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Pathology: the science behind the cure

# Standards and datasets for reporting cancers

## Dataset for histopathological reporting of endometrial cancer

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| **Comments** | This document will replace the 5th edition of the *Dataset for histological reporting of endometrial cancer*, published in 2017.<br>In accordance with the College's pre-publications policy, this document will be on the Royal College of Pathologists' website for consultation from 18 February to 18 March 2026. Responses and authors' comments will be available to view on publication.<br>**Dr Brian Rous and Sarah Davies**<br>**Clinical Leads for Guideline Review** |

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# Contents

# 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 and 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. Additionally, 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 stakeholders will be consulted for this document:

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

The information used to develop this dataset was obtained by undertaking a systematic search of journals (PubMed), conference proceedings, Cochrane reviews and NICE guidance for relevant evidence. Key terms searched included 'endometrial cancer', 'reporting guidelines' and 'update' and dates searched were between January 2021 and December 2024. 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] The new FIGO staging of endometrial carcinoma was published in June 2023.[2] Following a membership survey by the BGCS and BAGP, a decision to delay the implementation of this staging system was taken for the UK.[3]

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 3-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 2 weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Professional Guidelines team, Working Group on Cancer Services and Lay Advisory Group. It will be placed on the College website for consultation with the membership from 18 February to 18 March 2026. All comments received will be addressed by the authors to the satisfaction of the Chair of the Working Group and the Clinical Lead for Guideline Review.

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Professional Guidelines team 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 (required) and non-core (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.

This dataset includes a brief account of the major subtypes of endometrial cancer included in the 2020 World Health Organization (WHO) classification.[4] Carcinosarcoma, formerly included in the group of mixed epithelial and stromal tumours, is now classified as a distinct type of endometrial carcinoma and shows the typical biphasic pattern morphologically.

The 2020 WHO classification does not distinguish mucinous differentiation in endometrioid carcinoma as a separate variant. It is regarded as an endometrioid carcinoma due to their shared molecular features and natural history. The 2020 WHO classification includes novel tumour types, such as squamous cell carcinoma, mesonephric-like adenocarcinoma and gastrointestinal-type mucinous carcinoma. The variants of endometrioid carcinoma listed in previous editions are replaced by molecular groups.[5]

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

- 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 prognostic information.
- Accurate typing of endometrial cancers can allow epidemiological information to emerge especially regarding 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 5th 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:

- main histological tumour types, including the Cancer Genome Atlas molecular classification to align the dataset with the *WHO Classification of Female Genital Tumours*, 5th edition, 2020
- WHO recommendation for reporting lymphovascular space invasion (LVSI)
- assessment of myometrial invasion including invasion at uterine cornu, lower uterine segment (LUS) and invasion arising from adenomyosis
- lymph node including sentinel node assessment
- updated section on immunohistochemistry and molecular tests including mismatch repair (MMR) proteins, p53 and polymerase epsilon (POLE) testing as required
- recommendation to score oestrogen receptor (ER) by Allred score
- inclusion of the FIGO 2023 endometrial cancer staging.

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 with or without 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. Family history of cancer (particularly Lynch syndrome (LS) and other hereditary cancer syndromes), personal history of other cancers and history of other treatments including hormonal therapy is important. 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 total 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 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, 1 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 ovarian capsule.

Further specimens that may be received include omentum, lymph nodes (sentinel, pelvic, para-aortic), peritoneal biopsies, peritoneal washings.[6]

# 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.[7,8]

There are several ways of opening the uterus, depending on the preference and experience of the pathologist.[9] 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.

The practice of inking the specimen is variably used. When used, inking the peritoneal and nonperitoneal surfaces and extending the ink all the way to the vaginal cuff can be useful for measuring the vaginal cuff margin.[6]

## 4.1 Selection of blocks for histology

### 4.1.1 Tumour

At least 4 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.

In cases with biopsy proven carcinoma, but no visible tumour, the entire endometrium should be submitted for histological assessment including cornual sampling.

### 4.1.2 Isthmus/LUS

At least 1 block of isthmus/LUS should be taken in all cases. Anatomically, the LUS begins where the body funnels towards the cervix and ends at the internal os. This is especially important as tumour involvement of the isthmus is associated with MMR deficiency, predictive of lymph node involvement in early-stage carcinomas and an independent poor prognostic factor.[10,11]

### 4.1.3 Cornu

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 1 factor to consider when attempting to distinguish between metastatic and synchronous adnexal involvement (see below).

### 4.1.4 Parametria

Parametrial tissue is not included in simple hysterectomy procedures typically carried out for endometrial carcinoma. Parametrial tissue is described as fibrous and fatty connective tissue that separates the supravaginal portion of the cervix from the bladder. The parametrium lies in front of the cervix and extends laterally to the pelvic sidewalls between the layers of the broad ligaments. It connects the uterus to other tissues in the pelvis. It is

different from the perimetrium, which is the outermost layer of the uterus and which may be incorrectly sampled when parametrium is not sampled surgically.[1–3] Sampling of parametrial tissues as shave or radial sections is optional but must be carried out in case of macroscopic involvement of the isthmus or cervix, and in a way that allows accurate assessment of the surgical margin. Radical hysterectomy may be carried out for complete resection in endometrial cancers known or suspected preoperatively to involve the cervix; in such cases, the parametrial tissue may be blocked in its entirety if tumour is not seen macroscopically, and in a way that allows accurate assessment of margin clearance.[12]

#### 4.1.5 Cervix

2 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.

#### 4.1.6 Tubes and ovaries

1 or 2 blocks each of both ovaries and tubes should be submitted if grossly normal. The tubal blocks should include the fimbria. In cases of uterine serous carcinoma, sampling of the entire tube, or at least the distal tube using a SEE-FIM protocol should be considered.[13,14]

#### 4.1.7 Other abnormalities

Appropriate numbers of blocks should be taken to sample other abnormalities such as fibroids or adnexal masses.

#### 4.1.8 Omentum

1 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 a minimum of 4 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.

#### 4.1.9 Lymph nodes

All resected lymph nodes should be sampled. Every lymph node should be examined histologically in its entirety, unless obviously grossly involved by tumour. Only 1 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.[15,16]

#### 4.1.10 Peritoneal biopsies

All peritoneal biopsies should be blocked in toto. Representative blocks should be taken from any other tissues submitted. The origin/designation of all tissue blocks should be recorded and ideally documented in the final pathology report. If this information is not included in the final pathology report, it should be available on the laboratory computer system. This is important if there is an internal or external review and facilitates retrieval of blocks for further analysis as well as for research studies or clinical trials.

