.2 Target users and health benefits of this guidance

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 (MDT) meetings 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 highly desirable to provide 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.

3 Preparation of the 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. Good preservation of tumour morphology is of crucial importance for accurate subtyping and grading of any tumour and endometrial carcinomas are especially likely to be affected by autolysis. Prompt fixation is also necessary to ensure reliable immunohistochemistry. 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; in these cases, the ovaries should be handled in the same way as an ovarian tumour. Slicing may facilitate adequate fixation but this should only be done after careful inspection of the capsule.

4 Specimen handling and block taking

Many pathologists weigh and measure all solid organs. The measurements of the uterus and ovaries may vary with age, parity, body mass index, phase of the menstrual cycle and other associated pathologic processes.[5,6]

There are several ways of opening the uterus, depending on the preference and experience of the pathologist.[7] Some pathologists prefer to open the uterus in the sagittal plane while others open it coronally along the lateral border through 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.

4.1 Selection of blocks for histology

- Tumour – at least four blocks of tumour must be sampled. These blocks should include the full thickness of the uterine wall and the serosa at the site of deepest myometrial invasion. This may be as a number of conventional sized blocks or one big/mega block.
- At least one block of isthmus/lower uterine segment (LUS) should be taken in all cases.
- In cases with biopsy proven carcinoma, but no visible tumour, cornual blocks must be taken; the entire endometrium may need to be blocked depending on the histological findings in the initial sections.
- Cornual blocks may also be taken when there is adnexal involvement. The presence of carcinoma in the cornual mucosa or lumen may favour metastatic adnexal disease rather than synchronous adnexal involvement. However, this is only one factor to be taken into consideration when attempting to distinguish between metastatic and synchronous adnexal involvement.
- The parametrial tissue should be blocked in its entirety.
- Two longitudinal blocks each including a lip of the cervix should be submitted. The blocks should include the entire length of the endocervical canal. Additional blocks may be needed to include the vaginal cuff if present.
- One or two blocks each of both ovaries and tubes should be submitted if grossly normal. The tubal blocks should include the fimbria.[8]
- Appropriate numbers of blocks to sample other abnormalities such as fibroids or adnexal masses.

- Omentum – one block, taken from an area of obvious tumour, is adequate in cases where macroscopically visible tumour nodules are present. If the omentum is macroscopically normal, we recommend that two to 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 3 mm should be bisected or sliced perpendicular to the longest axis of the node, to maximise examination of the subcapsular sinus, while those smaller than 3 mm can be processed intact.[9,10]
- All peritoneal biopsies should be blocked *in toto.*
- Representative blocks should be taken from any other tissues submitted.

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

5 Core data items to be included in the histopathology report

5.1 Clinical core data items

5.1.1 Hysterectomy type

The type of hysterectomy should be documented: abdominal, vaginal or laparoscopic. 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. The clinical working diagnosis and results of previous biopsy as well as any relevant family history should be mentioned.

5.1.2 Relevant family history

Any relevant family history such as history of endometrial or colonic carcinoma should be mentioned.

5.2 Pathological core data: macroscopic data items

5.2.1 Details of hysterectomy specimen

The different components of the hysterectomy specimen (uterine corpus, cervix, ovaries and tubes) should be specified 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 of parametrial tissues should be recorded in case of radical hysterectomy specimens. Wispy connective tissue present on the lateral surface of the uterus removed at simple hysterectomy does not constitute parametrectomy.

Apart from the tumour details as below, the presence of any gross abnormalities in any anatomical structure should be documented. Absence of abnormality should be noted.

5.2.2 Accompanying specimens

The omentum, if received, should be measured and the presence and dimensions of the largest visible deposit 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.[9] The peritoneal biopsies from each submitted anatomical site must be described and measured and any gross abnormalities recorded.

5.2.3 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.

5.3 Pathological core data: microscopic data items

5.3.1 Tumour type

Endometrial carcinomas should be typed according to the WHO 2014 classification[3] (see Appendix A). Accurate typing is necessary on 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.[11–13] Information about mucinous carcinomas is still relatively limited but available information suggests that their clinical behaviour is similar to that of endometrioid adenocarcinoma.[14]

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 the WHO 2014 classification[3] and specialist textbooks of gynaecological pathology. A few points will, however, be highlighted for clarification. Mucinous adenocarcinoma refers to a subtype of endometrial adenocarcinoma in which more than 50% of the tumour cells contain abundant intracytoplasmic mucin in contrast to endometrioid adenocarcinomas that contain focal mucinous areas. Mucinous carcinomas are almost always well differentiated and have a good prognosis.[14]

Serous EIC is an intraepithelial neoplasm that usually arises in atrophic endometrium or sometimes in an endometrial polyp. It is characterised by cytology and immunophenotype similar to uterine serous carcinoma but the tumour is confined to the pre-existing endometrial epithelium with no invasion of the endometrial stroma or myometrium. Even in the absence of demonstrable invasion, serous EIC can shed cells and metastasise to extrauterine sites; this is the rationale for including this as a subtype of endometrial carcinoma in the WHO 2014 classification.[11–13,15,16]