*[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

Depending on the presumed stage of disease, a simple total hysterectomy (removal of all of uterus with cervix) or a radical/modified radical hysterectomy (en-bloc excision of uterus, cervix, vaginal cuff, parametria and uterosacral ligaments) is performed. Hysterectomy is accompanied by bilateral salpingo-oophorectomy in the vast majority. However, in a small subset of young pre-menopausal women with early-stage endometrial carcinoma, hysterectomy and bilateral salpingectomy with ovarian conservation may be performed.

Pelvic exenteration is occasionally performed in advanced and recurrent endometrial cancer.

Although subtotal hysterectomy (without cervix) and morcellated hysterectomy are not recommended, endometrial cancer may be incidentally diagnosed in hysterectomies performed for benign conditions.

The route of hysterectomy, whether total laparoscopic hysterectomy, laparoscopic-assisted vaginal hysterectomy, robotic-assisted laparoscopic or abdominal/laparotomy, should be documented. This information may be important for evaluation of histological parameters e.g. artefactual pseudovascular invasion related to the use of balloon manipulators in laparoscopic hysterectomies.

### 5.1.2 Specimen integrity

The state of the received specimen should be recorded as intact, open, morcellated or other. Opening the specimen for fixation or removal of fresh tissue can assist morphological assessment by optimising fixation, but hamper assessment of myoinvasive depth and sampling if the uterus becomes everted with retraction of the outer myometrium. Spillage of tumour and adherence to the external aspect of the specimen can cause difficulty in assessing serosal or parametrial involvement, and thereby pathological staging.

### 5.1.3 Relevant history

**Prior treatment**

Previous neoadjuvant or progesterone treatment affects pathological assessment and should be recorded.

**Personal history**

Relevant personal history – e.g. of previous cancer and cancer treatment, the clinical working diagnosis and results of previous biopsy – should be noted.

**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 lengths of the anterior and posterior peritoneal reflections, the relative anatomy of attached ligaments and adnexal structures (anterior to posterior: round ligaments, fallopian tube, ovary) or both.

Simple hysterectomy with bilateral salpingo-oophorectomy consists of uterine corpus, cervix, ovaries and tubes. Wispy connective tissue present on the lateral surface of the uterus removed at simple hysterectomy does not constitute parametrectomy.

Radical hysterectomy will include in addition vaginal cuff and parametrial tissues.[17] Inking of nonperitoneal surfaces (surgical margin) +/- peritoneal surfaces is recommended in hysterectomy specimens and is mandatory in radical hysterectomy and pelvic exenteration

specimens. In the latter 2, inking up to the vaginal cuff margin enables evaluation of status of the margin.

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

### 5.2.2 Accompanying specimens

Pelvic exenteration performed for advanced or recurrent endometrial cancer can be an anterior exenteration including uterus, cervix, adnexa, vagina and bladder; posterior exenteration including uterus, cervix, adnexa, vagina and rectum or total exenteration including uterus, cervix, adnexa, vagina, bladder and rectum.

#### Omentum

An omental biopsy is performed as part of staging procedure in some high-grade endometrial carcinomas (e.g. uterine serous carcinoma). The omentum should be measured. The presence and dimensions of the largest visible deposit should be recorded.

#### Lymph nodes

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.[15]

#### Peritoneal biopsies

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 location, maximum dimension and the presence or absence of macroscopic myometrial invasion, cervical involvement, parametrial and adnexal involvement or serosal surface involvement should be recorded.

#### 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 more commonly seen in association with hereditary non-polyposis colorectal cancer syndrome/LS.[18] 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.[11,10]

In addition to its prognostic significance, isthmic involvement also raises the possibility of upward spread of a cervical tumour that may need consideration depending on histology.

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

**Tumour size**

While tumour size is not included in risk stratification in British and European guidelines,[19] some guidelines state a 2 cm cut-off in the assessment of stage IA tumours.[17] Adjuvant treatment decisions may, therefore, be influenced by this parameter in some cases.

Histological assessment of myoinvasive depth, as well as of cervical, parametrial and serosal involvement may present challenges, and a record of the gross appearances can be helpful.[20]

## 5.3 Pathological core data: microscopic data items

### 5.3.1 Tumour type

Endometrial carcinomas should be typed according to the WHO 2020 classification[4] (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 non-endometrioid tumours.[21–23]

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 2020 classification[4] and specialist textbooks of gynaecological pathology. A few points will, however, be highlighted for clarification.

**Endometrioid carcinoma**

Although histology is reliable in the diagnosis of low-grade endometrioid carcinomas, there is considerable inter-observer variation in a subset of high-grade carcinomas. The diagnostic integrated histo-molecular classification for endometrial carcinomas,[4] although

applicable to all histological subtypes, is most relevant to endometrioid carcinoma; particularly grade 3/high-grade.

**Serous carcinoma**

Serous endometrial intraepithelial carcinoma (EIC) is regarded as a serous carcinoma, which grows along pre-existing glands but still has the potential to metastasise to extrauterine sites. Therefore, it is considered a carcinoma rather than a precursor lesion.

**Carcinosarcoma**

Carcinosarcoma (malignant mixed Mullerian tumours) are now known to be epithelial neoplasms that have undergone epithelial–mesenchymal transition (transdifferentiation) to give rise to a sarcomatous component. Predominance of the sarcomatous component and the presence of heterologous components such as rhabdomyosarcoma may confer a worse prognosis.[24]

Undifferentiated carcinoma has recently been highlighted as an aggressive form of uterine carcinoma. It is defined in the WHO 2020 classification as ‘a malignant epithelial neoplasm with no overt cell lineage differentiation’.[4] The undifferentiated carcinoma may occur in pure form or in combination with a differentiated component, typically low-grade (grade 1 or 2) endometrioid but rarely high grade endometrioid or serous (2351 and 1063 WHO REF) adenocarcinoma, when it is designated dedifferentiated carcinoma.

**Neuroendocrine neoplasms (NEN)**

The WHO 2020 classification considers NEN of all sites in the female genital tract collectively in a separate chapter. These are divided into neuroendocrine tumours (NET) and (small and large cell) neuroendocrine carcinoma (NEC). NEC can occur in pure form or in association with another morphological subtype of endometrial carcinoma. Primary endometrial NEC are rare and cervical origin and commoner histotypes should be considered before making this diagnosis

**Mixed carcinoma**

Mixed carcinoma refers to a carcinoma composed of >1 discrete morphological type, at least 1 of which is either serous or clear cell carcinoma identified by histology and immunohistochemistry. Unlike the 2014 WHO definition,[25] in the current 2020 WHO classification, any percentage of high grade carcinoma is sufficient to label the tumour as a mixed endometrial carcinoma as even a small percentage of serous or clear cell carcinoma may confer an adverse prognosis and outcome. Importantly, carcinosarcoma

and dedifferentiated carcinoma, which by definition contain a mixture of components, are considered specific entities that do not fall into this category.