Carcinosarcomas (malignant mixed Mullerian tumours) are now known to be epithelial neoplasms that have undergone sarcomatous metaplasia,[17,18] the epithelial elements being the 'driving force'. As stated previously, they are classified in the category of mixed epithelial and mesenchymal neoplasm but are staged like other endometrial cancers. Undifferentiated carcinoma has recently been highlighted as an aggressive form of uterine carcinoma. It is defined in the WHO 2014 classification[3] as 'a malignant epithelial neoplasm with no differentiation'.[19] Undifferentiated carcinoma may occur in pure form or in combination with a low-grade (grade 1 or 2) endometrioid adenocarcinoma; the combination of a low-grade endometrioid adenocarcinoma and undifferentiated carcinoma is referred to as dedifferentiated carcinoma. Undifferentiated carcinomas display evidence of epithelial differentiation only in occasional tumour cells. The WHO 2014 classification[3] includes neuroendocrine tumours and they are divided into low-grade neuroendocrine tumour (carcinoid tumour) and high-grade neuroendocrine carcinoma (small cell and large cell neuroendocrine carcinoma).[20–22] Neuroendocrine tumours may occur in pure form or in association with another morphological subtype of endometrial carcinoma.[23]

Mixed carcinoma refers to a tumour composed of more than one morphological type, at least one of which should be non-endometrioid/mucinous, typically serous carcinoma. Using the current WHO definition, the non-dominant type of differentiation must comprise at least 5% of the tumour. 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 5% of the neoplasm. This is of importance in that

oncologists would administer treatment for an aggressive tumour type, even if this comprises <5% of the neoplasm.

[Level of evidence B – prognostic importance of tumour type.]

[Level of evidence C – serous EIC, dedifferentiated, undifferentiated and neuroendocrine carcinomas.]

5.3.2 Tumour grade

The histologic FIGO grade[24,25] 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 Gynaecological Oncology Group and is primarily based on the architectural arrangement of the neoplastic cells that 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. The presence of grade 3 nuclei involving more than 50% of the tumour is associated with more aggressive behaviour and justifies upgrading of grade 1 or 2 tumours by one grade. Grade 3 nuclei are rounded, contain prominent, often multiple, nucleoli and show variability in size.[25] 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 reported as automatically grade 3 and should be recorded as grade 3.

The FIGO grading system has demonstrated prognostic utility but is unfortunately poorly reproducible.[26] The poor reproducibility of FIGO grading has led to attempts to devise two-tier grading systems that are likely to be more reproducible simply by reducing the number of categories.[27–29] However, for the time being, it is recommended that histopathologists continue to use the generally accepted, albeit imperfect, FIGO grading system.

In cases where there is a significant discrepancy between the reported tumour grade/type in the biopsy and in the hysterectomy, especially when there is no or minimal residual tumour in the hysterectomy specimen, it may be necessary to review the prior biopsy and take this into account when assigning the final tumour grade/type.

[Level of evidence B – prognostic importance of tumour grade.]

5.3.3 Myometrial invasion

Deep myometrial invasion by tumour has 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. The depth of myometrial invasion (inner or outer half) should be documented as this is required for tumour staging, prognostication and adjuvant therapy. 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).

Various methods of determining the extent of myometrial invasion have been evaluated.[30–32] 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. 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.[33] These last three parameters are included as non-core items in this dataset.

In most cases, determining the depth of myometrial invasion is not difficult. However, in some instances, this may be problematic. 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 does not seem to affect the outcome.[34] Morphologic features of the myoinvasive tumour such as a minimal deviation pattern, a microcystic elongated and fragmented pattern and associated smooth muscle metaplasia in polypoid neoplasms may result in problems in assessment of the presence and extent of myoinvasion.[30,35,36]

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 the recommended 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 the absolute depth of myometrial invasion cannot be ascertained, myometrial infiltration that reaches the arcuate vascular plexus of the uterus usually indicates >50% myometrial invasion.[31]

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

5.3.4 Lymphovascular space invasion

Lymphovascular space invasion (LVSI) within the myometrium has been demonstrated in repeated studies to be an independent prognostic factor in endometrial adenocarcinomas.[37–39] More recent evidence suggests that that substantial vascular invasion is predictive of pelvic regional recurrence, distant recurrence and overall survival.[40] However, evidence-based definitions of focal versus substantial vascular invasion are not universally agreed and for the purpose of this dataset we recommend that LVSI, when present, is noted. Presence of perivascular infiltrates correlates closely with LVSI but does not have independent prognostic significance.[40,41]

It is important to note that the presence of LVSI, whether within the uterus or outside it, does not upstage the tumour. For example, the presence of vascular invasion in the outer half of the myometrium or in cervical or adnexal vessels in a carcinoma with myoinvasion confined to the inner half would still be considered to be FIGO stage IA. However, the presence of vascular invasion at these sites should be recorded and should be taken into account at the MDT meeting when discussing the need for adjuvant therapy.

LVSI 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 LVSI 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. Immunohistochemistry for markers such as CD31 (which stains all vascular channels) and D2-40 (which stains lymphatic channels) may assist in identifying vascular invasion.[42]

True LVSI 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. Such vascular invasion may be disproportionate in comparison with 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 pseudoinvasion in total laparoscopic hysterectomy specimens using an intrauterine balloon manipulator has recently been highlighted.[43-45] 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. It is also suggested that this may be due to mechanical displacement of friable intraluminal tumour by the balloon and a subsequent grossing artefact. 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 essential.

[Level of evidence B – prognostic relevance of lymphovascular invasion.]

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

5.3.5 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, with deeper myometrial invasion, and a higher rate of lymphovascular invasion and nodal spread than tumours that are confined to the corpus.[46,47] 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.[47] 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[4] includes only cervical stromal invasion as stage II; tumours showing only cervical epithelial or crypt involvement directly or by drop metastasis remain within stage I. Assessment of cervical involvement is often difficult and has been shown to have low reproducibility even among specialised gynaecological pathologists.[48,49] 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. 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.[50] 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.

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

5.3.6 Vaginal involvement

Vaginal involvement may be identified as a distinct nodule and submitted separately by the gynaecologist at the time of operation. 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 <2 years.[51] Reporting of vaginal involvement thus provides prognostic information that is critical to appropriate management and it is considered a core data item.

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

5.3.7 Uterine serosal involvement

The uterine serosa is considered 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.[52,53]

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

5.3.8 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 preoperatively. In these cases, the entire parametrium should be submitted for microscopic examination.[54,55] 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.

5.3.9 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.[56] 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.[57] 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. The distinction between synchronous primary carcinomas and ovarian metastases from endometrial carcinomas has been based on morphological criteria. When early stage, low-grade endometrioid adenocarcinomas involve the uterus and one or both ovaries, they are regarded as most likely to represent synchronous independent primary neoplasms. Adjacent endometrial hyperplasia, in the case of the uterine tumour, and endometriosis or a component of benign or borderline 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 has been regarded as likely. Emerging molecular studies indicate that ovarian and endometrial endometrioid carcinomas have distinct genetic profiles.[58] In many cases these are clonally related, and therefore more likely to be primary and metastatic rather than synchronous independent tumours, although the directionality of the metastasis is not proven.[59–61] However, as molecular studies are not performed routinely, and, more importantly, these combinations show clinically indolent

behaviour, their continued classification as 'synchronous' based on morphology should dictate their clinical management.

With a high-grade carcinoma involving the uterus and one or both ovaries, the situation is different. Uterine serous carcinoma has a marked propensity for extrauterine 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 uterine serous carcinoma with metastasis to the adnexa, an adnexal primary with spread to the endometrium or independent primaries. Most ovarian and tubal high-grade serous carcinomas exhibit diffuse strong nuclear positivity with WT1. By contrast, uterine serous carcinoma is usually negative, although some cases are positive.[62,63] With a high-grade carcinoma involving more than one location, the likely site of origin should be based on disease distribution and immunohistochemical results and an appropriate stage applied; these should not be considered to be synchronous independent primaries unless they are distinct morphologically and on immunohistochemistry.

[Level of evidence C – assessment of synchronous and metastatic involvement.]

5.3.10 Omental involvement

Omental involvement by endometrial carcinoma is associated with an adverse outcome with a decreased overall survival; it is categorised as FIGO stage IVB.[64] Omental involvement correlates with deep myometrial invasion, high tumour grade, non-endometrioid histology, lymph node metastasis and adnexal involvement.[65]

[Level of evidence C – prognostic value of omental involvement.]

5.3.11 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 this does occur occasionally. In the 2009 revision of the FIGO staging system, stage IIIC is divided into stage IIIC1 (positive pelvic nodes) and stage IIIC2 (positive para-aortic nodes with or without positive pelvic nodes).[65,66]

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.

[Level of evidence C – Importance of lymph node counts.]

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

5.3.12 Peritoneal involvement

Peritoneal involvement is more common with non-endometrioid carcinomas, especially of serous type. Peritoneal involvement is not specifically referred to in the 2009 FIGO staging system[4] but should be documented; if present, the site of the peritoneal involvement should also be documented. Spread to pelvic peritoneum including bladder, sigmoid serosa and cul-de-sac is FIGO stage IIIA while spread to the abdominal peritoneum is FIGO stage IVB. Occasionally, keratin granulomas are identified in the peritoneum, 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.[67]

5.3.13 Distant metastases

Distant spread refers to metastasis beyond the pelvic cavity and signifies stage IV disease. Common sites of distant spread are the omentum, the lungs, the peritoneal lining of the paracolic gutters and the peritoneum covering the bowel and diaphragm. Less common

sites are the liver, brain and bone. The pathology report includes only microscopically identified disease for the purposes of staging. However, clinical or imaging findings may reveal distant disease and this should be noted at the MDT meeting and the final stage assigned here.

5.3.14 Provisional FIGO stage

Two staging systems are in widespread use for gynaecological cancers: the FIGO system, which is specific for gynaecological cancers, and TNM,[68] which is applicable to all tumour sites. A survey undertaken in the UK showed that most gynaecological pathologists report gynaecological cancers exclusively using FIGO staging systems and most gynaecological oncologists and other specialists dealing with patients with gynaecological malignancies likewise use FIGO.[69] Worldwide, most clinical trials and retrospective and prospective studies use FIGO rather than TNM.

The 2009 provisional FIGO stage 4 (provisional on the basis of the material submitted for pathologic examination) of all endometrial carcinomas should be documented on the pathology report; TNM staging is considered a non-core element. The final FIGO stage should be assigned at the MDT meeting.

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 C or Level D evidence. They may be included in the report depending on the preference of individual laboratories, individual groups of pathologists or to assist clinical research. They 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 with relation to the cancer prognosis or management and are therefore not included in the core data items.[5,6]

6.1.2 Location of tumour

The location of the tumour within the uterus is important. This can be recorded as LUS/isthmus, body, fundus or cornu. LUS/isthmus is defined as the area between the narrowing of the uterine body to the top of the endocervical canal. The fundus is the part of the uterus above the fallopian tubes. Approximately 14% of endometrial carcinomas arise in the LUS/isthmus. An isthmic location is seen more commonly in association with hereditary non-polyposis colorectal cancer syndrome/Lynch syndrome.[70] LUS involvement has also been shown to be an independent prognostic factor in conferring a higher risk of adverse outcomes including distant recurrence and death.[71,72]

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

[Level of evidence C – correlation of site of tumour with prognosis.]