**Novel subtypes**

The WHO 2020 classification includes novel subtypes such as mesonephric-like adenocarcinoma and gastric (gastrointestinal) type mucinous carcinoma. Mesonephric-like carcinoma resembles the mesonephric carcinomas more commonly identified in the cervix, but is a tumour centred in the endometrium, rather than the lateral wall of the uterus.[4] There is usually completely negative staining for ER and progesterone receptor (PR), with strong expression of either GATA-3 or TTF1, but not both. Lack of ER expression is especially useful to differentiate it from low-grade endometrioid carcinoma.[26]

**Mucinous carcinoma of gastric (gastrointestinal) type**

In previous years the significance of mucinous differentiation in endometrial carcinomas was poorly understood; the current classification allows mucinous differentiation of any extent in endometrioid carcinomas, provided there is good evidence of endometrioid differentiation based on morphology and/or diffuse ER expression, as this does not affect their behaviour.

Gastric (gastrointestinal) type mucinous carcinoma, on the other hand, is generally completely negative for ER, shows a gastrointestinal-type phenotype and is similar to gastric-type HPV-independent cervical carcinomas in many respects, including aggressive clinical behaviour.[27]

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

*[Level of evidence C – serous EIC, dedifferentiated, undifferentiated and NECs.]*

### 5.3.2 Tumour grade (only for endometrioid carcinoma)

**FIGO grade**

The histologic FIGO grade[28,29] has been consistently identified as 1 of the more important prognosticators for women with endometrial carcinoma. FIGO grade 1 is defined as a gland forming tumour in which <5% of the neoplastic cells form solid sheets, FIGO grade 2 as a tumour in which 5–50% of the neoplasm forms solid sheets and FIGO grade 3 as a tumour in which >50% of the neoplasm is formed of solid sheets of neoplastic cells. Apart from completely solid architecture, a confluent microacinar pattern should also be interpreted as solid.[30]

The presence of grade 3 nuclei involving >50% of the tumour is associated with more aggressive behaviour and justifies upgrading of grade 1 or 2 tumours by 1 grade. Grade 3 nuclei are rounded, contain prominent, often multiple, nucleoli and show variability in size.[29] 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.

**Squamous differentiation**

In tumours showing squamous differentiation, the squamous elements should be excluded from the architectural assessment.

**Endometrioid carcinoma with spindle cells and corded and hyalinised endometrioid carcinomas**

Similarly, although not addressed specifically in the FIGO grading system and lacking a firm evidence base due to the rarity of these carcinomas, it is recommended that architectural assessment in endometrioid carcinoma with spindle cells and corded and hyalinised endometrioid carcinomas should be confined to areas showing conventional morphology.[31]

**Binary grading**

Binary grading, as recommended by WHO (2020), is generally applied in clinical decision-making, whereby FIGO grades 1 and 2 are considered low-grade, and FIGO grade 3 is considered high grade. Inter-observer reproducibility is imperfect.[32] Pathologists are directed to expert consensus guidance issued by the International Society of Gynecological Pathologists to optimise their grading thresholds.[33]

However, for the time being, especially as the distinction between grades 1 and 2 may be important in guiding the decision for fertility-sparing surgery in some centres, it is recommended that histopathologists continue to use the generally accepted, albeit imperfect, FIGO grading system.

**Non-endometrioid carcinomas**

FIGO grading is not applicable to non-endometrioid carcinomas, including the newly described mesonephric-like and gastric (gastrointestinal) type carcinomas; management as high-grade tumours should be recommended for all these histotypes.[34–36]

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 Core ancillary studies including screening for LS and the molecular classification of endometrial carcinomas (please also refer to sections 10 and 11)

It is recommended to perform a minimal panel of immunohistochemistry including p53, ER, PR and the MMR proteins on all endometrial carcinomas. This panel will assist with the accurate typing of endometrial carcinomas as per the WHO classification outlined in section 5.3.1, and the p53 and the MMR status will form the basis for the molecular classification of these tumours required for guiding oncological decisions in the adjuvant setting.

Similar to interpretation of p53 immunohistochemistry in tubo-ovarian carcinoma,[39] it is recommended to report p53 immunostain in endometrial carcinoma as either wild type or mutation/aberrant pattern which includes overexpression, null type and cytoplasmic type. A small proportion of mutant p53 endometrial cancers can show wild type immunohistochemical staining pattern.

There is evidence for integrating hormone receptor ER and PR status evaluation into clinical risk stratification to improve prognosis in endometrial carcinoma.[38] ER and PR status may also be useful in the management of recalcitrant or recurrent disease or low-grade adenocarcinomas where surgery is contraindicated, for example, owing to comorbidities or fertility conservation.

There are 3 different methods used to assess the degree of ER staining – the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) criterion, histochemistry score (H-score), and Allred scoring system. To enable uniform reporting across various tumour sites, it is recommended to use the Allred score to interpret ER (and PR staining) with ER and PR status recorded as Allred score 0–2 as negative and score 3–8 as positive.

In 2020, NICE recommended[39] that immunohistochemistry for MMR proteins should be performed on all cases of endometrial carcinoma, regardless of the histotype, including carcinosarcoma, as a screening test to detect LS.

A comprehensive genomic analysis performed by the Cancer Genome Atlas provides a molecular classification of the endometrial carcinomas into 4 main biologically distinct groups, all of clinical importance as they provide prognostic and therapeutic value:[5]

- POLE mutant group also known as ultramutated
- MMR deficient group also known as hypermutated
- a copy number low group also known as no specific molecular profile (NSMP)
- a copy number high or serous-like tumours.

Group 1 endometrial carcinomas are characterised by somatic inactivating hotspot mutations in the exonuclease domain of the DNA polymerase epsilon (*POLE*) gene which, irrespective of grade, have been reported in retrospective studies to show an excellent prognosis.[40] Prospective studies (i.e. PORTEC 4a) are underway, which will help to further inform on the outcome of this tumour group and testing criteria.

The second group is represented by the MMR deficient tumours. Apart from identifying patients at risk of LS, the MMR status has therapeutic and prognostic utility as it helps to select patients likely to respond to immune check-point inhibitors in particular. The MMR status is also useful in cases that are morphologically challenging as endometrioid carcinomas are more likely to harbour this aberration. This group shows intermediate prognosis between groups 1 and 4.