6.2 Microscopic non-core data items

6.2.1 Percentages of different components of mixed carcinomas

In the case of mixed carcinomas, it is recommended that the percentage of each component be recorded in the pathology report even if the minor component comprises <5% 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, e.g. 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] A recent study has suggested that in stage I uterine carcinosarcomas, the presence of a heterologous mesenchymal component is a powerful adverse prognostic indicator.[75] Given this, it is suggested 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,[4] involvement of the cervical surface epithelium or glands (crypts) without stromal invasion represents stage I. It is advisable to document the presence or absence of cervical surface epithelial or crypt involvement.

6.2.4 Distance of tumour from cervical (or vaginal) margin

General oncological principles indicate that the margin of excision of tumours dictate 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 Myometrial involvement: absolute depth of myoinvasion

This is the distance between the endomyometrial junction and the deepest point of myometrial invasion.[33]

6.2.6 Myometrial involvement: percentage of myometrium involved

This is recorded as a percentage of myometrial thickness invaded by the tumour and is calculated by dividing the depth of invasion by the myometrial thickness and expressed as a percentage.[33]

6.2.7 Myometrial involvement: 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.[76–79] 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. All studies have shown this to be a significant predictive factor, although its performance relative to myometrial depth of invasion and percentage of infiltration has varied. Various cut-off measures have been put forward as being predictive of outcome but their evaluation requires larger prospective studies.

6.2.8 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 it is suggested that the presence of hyperplasia, atrophy and polyps be recorded.

6.2.9 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. Any report on peritoneal washings, if done, can be cross-referenced to the histology report. Advanced stage disease (stage III or IV) is associated with positive peritoneal cytology in approximately 30% of cases.

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 prospectively in the pathology report.

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 receptor [ER] and progesterone receptor [PR]) 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, owing to comorbidities or fertility conservation.

6.2.12 Provisional TNM stage

The updated version of the TNM classification for endometrial carcinoma[68] mirrors most of the changes in the 2009 FIGO staging system[4] and may be recorded as a non-core data item. The TNM system includes individual parameters that 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 it is preferable that this information be documented on the final pathology report. This is particularly important should the need for internal or external review arise. If the tumour has been submitted *in toto* for histological examination then this should be documented.

7 Diagnostic coding and staging

Primary endometrial carcinomas should be subtyped according to the WHO 2014 classification[3] and coded using SNOMED codes (Appendix A). Tumours should be staged using the 2009 FIGO staging system[4] (Appendix B) with the option to include TNM8 staging[68] (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 endometrial curettage under anaesthesia. The outpatient sample is a blind procedure and samples less of the endometrium. However, there is evidence that its reliability is similar to the curettage in generalised endometrial disorders. In some cases, though, 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 the submitted tissue should be processed.[80] When 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.

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 MDT meeting and their management should be based on the results of clinical, pathological and imaging findings.

9 Reporting of frozen sections

In most institutions in the UK, intraoperative 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 extrauterine 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, Ber-EP4, PAX8 and CK7, 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.

10.1 Typing endometrial carcinomas

Serous endometrial carcinomas can show an architecturally well-differentiated glandular pattern mimicking endometrioid adenocarcinoma. An immunohistochemical panel that is helpful in this differential includes p53, PR and PTEN. Mutant/aberrant p53 staining (overexpression or null) with lack of PR and PTEN staining favours serous carcinoma.[82,83] Clear cell carcinomas of the endometrium can be difficult to distinguish from serous and endometrioid carcinomas with clear cell change. Clear cell carcinomas are generally positive for Napsin A and hepatocyte nuclear factor 1B (HNF-1B). Napsin A is more specific than HNF-1B since the latter is not uncommonly positive. Caution is advised when interpreting HNF-1B as it can be positive in clear cell metaplasia and secretory endometrium, secretory variants of endometrioid carcinoma and serous carcinoma. Clear cell carcinomas are typically ER negative and show wild-type p53 staining.[84,85]

It is recognised that a subset of endometrial carcinomas show ambiguous morphology and are challenging to subtype. The TCGA analysis has revealed four major molecular types of endometrial carcinoma: POLE ultramutated (POLE), microsatellite instability-hypermutated (MSI/hypermutated), copy number-low and copy number-high.[86] Of these the POLE/ultramutated and MSI/hypermutated types are most likely to show confounding morphological features.[87] Diagnostic algorithms are being developed that will enable accurate subtyping[88] and these should become available in future practice.

10.2 Endometrial versus endocervical carcinomas

Immunohistochemistry to distinguish between endometrial and cervical adenocarcinoma is more often necessary in biopsies rather than in resection specimens. Generally, endometrioid and mucinous endometrial carcinomas are strongly and diffusely positive for vimentin, ER and PR and are largely negative for CEA.[89,90] The converse profile is usual in

cervical adenocarcinomas. P16 is expressed strongly and diffusely (block positivity)[91] in endocervical carcinomas, while patchy positive staining in a mosaic pattern is typically seen in endometrial endometrioid carcinomas. Vimentin expression in endometrioid adenocarcinomas is usually strong and expressed on the lateral membranes, but endometrial carcinomas with mucinous differentiation express vimentin less frequently.[89] 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.