It is recommended to report MMR immunostains in endometrial carcinoma as either MMRp (MMR proficient) or MMRd (MMR deficient).[41]

- If MMRp – report as ‘MMRp’. If there is a strong family/clinical history suggestive of Lynch and related syndromes, consider referral to clinical genetics services.
- If MMRd with loss of MLH1 and PMS2 or loss of MLH1 only – report as ‘loss of MLH1 and PMS2 or loss of MLH1, awaiting promoter methylation testing’. If methylation test is negative, recommend referral to clinical genetics.
- If MMRd with loss of MSH6 and/or MSH2 or MSH6 only – report as ‘MMRd’ (mention the particular loss of MMR) and ‘recommend referral to clinical genetics’ for consideration of germline testing.

Group 3 has a similar prognosis to group 2; it includes tumours with no MMR deficiency, POLE or p53 mutation. In contrast, the p53 mutant subgroup, group 4, have a poor

prognosis, may present in advanced stage and definitionally lack MMRd or POLE mutations.

Most tumours could be classified and placed into an individual group based on a single abnormality known as a single classifier, but a small proportion (3%) may show a POLE mutation or MMRd in addition to aberrant p53. These are known as “multiple-classifier” endometrial carcinomas and based on outcome, there is support to classify the MMRd+p53 aberrant endometrial carcinomas as MMRd and POLE mutant+p53 aberrant ones as POLE mutant, suggesting that p53 is a secondary event in tumour progression.[42]

Testing can be implemented into routine clinical practice using a combination of immunohistochemistry for p53 and MMR and DNA mutation testing for POLE. MMR immunohistochemistry is the preferred and recommended method by the European Society for Medical Oncology and NICE to determine the MMR status. The category of p53-abnormal endometrial carcinoma carries the worst prognosis of all molecular groups. This category is largely formed by serous carcinoma, carcinosarcoma and grade 3 endometrioid carcinoma, however tumours of all histotypes, including those diagnosed as low-grade endometrioid carcinoma, may fall into this molecular group. Correct identification of p53-abnormal tumours places the case into an intermediate-risk (cases with no myometrial invasion) or high-risk category (stage IA with myometrial invasion and all other stages), regardless of tumour type or grade. For these reasons, immunohistochemistry for p53 should be carried out on all cases. TP53 mutation testing may be required in a small proportion of cases with an equivocal or unusual staining patterns. Testing for POLE mutations should be restricted to those cases in which this will change management; this decision should be made following MDT discussion.

Owing to better fixation, this is best carried out on biopsy material; testing does not need to be repeated on hysterectomy specimens unless not done previously, or inconclusive on the biopsy sample.

### 5.3.4 Myometrial invasion

**Depth of myometrial invasion**

Depth of myometrial invasion is an important independent prognostic predictor of regional lymph node metastasis and overall survival. It is used in staging systems (FIGO and TNM) and for risk stratification and is an important determinant of adjuvant therapy.

## Documentation

Myometrial invasion should be documented as absent or infiltrating the inner half of the myometrium i.e. <50% of myometrial thickness, or invasion of ≥50% of myometrial thickness. Absent or inner myometrial invasion are both staged as FIGO 2009 stage IA in the absence of other sites of involvement; however, absence of myoinvasion in non-endometrioid and/or p53-abnormal endometrial carcinomas affects European Society of Gynaecological Oncology (ESGO) risk stratification;[19] distinction between these in stage IA tumours should, therefore, be clearly recorded. Involvement of half or more of myometrial thickness indicates stage IB disease in the absence of tumour at other locations. In the 2023 FIGO staging, both the tumour grade and myometrial invasion determine the stage.

## Methods of determining the extent of myometrial invasion

Various methods of determining the extent of myometrial invasion have been evaluated.[43–45] These include 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 3 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.[46] These last 3 parameters are included as non-core items in this dataset.

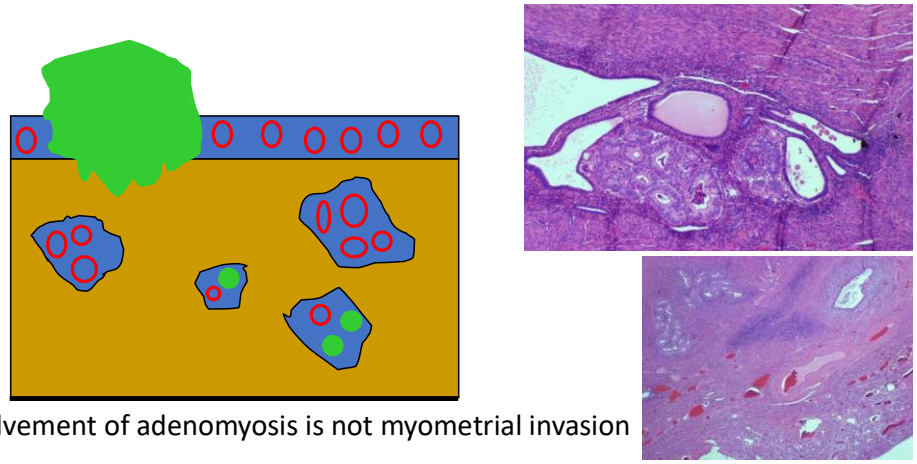
## Issues in assessing depth of myometrial invasion

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.[47]

Evaluation of myoinvasion beyond the confines of the adenomyosis is controversial, but in accordance with the ISGyP guidelines, the following is recommended: irrespective of the location of the adenomyotic focus, invasion into the inner half of the myometrium would remain as FIGO stage 1A, but invasion into the outer half of the myometrium should be

staged FIGO stage 1B with a comment to state that the significance of this is uncertain and may be an overestimation of the true depth of invasion (see Figures 1 and 2).

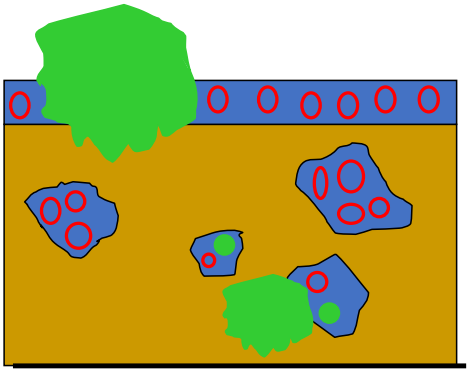
**Figure 1: Tumour involving adenomyosis.**



Involvement of adenomyosis is not myometrial invasion

FIGO stage 1A

**Figure 2: Tumour involving adenomyosis but infiltrating beyond into deep myometrium.**



FIGO stage 1B, but whether it confers same risk as deep myometrial invasion from surface is not known. Therefore state "focal invasion from adenomyosis" and specify whether arising from superficial or deep adenomyosis.

Morphologic features of the myoinvasive tumour such as a minimal deviation pattern (adenoma malignum pattern), a microcystic elongated and fragmented (MELF) pattern and smooth muscle metaplasia in polypoid neoplasms may result in problems in assessment of the presence and extent of myoinvasion.[43,48,49]

Although in a large meta-analysis, there was no overall or disease-specific survival benefit or increase in vaginal recurrence rates, identification of MELF pattern of invasion has diagnostic implications. In addition to underestimation of depth of myometrial invasion, MELF foci may be mistaken for LVSI. Awareness that lymph node involvement (associated with MELF pattern) may be subtle and in a subset that mimics a histiocytic infiltrate, helps

identify nodal disease in such cases. Documentation of this pattern of myoinvasion is useful, but remains a non-core item.

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 a reliable 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.[44]

As recommended by ISGyP, if the deepest site of infiltration is at the LUS, assessment of depth of invasion should be performed as for other non-cornual sites. If it involves a leiomyoma, the thickness of the involved myometrium should include the thickness of the involved leiomyoma (i.e. similar to the measurement performed in non-leiomyomatous myometrium). LVSI is not included in the assessment of the depth of invasion.

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

### 5.3.5 LVSI

LVSI within the myometrium has been demonstrated in repeated studies to be an independent prognostic factor in endometrial adenocarcinomas.[50–52]

Documentation of the presence or absence of LVSI is a core item. More recent evidence suggests that substantial vascular invasion is predictive of pelvic regional recurrence, distant recurrence and overall survival.[53]

Distinction between focal and extensive or substantial LVSI determines the requirement for adjuvant radiotherapy.

In most instances, extensive LVSI is visible at scanning magnification. The WHO (2020) has stated a cut-off of 5 or more vessels as the threshold for defining extensive/substantial. The 5 or more vessel cut-off is also endorsed as substantial LVSI in the 2023 FIGO staging. A recent comprehensive analysis of multiple cut-points and the

number of sections in which LVSI foci were seen has concluded that the presence of 4 or more foci of LVSI in at least 1 H&E slide is a numeric threshold that correlates with a clinically relevant cut-point. Separately the ICCR and ISGyP recommend 3 or more LVSI foci as the definition of 'extensive/substantial'.[54]

Although there have been different proposals for what constitutes extensive LVSI, it is a good rule of thumb to diagnose extensive LVSI when it is easily recognisable at scanning magnification (and artefact is excluded).

The following categories are recommended for reporting of LVSI:

- Absent
- Focal: <5 vessels in total or <4 vessels per section
- Substantial/extensive: 5 or more vessels in total or >4 vessels per section.

Since there is no consensus regarding the best definition for focal and substantive/extensive LVSI, we recommend specifying within the focal category if there were <5 vessels involved in the total in all sections of uterus or <4 vessels per section, similarly specifying within the substantial/extensive category if 5 or more vessels in total or >4 vessels per section was seen. This may help future prognostic studies on LVSI.[38]

As stated in section 5.3.3, it is important to note that the presence of LVSI, whether within the uterus or outside it, does not upstage the tumour. The presence of LVSI 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 LVSI at these sites should be recorded and mentioned at the MDT meeting when discussing the need for adjuvant therapy.

LVSI may be confidently diagnosed when the tumour embolus is within a channel lined by endothelium and tumour adherent to the vessel wall. Nevertheless there are pitfalls in evaluation of LVSI.

Tumour emboli in lymphovascular channels tend to resemble the endometrial carcinoma. However, in cases with a MELF pattern of invasion, the tumour within lymphovascular spaces may consist of single or small clusters of histiocytoid or metaplastic-squamoid cells similar to the myoinvasive cells of MELF.

Genuine LVSI may need to be distinguished from a variety of artefacts.

**Retraction artefacts**

This distinction may be difficult, but retraction artefacts are often more widespread than true LVSI and are characterised by a smooth round contour; with true LVSI, 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 LVSI.[55]

**MELF pattern of invasion**

In addition to the difficulty in identifying true LVSI associated with MELF, the cysts lined by flattened epithelium may contain free floating tumour, misdiagnosed as LVSI. This may be resolved by immunohistochemical evaluation with a pancytokeratin to highlight the epithelium and endothelial markers, which would be negative.

**Extensive smearing artefact or 'toothpaste/buttering' effect in autolysed samples**

Clues to smear artefact are the following: discrepancy between stage/grade and extent of LVSI, often involvement of vessels in outer myometrium and smearing of tumour in tissue clefts and on the serosa.

**Pseudovascular invasion related to mechanical displacement of tumour into vessels**

This may be seen in total laparoscopic or robotic-assisted hysterectomy specimens where a balloon manipulator has been used. As in smear artefact there may be discrepancy between stage and extent of LVSI, tumour in tissue clefts and preferential involvement of thick-walled vessels in outer myometrium and ectatic vessels anywhere in the myometrium. The presence of benign stroma accompanying the tumour in vessels, the lack of adherence to the vessel walls and the absence of surrounding inflammatory response may help identify it as artefact. Disruption to the endometrial lining and intratubal contaminants are clues that an intrauterine manipulator has been used.

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

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

### 5.3.6 Cervical stromal invasion

Cervical stromal 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 LVSI and nodal spread than tumours that are confined to the corpus.[56,57]

For this reason, the true significance of cervical involvement has been difficult to determine and some studies have cast some doubt on cervical stromal invasion as an independent prognosticator.[57] The presence of cervical stromal involvement is an indication for most oncologists to administer adjuvant brachytherapy and reporting of this parameter is therefore mandatory. In the presence of cervical involvement, the depth of involvement and the distance from the closest cervical circumferential resection margin should also be mentioned (see below in non-core data items).

The 2009 revision of FIGO staging[58] 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.[29,59]

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. In accordance with the ICCR dataset recommendations, ‘any invasion identified at the level of, or distal to, a benign endocervical crypt should be considered cervical stromal invasion’. Adherence to these criteria would enhance reproducibility.

The 2 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.[60] 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.

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Uterine Neoplasms list deep cervical stromal invasion as an adverse risk factor in patients with stage II endometrial carcinoma.[17] There is no clear definition of what constitutes ‘minimal cervical stromal invasion’. Absolute depth of cervical stromal invasion and percentage of cervical stromal invasion are non-core elements.

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

### 5.3.7 Vaginal involvement

Vaginal involvement occurs mainly as recurrent disease and only very rarely presents at diagnosis when it 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 2009 stage IIIB disease.

The reported 5-year survival for women with isolated vaginal metastasis is only about 25% and the median survival is <2 years.[61] 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.]*

### 5.3.8 Uterine serosal involvement

According to ESGO/ESTRO/ESP and ISGyP guidelines, tumour infiltrating the full myometrial thickness and reaching submesothelial fibroconnective tissue or the mesothelial layer should be reported as serosal involvement.[19]

Where stromal desmoplasia hinders evaluation of serosal involvement, the ICCR recommends identifying the adjacent serosal plane and extending it through the desmoplastic focus; if carcinoma disrupts or extends beyond this plane, it should be interpreted as serosal involvement.