11 Endometrial carcinomas associated with Lynch syndrome

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 include lower uterine segment location, undifferentiated areas and abundant tumour infiltrating lymphocytes. Loss of expression of mismatch repair proteins (MLH1/PMS2 or MSH2/MSH6) usually occurs.[92,93] On the basis of the immunohistochemical results, additional testing may follow. There are no guidelines currently and pathologists may need to carry out staining for mismatch repair proteins according to clinical or morphological triggers dictated by local protocols and preferences.

12 Criteria for audit of dataset

This dataset can be used as a standard in audits. Examples of audits include completeness of recording of all data items in histopathology reports, audits of numbers of lymph nodes retrieved and of variation between diagnostic biopsies and final histopathology reports.

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/profession/clinical-effectiveness/key-performance-indicators-kpi.html):

- cancer resections must be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPath cancer datasets. English Trusts were required to implement the structured recording of core pathology data in the COSD by January 2016
  - standard: 95% of reports must contain structured data.
- histopathology cases 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.

13 References

1 McCluggage WG, Colgan T, Duggan M, Hacker NF, Mulvany N, Otis C *et al*. Data set 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 The Royal College of Pathologists. *Guidance on Writing Cancer Datasets.* Accessed December 2017. Available at: www.rcpath.org/resourceLibrary/guidance-on-writing-cancer-datasets.html

3 Kurman RJ, Carcangiu ML, Herrington CS, Young RH. *WHO classification of tumours of the Female Reproductive Organs (4th edition)*. Lyon, France: IARC, 2014.

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

5 Dandolu V, Singh R, Lidicker J, Harmanli O. BMI and uterine size: is there any relationship? *Int J Gynecol Pathol* 2010;29:568–571.

6 Hauth EA, Jaeger HJ, Libera H, Lange S, Forsting M. MR imaging of the uterus and cervix in healthy women: determination of normal values. *Eur Radiol* 2007;17:734–742.

7 Robboy SJ, Kraus FT, Kurman RF. Gross description, processing, and reporting of gynaecologic and obstetric specimens. *In*: Kurman RJ (ed.). *Blaustein's Pathology of the Female Genital Tract (4th edition)*. New York, USA: Springer, 2002.

8 Kulac I, Usubutun A. Microscopic lesions of fallopian tubes in endometrioid carcinoma of the endometrium: How effective are the macroscopic tubal sampling techniques? *J Gynecol Oncol* 2013;24:114–119.

9 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.

10 Horn LC, Einenkel J, Höckel M, Kölbl H, Kommoss F, Lax SF *et al*. Recommendations for the handling and oncologic pathology report of lymph node specimens submitted for evaluation of metastatic disease in gynecologic malignancies. *Pathologe* 2005;26:266–272.

11 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.

12 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.

13 Wheeler DT, Bell KA, Kurman RJ, Sherman ME. Minimal uterine serous carcinoma: diagnosis and clinicopathologic correlation. *Am J Surg Pathol* 2000;24:797–806.

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

15 Zheng W, Schwartz PE. Serous EIC as an early form of uterine papillary serous carcinoma: recent progress in understanding its pathogenesis and current opinions regarding pathologic and clinical management. *Gynecol Oncol* 2005;96:579–582.

16 Rabban JT, Zaloudek CJ. Minimal uterine serous carcinoma: current concepts in diagnosis and prognosis. *Pathology* 2007;39:125–133.

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

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

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

20 Koo YJ, Kim DY, Kim KR, Kim JH, Kim YM, Kim YT *et al*. Small cell neuroendocrine carcinoma of the endometrium: a clinicopathologic study of six cases. *Taiwan J Obstet Gynecol* 2014;53:355–359.

21 Nguyen ML, Han L, Minors AM, Bentley-Hibbert S, Pradhan TS, Pua TL *et al.* Rare large cell neuroendocrine tumor of the endometrium: A case report and review of the literature. *Int J Surg Case Rep* 2013;4:651–655.

22 Albores-Saavedra J, Martinez-Benitez B, Luevano E. Small cell carcinomas and large cell neuroendocrine carcinomas of the endometrium and cervix: polypoid tumors and those arising in polyps may have a favorable prognosis. *Int J Gynecol Pathol* 2008;27:333–339.

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

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

25 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.

26 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.

27 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.

28 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.

29 Alkushi A, Abdul-Rahman ZH, Lim P, Schulzer M, Coldman A, Kalloger SE *et al*. Description of a novel system for grading of endometrial carcinoma and comparison with existing grading systems. *Am J Surg Pathol* 2005;29:295–304.

30 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.

31 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.

32 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.

33 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.

34 Hanley KZ1, 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.

35 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.

36 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.

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

38 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.

39 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.

40 Bosse T, Peters EE, Creutzberg CL, Jürgenliemk-Schulz IM, Jobsen JJ, Mens JW *et al*. Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer – A pooled analysis of PORTEC 1 and 2 trials. *Eur J Cancer* 2015; 51:1742–1750.

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

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

43 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.

44 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.

45 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.

46 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.

47 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.

48 Zaino R, Zhu J, Abendroth C, Yemelyanova A, Oliva E, Lim D *et al*. Stage II endometrial carcinoma: Endocervical gland spread is not reproducibly distinguished from endocervical stromal invasion. *Mod Pathol* 2011;24:272A (suppl 1).

49 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.

50 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.

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

52 Jobsen JJ, Naudin TC L, Lybeert ML, Scholten A, van der Steen-Banasik EM, van der Palen J *et al.* Outcome of Endometrial Stage IIIA with Adnexa or Serosal Involvement Only. *Obstet Gynecol Int 2011*;2011:962518.