It most commonly occurs secondary to full-thickness myometrial invasion but occasionally represents discontinuous tumour involvement. For staging purposes, serosal lymphovascular involvement, unaccompanied by tissue infiltration, is not considered to represent 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.[62,63]

Uterine perforation does not constitute serosal involvement and tumours with iatrogenic perforation should be staged based on usual parameters.

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

### 5.3.9 Parametrial involvement

The majority of endometrial carcinomas are surgically managed by a simple hysterectomy. Surgically dissected parametrium is not part of a simple hysterectomy specimen. In simple hysterectomy specimens, similar to serosal involvement, parametrial involvement can be seen when there is full-thickness penetration of the lower uterine wall and this can be confirmed within the scant parametrial tissue included. Involvement of loose connective tissue in the parametrial shave is considered parametrial involvement and upstages the carcinoma. Care must be taken that the parametrial shave does not include the outer myometrium. Please refer to core item 4.1 for how to identify and define parametrium.

Radical hysterectomy or modified radical hysterectomy with parametrial resection is sometimes performed for endometrial carcinoma when cervical involvement is suspected preoperatively. In these cases, the entire parametrium should be submitted for microscopic examination.[64,65]

For staging purposes and in common with LVSI at other sites, parametrial lymphovascular involvement unaccompanied by tissue infiltration is not considered to represent parametrial involvement. Parametrial involvement signifies FIGO stage IIIB disease.

### 5.3.10 Adnexal involvement

Adnexal involvement has been identified as an independent poor prognostic factor for both recurrence-free and overall survival and signifies FIGO stage IIIA disease.[66] Adnexal involvement, however, is frequently associated with other poor prognostic factors and other sites of metastatic disease.

It is important to distinguish between endometrial carcinoma with ovarian metastasis and synchronous primary tumours of the endometrium and the ovary.

**For high-grade carcinomas**

Ovarian involvement is almost always considered metastatic. The possibility of coincidental independent primary serous carcinomas in the endometrium and the tube/ovary is exceedingly rare. Metastasis from the adnexa to the endometrium is also very rare. Ancillary techniques (such as WT1 and p53 staining) and evaluation of the fallopian tube by sectioning and extensively examining the fimbria (SEE-FIM) protocol may be helpful.

**For low-grade endometrioid carcinomas**

Recent molecular studies have shown that for low-grade endometrioid carcinomas, there is a clonal relationship between the endometrial and ovarian tumour in the vast majority of cases, suggesting that the tumour arises in the endometrium, and secondarily extends to the ovary.[67]

In the 2020 edition of the WHO classification, it is suggested that patients with clonally related low-risk tumours be managed conservatively (as if they were 2 independent primaries) when the following criteria are met: 1) low-grade endometrioid morphology, 2) no more than 50% of myometrial thickness myometrial invasion, 3) absence of LVSI, and 4) absence of additional metastases.[4] This has been addressed in the FIGO 2023 endometrial cancer staging. Cases with minor deviation from these criteria should be discussed and treatment individualised.[2]

Presence of detached aggregates of tumour cells in the tubal lumen, without involvement of the fallopian wall, should not be considered tubal involvement but is often associated with peritoneal metastasis.[68] Staging of carcinomas extending only to the tubal epithelium is problematic; such cases should be discussed and treatment individualised. Endometrial carcinomas involving the fallopian tube wall or its serosa should be interpreted as metastatic unless there is evidence of an origin in endometriosis.

Involvement of the fallopian tube upstages a carcinoma, although, as indicated above, it is uncertain whether solely epithelial/mucosal involvement in continuity with the main tumour has adverse prognostic significance.[20] The presence of LVSI in ovarian hilar, parenchymal vessels or tubal vessels without stromal invasion does not affect the stage.

### 5.3.11 Margin status (only in cases with cervical stromal involvement)

In cases showing cervical stromal involvement, whether the tumour reaches the surgical margin should be recorded.

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

### 5.3.12 Omental involvement

Omentectomy is part of the surgical staging procedure for some high-grade endometrial cancers. Omental involvement by endometrial carcinoma is associated with an adverse outcome with a decreased overall survival; it is categorised as FIGO stage IVB.[69]

Omental involvement correlates with deep myometrial invasion, high tumour grade, non-endometrioid histology, lymph node metastasis and adnexal involvement.[70]

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

### 5.3.13 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).[70,71]

Involvement of non-regional lymph nodes is regarded as distant metastasis (stage IVB). Please note that inguinal lymph nodes are non-regional. The FIGO staging system is similar to the TNM, which classifies regional lymph nodes in the N category (pN1, pelvic; pN2, para-aortic) and non-regional nodes in the M category. However, although the size of the nodal metastasis does not affect the FIGO stage, as per TNM8, metastases >2 mm are macrometastases and 0.2–2 mm and/or >200 cells are micrometastases and documented as pN1 and pN1mi (pelvic) and pN2 and pN2mi (para-aortic) respectively and regarded as metastatic involvement. Isolated tumour cells (ITCs), which are foci <0.2 mm or $\leq$200 cells are documented as pN0 (i+), as there is no evidence to suggest that nodal involvement by ITCs has prognostic implications.[74]

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 and the size of the largest metastatic deposit (maximum diameter in millimetres), considered core items.

Sentinel lymph node (SLN) biopsy is an alternative to systematic and selective lymphadenectomy and is recommended in low and intermediate-risk prognostic groups. Indocyanine green, the tracer currently in use, yields a high detection rate when injected into the cervix. An advantage of the SLN biopsy is the detection of a high percentage of positive lymph nodes by accurate evaluation of a single/few lymph node(s). Studies have confirmed the high sensitivity of the SLN approach in detecting nodal disease in early-stage endometrial carcinomas. Ultrastaging is recommended for SLNs that are negative for metastases by routine histologic evaluation. If pelvic lymph nodes are negative by ultrastaging, para-aortic nodal involvement is unlikely. As per BAGP protocol for pathological processing of SLN, the following is recommended for ultrastaging of SLN in endometrial carcinoma.

- Ultrastaging is undertaken once a single H&E section of each slice of the SLN (with minimal trimming to avoid tissue wastage) is examined and confirmed to be negative for tumour.
- In a bilateral procedure, if 1 SLN is positive on initial H&E, but the node(s) on the contralateral side are negative, ultrastaging should be carried out only on the contralateral node(s).
- If SLN is accompanied by a full lymphadenectomy, there is no need to carry out SLN ultrastaging.
- For ultrastaging, 2 additional pairs of sections are cut at 50-micron intervals.
- 1 section from each of the 2 pairs is stained with H&E and the other with immunohistochemistry for a broad-spectrum cytokeratin (CK); AE1/AE3 is currently widely used.