53 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.

54 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.

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

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

57 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.

58 McConechy MK, Ding J, Senz J, Yang W, Melnyk N, Tone AA *et al.* Ovarian and endometrial endometrioid carcinomas have distinct CTNNB1 and PTEN mutation profiles. *Mod Pathol* 2014;27:128–134.

59 Anglesio MS, Wang YK, Maassen M, Horlings HM, Bashashati A, Senz J *et al.* Synchronous Endometrial and Ovarian Carcinomas: Evidence of Clonality. *J Natl Cancer Inst* 2016; 108:428.

60 Schultheis AM, Ng CK, De Filippo MR, Piscuoglio S, Macedo GS, Gatius S *et al.* Massively parallel sequencing-based clonality analysis of synchronous endometrioid endometrial and ovarian carcinomas. *J Natl Cancer Inst* 2016;108:427.

61 Guerra F, Girolimetti G, Perrone AM, Procaccini M, Kurelac I, Ceccarelli C *et al.* Mitochondrial DNA genotyping efficiently reveals clonality of synchronous endometrial and ovarian cancers. *Mod Pathol* 2014;27:1412–1420.

62 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.

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

64 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.

65 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.

66 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.

67 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.

68 Brierley JD, Gospodarowicz M, Wittekind C (eds.) *TNM Classification of Malignant Tumours (8th edition)*. Oxford, UK: Wiley-Blackwell, 2017.

69 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.

70 Bartosch C, Pires-Luís AS, Meireles C, Baptista M, Gouveia A, Pinto C *et al.* Pathologic Findings in Prophylactic and Nonprophylactic Hysterectomy Specimens of Patients With Lynch Syndrome. *Am J Surg Pathol* 2016;40:1177–1191.

71 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.

72 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.

73 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* 2015;38:272–277.

74 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.

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 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.

77 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.

78 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.

79 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 tumor-free distance from the uterine serosa in endometrial cancer? *Gynecol Oncol* 2003;91:547–551.

80 Hirschowitz L, Faruqi A, Fulmali R, Ganesan R, McCluggage WG. *Tissue pathways in gynaecological pathology.* London, UK: The Royal College of Pathologists, 2015.

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 Darvishian F, Hummer AJ, Thaler HT, Bhargava R, Linkov I, Asher M *et al*. Serous endometrial cancers that mimic endometrioid adenocarcinomas: a clinicopathologic and immunohistochemical study of a group of problematic cases. *Am J Surg Pathol* 2004;28:1568–1578.

83 Gatius S, Matias-Guiu X. Practical issues in the diagnosis of serous carcinoma of the endometrium. *Mod Pathol* 2016;29:S45–S58 (suppl 1).

84 Fadare O, Desouki MM, Gwin K, Hanley KZ, Jarboe EA, Liang SX *et al.* Frequent expression of napsin A in clear cell carcinoma of the endometrium: potential diagnostic utility. *Am J Surg Pathol* 2014;38:189–196.

85 Hoang LN, Han G, McConechy M, Lau S, Chow C, Gilks CB *et al.* Immunohistochemical characterization of prototypical endometrial clear cell carcinoma – diagnostic utility of HNF-1β and oestrogen receptor. *Histopathology* 2014;64:585–596.

86 Cancer Genome Atlas Research Network, Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y *et al.* Integrated genomic characterization of endometrial carcinoma. *Nature* 2013;2:67–73.

87 Hussein YR, Weigelt B, Levine DA, Schoolmeester JK, Dao LN, Balzer BL *et al.* Clinicopathological analysis of endometrial carcinomas harboring somatic POLE exonuclease domain mutations. *Mod Pathol* 2015;28:505–514.

88 Talhouk A, McConechy MK, Leung S, Li-Chang HH, Kwon JS, Melnyk N *et al.* A clinically applicable molecular-based classification for endometrial cancers. *Br J Cancer* 201514;113:299–310.

89 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.

90 O'Neill CJ, McCluggage WG. p16 expression in the female genital tract and its value in diagnosis. *Adv Anat Pathol* 2006;13:8–15.

91 Darragh TM, Colgan TJ, Thomas Cox J, Heller DS, Henry MR, Luff RD *et al.* The Lower Anogenital Squamous Terminology Standardization project for HPV-associated lesions: background and consensus recommendations from the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology. *Int J Gynecol Pathol* 2013;32:76–115.

92 Rabban JT, Calkins SM, Karnezis AN, Grenert JP, Blanco A, Crawford B *et al.* Association of tumor morphology with mismatch-repair protein status in older endometrial cancer patients: implications for universal versus selective screening strategies for Lynch syndrome. *Am J Surg Pathol* 2014;38:793–800.

93 Garg K, Leitao MM Jr, Kauff ND, Hansen J, Kosarin K, Shia J *et al.* Selection of endometrial carcinomas for DNA mismatch repair protein immunohistochemistry using patient age and tumor morphology enhances detection of mismatch repair abnormalities. *Am J Surg Pathol* 2009;33:925–933.

Appendix A WHO classification[3] of endometrial tumours (2014) and SNOMED M coding

Tumour site	ICD-10	SNOMED 2/3 code	SNOMED-CT terminology	SNOMED-CT code
Endometrium	C54.1	T-83400	Endometrial structure (body structure)	2739003

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O)

Morphological codes	SNOMED 2/3/ICD-O code	SNOMED-CT terminology	SNOMED-CT code
Endometrioid carcinoma	M-83803	Endometrioid carcinoma (morphologic abnormality)	30289006
Endometrioid carcinoma with squamous differentiation	M-85703	Adenocarcinoma with squamous metaplasia (morphologic abnormality)	15176003
Endometrioid carcinoma, villoglandular variant	M-82623	Villous adenocarcinoma (morphologic abnormality)	28558000
Endometrioid carcinoma, secretory variant	M-83823	Endometrioid adenocarcinoma, secretory variant (morphologic abnormality)	128680006
Mucinous carcinoma	M-84803	Mucinous adenocarcinoma (morphologic abnormality)	72495009
Serous endometrial intraepithelial carcinoma	M-84412	No code yet	No code yet
Serous carcinoma	M-84413	Serous cystadenocarcinoma (morphologic abnormality)	90725004
Clear cell carcinoma	M-83103	Clear cell adenocarcinoma (morphologic abnormality)	30546008
Carcinoid tumour	M-82403	Carcinoid tumour, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	81622000
Small cell neuroendocrine carcinoma	M-80413	Small cell carcinoma (morphologic abnormality)	74364000
Large cell neuroendocrine carcinoma	M-80133	Large cell neuroendocrine carcinoma (morphologic abnormality)	128628002
Mixed cell adenocarcinoma	M-83233	Mixed cell adenocarcinoma (morphologic abnormality)	38958001
Undifferentiated carcinoma	M-80203	Carcinoma, undifferentiated (morphologic abnormality)	38549000
Dedifferentiated carcinoma	No specific code. Code according to tumour that has undergone dedifferentiation.		

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 B FIGO stage[4] (2009)

IA	Tumour confined to the uterus, none or <50% myometrial invasion
IB	Tumour confined to the uterus, ≥50% 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

Appendix C TNM staging classification[68] (8th edition)

Primary tumour (T)

Tx Primary tumour cannot be assessed

T0 No evidence of primary tumour

T1 Carcinoma confined to corpus uteri

- T1a Tumour limited to endometrium or invading less than half of myometrium
- T1b Tumour invades one half or more of the myometrium

T2 Tumour invades cervical stroma, but does not extend beyond the uterus

T3 Local and/or regional spread as specified here:

- T3a Tumour involves serosa of the corpus uteri or adnexae (direct extension or metastases)
- T3b Vaginal or parametrial involvement (direct extension or metastases)

T4 Tumour invades bladder/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 Metastases to pelvic lymph nodes

N2 Metastasis to para-aortic nodes, with or without metastasis to pelvic lymph nodes

Distant metastases (M)

M0 No distant metastases

M1 Distant metastases
(excluding metastases to vagina, pelvic serosa or adnexa, including metastasis to inguinal lymph nodes and intra-abdominal lymph nodes other than para-aortic or pelvic nodes)

Positive peritoneal cytology has to be reported separately without changing 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 III	T1, T2, T3	N1, N2	M0
Stage IIIC1	T1, T2, T3	N1	M0
Stage IIIC2	T1, T2, T3	N2	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Appendix D Reporting proforma for endometrial carcinoma excision specimens

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

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

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

Clinical items

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

Relevant family history ……

Macroscopic items

Specimen components Adnexa ☐ Vaginal cuff ☐ Parametrium ☐

Other ☐ (specify): ….....

Accompanying specimens: Omentum ☐

Lymph nodes: Pelvic ☐ Para-aortic ☐

Other ☐ (specify) ……..……

Tumour details

Maximum dimension of tumour†: ….....mm

Involvement of (tick all that apply):

Myometrium ☐ Cervix ☐ Serosa ☐ Parametrium ☐

Microscopic items

Tumour type†: Endometrioid ☐ Mucinous ☐ Serous EIC ☐ Serous ☐

Clear cell ☐ Undifferentiated ☐ Neuroendocrine ☐

Mixed ☐ (specify components) Carcinosarcoma ☐ Other ☐

If mixed or other, specify …….

FIGO grade† (non-endometrioid/mucinous tumours automatically grade 3)

1 ☐ 2 ☐ 3 ☐

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

Lymphovascular space invasion†: Present ☐ Not identified ☐

Microscopic involvement of:

Cervical stroma†	Involved ☐	Not involved ☐	Not assessable ☐
Vagina	Involved ☐	Not involved ☐	Not assessable ☐
Adnexa	Involved ☐	Not involved ☐	Not assessable ☐

(If adnexa involved, is this considered to be a separate primary neoplasm? Yes ☐ No ☐ Uncertain ☐)

Uterine serosa†	Involved ☐	Not involved ☐	Not assessable ☐
Parametrium†	Involved ☐	Not involved ☐	Not assessable ☐

Lymph nodes: Not sampled ☐ Sampled ☐

Right pelvic lymph nodes† (no. positive/total no.):……/……

Left pelvic lymph nodes† (no. positive/total no.): ……/……

Para-aortic lymph nodes† (no. positive/total no.):……/……

Omentum†: Not sampled ☐ Involved by tumour ☐ Not involved by tumour ☐

Peritoneal involvement: Involved ☐ Not involved ☐ Not assessable ☐

If yes, site of involvement: Pelvic ☐ Abdominal ☐

Distant metastases†: Yes ☐ No ☐ Not assessable ☐

Site (if known): ……

Comments

Provisional FIGO stage†‡:

SNOMED code† T …… M……

Signature .....…….. Date……...../……...../……..

Notes

†Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 6.

‡Data items that are used in version 2.0 of the ICCR endometrial cancer dataset.