*[Level of evidence C – importance of lymph node counts.]*

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

### 5.3.14 Peritoneal involvement

Peritoneal involvement is more common with non-endometrioid carcinomas, especially of serous type. 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.[73]

### 5.3.15 Distant metastases

Distant spread refers to metastasis beyond the pelvic cavity and signifies stage IV disease. Common sites of distant spread are the omentum, lungs, peritoneal lining of paracolic gutters and 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 on this basis.

### 5.3.16 Provisional FIGO stage

For gynaecological cancers, 2 staging systems are in widespread use: the FIGO system, which is specific for gynaecological cancers, and TNM,[72] which defines staging parameters for tumours arising at all anatomical 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.[74] Worldwide, most clinical trials and retrospective and prospective studies use FIGO rather than TNM.

The new FIGO staging of endometrial carcinoma was published in June 2023.[2] Following a membership survey by the BGCS and BAGP, a decision to delay the implementation of this staging system was taken.

It is noted that the following changes have been incorporated in the 2023 FIGO staging of endometrial carcinoma.

- New staging system accounts for histological type: Non-aggressive histological types are grade 1 and grade 2 endometrioid carcinomas. Other histological types are considered ‘aggressive’. Histological type affects stage I and II tumours but does not affect stage III or IV tumours.
- Simultaneous presence of low-grade endometrioid carcinoma involving endometrium and ovary/fallopian tube has been incorporated.
- New staging system takes into account molecular classification – stage is modified for stage I and II tumours showing either POLEmut or p53abn. Please note that in the staging system POLEmut and P53abn refer to molecular classification rather than individual molecular findings; as such, tumour which show both POLE mutation and a P53 abnormality are considered POLEmut.
- The presence or absence of extensive/substantial LVSI (≥5 vessels) affects stage for non-aggressive histological types.
- There is a new category for metastasis to pelvic peritoneum.
- Nodal involvement is sub-categorised according to the presence of micro- or macro-metastasis.

- There is a new category of stage IVC for metastasis to sites other than bladder/bowel mucosa and peritoneal metastases.

The provisional FIGO stage (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 comprise the following.

## 6.1 Macroscopic non-core data items

### 6.1.1 Specimen weight and measurements

Many pathologists routinely weigh and measure all solid organs. The variability in dimensions and weight of the uterus relative to age, parity, phase of the menstrual cycle and associated benign abnormalities such as fibroids or adenomyosis mean that these parameters have no significance in relation to the cancer prognosis or management and are therefore not included in the core data items.[7,8]

## 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 or clear cell carcinoma. 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.[19]

### 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.[75,76] A recent study has suggested that in stage I uterine carcinosarcomas, the presence of a heterologous mesenchymal component is a powerful adverse prognostic indicator.[77] 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 Adenomyosis: presence and involvement by tumour

The presence of adenomyosis and whether or not it is involved by tumour may be recorded as a non-core element. The presence of adenomyosis can occasionally result in overestimation of the depth of myometrial invasion macroscopically and/or on imaging. The presence of myometrial invasion arising from adenomyosis has been discussed above.

### 6.2.4 Cervical surface and gland (crypt) involvement

With the introduction of the 2009 FIGO staging system,[58] 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.

### 6.2.5 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.

### 6.2.6 Myometrial involvement: absolute depth of myoinvasion

This is the distance between the endomyometrial junction and the deepest point of myometrial invasion.[46]

### 6.2.7 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.[46]

### 6.2.8 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.[78–80] 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 measurement 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.

### 6.2.9 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.

### 6.2.10 Peritoneal cytology

The significance of positive peritoneal cytology as an independent prognostic factor is controversial; 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.

### 6.2.11 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.

### 6.2.12 Provisional TNM stage

The updated version of the TNM classification for endometrial carcinoma[72] mirrors most of the changes in the 2009 FIGO staging system[58] 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 and Appendix C).

### 6.2.13 Block key

The origin/designation of all tissue blocks should be recorded; 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 2020 classification[4] and coded using SNOMED codes (Appendix A). Tumours should be staged using the 2009 FIGO staging system.[58] (Appendix B) with the option to include TNM8 staging[72] (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.

All the submitted tissue should be processed.[81]

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.

MMR repair immunohistochemistry must be carried out on all endometrial carcinomas.[39] There is no recommendation for MMR testing in hyperplasia.

# 9 Reporting of frozen sections

In most institutions in the UK, intraoperative frozen sections are rarely performed in patients with endometrial carcinoma.[82]

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

Most endometrial carcinomas express pan-cytokeratins, EMA, Ber-Ep4, PAX8 and CK7 and 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 consolidating the diagnosis of endometrial carcinomas or subtyping of endometrial carcinomas.

## 10.1 Typing endometrial carcinomas

Typing endometrial carcinomas can be done by careful histological assessment and additional confirmatory immunohistochemistry.

Serous endometrial carcinomas can show an architecturally well-differentiated glandular pattern mimicking endometrioid adenocarcinoma. High-grade endometrioid carcinomas tend to show typically more solid and less papillary morphology and a lesser degree of cytonuclear atypia. In cases that are morphologically ambiguous, an immunohistochemical

panel that is helpful in this differential includes p53, ER, PR, p16, PTEN and MMR antibodies. The majority of serous carcinomas are negative for ER and PR, positive for PTEN, retain expression of the MMR proteins and show, in addition to an aberrant p53 pattern, diffuse staining with p16, whereas endometrioid carcinomas are more likely to show positivity for ER, PR, lack of PTEN staining (if abnormal phenotype), a wild-type phenotype for p53, MMR deficiency (in up to 30% of cases) and patchy and focal p16 positivity.[5,83]

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, hepatocyte nuclear factor 1B (HNF-1B) and alpha-methylacyl-CoA racemase.[84] 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 usually ER and PR negative or focally positive and up to a third may show abnormal p53 staining.[83]

Some of the newly described variants of endometrial carcinomas included in the 2020 WHO classification show a unique immunophenotype. Primary uterine mesonephric carcinomas resemble mesonephric carcinomas with a morphologically predominant pattern of small glands and tubules with luminal colloid-like material. Characteristically, these tumours lack ER and PR staining, are p53 wild type and show diffuse positive staining for GATA3. A number of cases may also show positive staining for TTF1 and calretinin.[25]

Staining for ER +/- PR is recommended in all cases of endometrioid carcinoma, as this may help to identify rare and newly described histotypes that mimic endometrioid carcinoma (please also see section 6.2.12).