Appendix E Reporting proforma for endometrial biopsies containing carcinoma

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

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

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

Type of sample: Pipelle ☐ Currettings ☐ Other/not stated ☐

Diagnosis

Tumour type†: Endometrioid ☐ Mucinous ☐ Serous EIC ☐ Serous ☐

Clear cell ☐ Undifferentiated ☐ Neuroendocrine ☐

Mixed ☐ (specify components) Carcinosarcoma ☐ Other ☐

If mixed or Other specify …….

FIGO grade (non-endometrioid/mucinous tumours automatically grade 3)†

1 ☐ 2 ☐ 3 ☐

Comments

SNOMED code† T …… M……

Signature .....…….. Date……...../……...../…….

Notes

†Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 6.

Appendix F Reporting proforma for endometrial carcinoma excision specimens in list format

Element name	Values	Implementation notes
Hysterectomy type	Single selection value list: • Abdominal • Vaginal • Laparoscopic • Not known	
Relevant family history	Free text	
Specimen components	Multiple selection value list: • Adnexa • Vaginal cuff • Parametrium • Other	
Specimen components, other specify	Free text	Only applicable if 'Specimen components, Other' is selected.
Accompanying specimens	Multiple selection value list: • Omentum • Lymph nodes: pelvic • Lymph nodes: para-aortic • Other	
Accompanying specimens, other specify	Free text	Only applicable if 'Accompanying specimens, Other' is selected.
Maximum dimension of tumour	Size in mm	
Macroscopic involvement	Multiple selection value list: • Myometrium • Cervix • Serosa • Parametrium	
Tumour type	Single selection value list: • Endometrioid • Mucinous • Serous EIC • Serous • Clear cell • Undifferentiated • Neuroendocrine • Mixed • Carcinosarcoma • Other	
Tumour type, mixed or other specify	Free text	Only applicable if 'Tumour type, Mixed' or 'Tumour type, Other' is selected.

Element name	Values	Implementation notes
FIGO grade	Single selection value list: • 1 • 2 • 3	
Myometrial invasion	Single selection value list: • None or <50% • ≥50%	
Lymphovascular invasion	Single selection value list: • Present • Not identified	
Microscopic involvement of cervical stroma	Single selection value list: • Involved • Not involved • Not assessable	
Microscopic involvement of vagina	Single selection value list: • Involved • Not involved • Not assessable	
Microscopic involvement of adnexa	Single selection value list: • Involved • Not involved • Not assessable	
If adnexa involved, is this considered to be a separate primary neoplasm	Single selection value list: • Yes • No • Uncertain	Only applicable if 'Microscopic involvement of adnexa, Involved' is selected.
Microscopic involvement of uterine serosa	Single selection value list: • Involved • Not involved • Not assessable	
Microscopic involvement of parametrium	Single selection value list: • Involved • Not involved • Not assessable	
Lymph nodes	Single selection value list: • Not sampled • Sampled	
Right pelvic lymph nodes, number positive	Integer	Only applicable if 'Lymph nodes, Sampled' is selected.
Right pelvic lymph nodes, total number	Integer	Only applicable if 'Lymph nodes, Sampled' is selected.

Element name	Values	Implementation notes
Left pelvic lymph nodes, number positive	Integer	Only applicable if 'Lymph nodes, Sampled' is selected.
Left pelvic lymph nodes, total number	Integer	Only applicable if 'Lymph nodes, Sampled' is selected.
Para-aortic lymph nodes, number positive	Integer	Only applicable if 'Lymph nodes, Sampled' is selected.
Para-aortic lymph nodes, total number	Integer	Only applicable if 'Lymph nodes, Sampled' is selected.
Omentum	Single selection value list: • Not sampled • Involved by tumour Not involved by tumour	
Peritoneal involvement	Single selection value list: • Involved • Not involved Not assessable	
Distant metastases	Single selection value list: • Yes • No Not assessable	
Distant metastases, site	Free text	Only applicable if 'Distant metastases, Yes' is selected.
Comments	Free text	
Provisional FIGO stage	Single selection value list: • IA • IB • II • IIIA • IIIB • IIIC1 • IIIC2 • IVA IVB	
SNOMED T code	May have multiple codes. Look up from SNOMED tables.	
SNOMED M code	May have multiple codes. Look up from SNOMED tables.	

Appendix G Reporting proforma for endometrial biopsies containing carcinoma in list format

Element name	Values	Implementation notes
Type of sample	Single selection value list: • Pipelle • Currettings • Other/not stated	
Tumour type	Single selection value list: • Endometrioid • Mucinous • Serous EIC • Serous • Clear cell • Undifferentiated • Neuroendocrine • Mixed • Carcinosarcoma • Other	
Tumour type, mixed or other specify	Free text	Only applicable if 'Tumour type, Mixed' or 'Tumour type, Other' is selected.
FIGO grade	Single selection value list: • 1 • 2 • 3	
Comments	Free text	
SNOMED T code	May have multiple codes. Look up from SNOMED tables.	
SNOMED M code	May have multiple codes. Look up from SNOMED tables.	

Appendix H Summary table – Explanation of grades 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 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, and directly applicable to the target 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 type or Extrapolation of 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 type or Extrapolation of evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation of 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 I AGREE guideline monitoring sheet

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

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	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
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	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 for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword, 1
12 There is an explicit link between the recommendations and the supporting evidence	4–11
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	2–11
16 The different options for management of the condition or health issue are clearly presented	2–11
17 Key recommendations are easily identifiable	2–11
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword, 1
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	Appendices A–G
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	12
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