## 10.2 Endometrial versus endocervical carcinomas

Immunohistochemistry to distinguish between endometrial and cervical adenocarcinoma is more often necessary in biopsies than in resection specimens. Generally, endometrioid and mucinous endometrial carcinomas are strongly and diffusely positive for vimentin, ER and PR and largely negative for CEA.[85,86] They may also show MMRd. The converse profile is usual in cervical adenocarcinomas. P16 is expressed strongly and diffusely (block positivity)[87] 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.[85] 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 LS

Gynaecological malignancies occur commonly in women with LS, with approximately 3% of endometrial carcinomas being the result of germline mutations in 1 of the MMR genes or the closely related gene EPCAM.

The NICE diagnostic guidance DG42[39] recommends systematic screening of all endometrial carcinomas for LS using immunohistochemistry at the time of diagnosis. A panel of 4 antibodies is both cost and clinically effective in identifying MMR deficiency. Loss of MLH1 protein expression should prompt MLH1 promoter hypermethylation testing. If MLH1 promoter hypermethylation is not detected or the tumour shows loss of MSH6, MSH2 or isolated PMS2 protein expression, a recommendation should be made for the patient to be offered genetic counselling for consideration of germline testing.

Testing strategies may also include microsatellite instability in addition to immunohistochemistry, particularly when there is a strong clinical suspicion of LS and the immunohistochemistry results show no loss of MMR protein expression. The latter may be due to germline mutations in the MMR genes with no detectable loss of protein expression by immunohistochemistry.

# 12 Criteria for audit of dataset

The following are recommended by the RCPath as key assurance indicators and key performance indicators:[88,89]

- cancer resections should 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

  - standard: 95% of reports must contain structured data

- histopathology cases must be reported, confirmed and authorised within 7 and 10 calendar days of the procedure
  - standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days.

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 assurance indicators:[88]

- 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 7 and 10 calendar days of the procedure
  - standard: 80% of cases must be reported within 7 calendar days and 90% within 10 calendar days.

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# Appendix A WHO classification[3] of endometrial cancer

| 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 | Serous intraepithelial carcinoma (morphologic abnormality) | 703558002 |
| Serous carcinoma | M-84413 | Serous cystadenocarcinoma (morphologic abnormality) | 90725004 |
| Clear cell carcinoma | M-83103 | Clear cell adenocarcinoma (morphologic abnormality) | 30546008 |
| Carcinoid tumour | M-82403 | Well-differentiated neuroendocrine tumour (morphologic abnormality) | 1286768001 |
| Small cell NEC | M-80413 | Small cell carcinoma (morphologic abnormality) | 74364000 |
| Large cell NEC | M-80133 | Large cell NEC (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[59] (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 (9th 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 1 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:..... CHI/NHS 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 ☐
If present, Focal ☐ Substantive ☐

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 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: ..... CHI/NHS no: .....

Date of receipt: ..... Report no: ..... Surgeon: .....

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

## Diagnosis

Tumour type:

Endometrioid ☐ 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……...../……...../……..**

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

| Element name | Values | Implementation notes |
|---|---|---|
| Hysterectomy type | Single selection value list:<br>• Abdominal<br>• Vaginal<br>• Laparoscopic<br>• Not known | |
| Relevant family history | Free text | |
| Specimen components | Multiple selection value list:<br>• Adnexa<br>• Vaginal cuff<br>• Parametrium<br>• Other | |
| Specimen components, other specify | Free text | Only applicable if 'Specimen components, Other' is selected. |
| Accompanying specimens | Multiple selection value list:<br>• Omentum<br>• Lymph nodes: pelvic<br>• Lymph nodes: para-aortic<br>• 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:<br>• Myometrium<br>• Cervix<br>• Serosa<br>• Parametrium | |
| Tumour type | Single selection value list:<br>• Endometrioid | |

| | | |
|---|---|---|
| | • Mucinous<br>• Serous EIC<br>• Clear cell<br>• Undifferentiated<br>• Neuroendocrine<br>• Mixed<br>• Carcinosarcoma<br>• 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:<br>• 1<br>• 2<br>• 3 | |
| Myometrial invasion | Single selection value list:<br>• None or <50%<br>• ≥50% | |
| LVSI | Single selection value list:<br>• Present (< or >4 foci)<br>• Not identified | |
| LVSI is present | Single selection value list:<br>• Focal<br>• Substantive | |
| Microscopic involvement of cervical stroma | Single selection value list:<br>• Involved<br>• Not involved<br>• Not assessable | |
| Microscopic involvement of vagina | Single selection value list:<br>• Involved<br>• Not involved<br>• Not assessable | |
| Microscopic involvement of adnexa | Single selection value list:<br>• Involved<br>• Not involved<br>• Not assessable | |
| If adnexa involved, is this considered to be a separate primary neoplasm | Single selection value list:<br>• Yes<br>• No | Only applicable if 'Microscopic involvement of |

| | | |
|---|---|---|
| | • Uncertain | adnexa, Involved' is selected. |
| Microscopic involvement of uterine serosa | Single selection value list:<br>• Involved<br>• Not involved<br>• Not assessable | |
| Microscopic involvement of parametrium | Single selection value list:<br>• Involved<br>• Not involved<br>• Not assessable | |
| Lymph nodes | Single selection value list:<br>• Not sampled<br>• 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. |
| 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:<br>• Not sampled<br>• Involved by tumour<br>• Not involved by tumour | |
| Peritoneal involvement | Single selection value list:<br>• Involved | |

| | | |
|---|---|---|
| | • Not involved<br>• Not assessable | |
| Distant metastases | Single selection value list:<br>• Yes<br>• No<br>• 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:<br>• IA<br>• IB<br>• II<br>• IIIA<br>• IIIB<br>• IIIC1<br>• IIIC2<br>• IVA<br>• 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:<br>• Pipelle<br>• Currettings<br>• Other/not stated | |
| Tumour type | Single selection value list:<br>• Endometrioid<br>• Serous<br>• Clear cell<br>• Undifferentiated/Dedifferentiated<br>• Neuroendocrine<br>• Mixed<br>• Carcinosarcoma<br>• 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:<br>• 1<br>• 2<br>• 3 | |
| Comments | Free text | |
| SNOMED T code | May have multiple codes.<br>Look up from SNOMED tables. | |
| SNOMED M code | May have multiple codes.<br>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 1 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 population<br>or<br>A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type. |
| 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 population<br>or<br>Extrapolation evidence from studies described in A. |
| Grade C | A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high- quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population<br>or<br>Extrapolation evidence from studies described in B. |
| Grade D | Non-analytic studies such as case reports, case series or expert opinion<br>or<br>Extrapolation evidence from studies described in C. |
| Good practice point (GPP) | Recommended best practice based on the clinical experience of the authors of the writing group. |

# Appendix I AGREE II guideline monitoring sheet

The autopsy guidelines of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this autopsy 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 |