** Endometrial Cancer Histopathology Reporting Guide**

**Elements in black text are CORE Elements in grey text are NON-CORE o indicates single select values □ indicates multi-select values**

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| Definition of Core elements | CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council levels of evidence1). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement by the Dataset Authoring Committee (DAC). An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.  Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.  The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.  **Reference**  1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34. |
| Definition of Non-core elements | NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.  Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC. |
| Scope of this dataset | The dataset has been developed for the pathology reporting of resection specimens of endometrial cancers, including carcinosarcomas. It is not applicable for small endometrial biopsy specimens. Haematopoietic neoplasms, mesenchymal neoplasms, adenosarcomas, malignant melanomas, other non-epithelial malignancies and metastatic tumours are excluded from this dataset. Adenosarcoma and other mesenchymal neoplasms are included in the ICCR Uterine malignant and potentially malignant mesenchymal tumours dataset.[1](#_ENREF_1)  The 5th edition of the ICCR Endometrial cancer dataset incorporates the International Federation of Gynaecology and Obstetrics (FIGO) staging for endometrial cancer (2023).[2](#_ENREF_2) This dataset also includes changes to align the dataset with the World Health Organization (WHO) Classification of Tumours, Female Genital Tumours, 5th edition, 2020.[3](#_ENREF_3)The ICCR dataset includes 5th edition Corrigenda, July 2024.[4](#_ENREF_4) References 1 International Collaboration on Cancer Reporting (2021). *Uterine Malignant and Potentially Malignant Mesenchymal Tumours Histopathology Reporting Guide. 1st edition*. Available from: http://www.iccr-cancer.org/datasets/published-datasets/female-reproductive (Accessed 10th July 2024).  2 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  3 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  4 WHO Classification of Tumours Editorial Board (2024). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4 - Corrigenda July 2024*. Available from: https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Female-Genital-Tumours-2020 (Accessed 18th July 2024). |

| **Core/**  **Non-core** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
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| Non-core | CLINICAL INFORMATION | * Information not provided * Family history of cancer or cancer-associated syndrome,   *specify*   * Previous history of cancer, *specify* * Previous therapy, *specify* * Other clinical information, *specify* | Clinical information regarding history of familial cancer (particularly for Lynch syndrome, but also for other hereditary cancer syndromes) is important. In addition, the history of previous cancer, previous neoadjuvant therapy (including hormonal therapy), or any other clinical data that can be relevant for pathologic interpretation is of benefit to report. |  |
| Core | OPERATIVE PROCEDURE | * Not specified * Hysterectomy * Simple * Simple supracervical /subtotal * Radical * Type not specified * Other, *specify* | Depending on the presumed extent of spread of the carcinoma as assessed clinically or radiologically, either a simple or radical hysterectomy is performed, which may or may not be part of a staging procedure. A simple hysterectomy is defined as the removal of the total uterus (including the cervix). Radical hysterectomy entails en bloc resection of the uterus and cervix along with the surrounding parametria, upper vagina and uterosacral ligaments. These procedures can either be performed through a laparoscopy, robot-assisted laparoscopy or laparotomy. Finally, a debulking procedure can be performed, if the tumour is macroscopically disseminated, to remove all visible tumour. Pelvic exenteration is not a frequent procedure, but is occasionally used in advanced and recurrent endometrial cancer, and recognised in the 2020 European Society of Gynaecological Oncology (ESGO)-European Society for Radiotherapy and Oncology (ESTRO)-European Society of Pathology (ESP) guidelines.[1](#_ENREF_1) In some instances, malignancy can be found in a morcellated hysterectomy specimen.[2](#_ENREF_2) Morcellation should be avoided whenever there is suspicion of endometrial carcinoma. Primary hormonal treatment may be considered in a woman who desires fertility conservation. References 1 Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X (2021). ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch*:153-190.  2 Picerno TM, Wasson MN, Gonzalez Rios AR, Zuber MJ, Taylor NP, Hoffman MK and Borowsky ME (2016). Morcellation and the incidence of occult uterine malignancy: a dual-institution review. *Int J Gynecol Cancer* 26(1):149-155. |  |
| Core | SPECIMEN(S) SUBMITTED | * Not specified * Fallopian tube * Left * Right * Laterality not specified * Ovary * Left * Right * Laterality not specified * Parametrium * Left * Right * Laterality not specified * Vaginal cuff * Vaginal nodules * Omentum * Peritoneal biopsies * Peritoneal washings//peritoneal fluid * Lymphadenectomy specimen(s) * Sentinel node(s) * Left * Right * Laterality not specified * Regional node(s): pelvic * Left * Right * Laterality not specified * Regional node(s): para-aortic * Non-regional node(s): inguinal * Left * Right * Laterality not specified * Other node group, *specify* * Other, *specify* | Attached anatomical structures may include vaginal cuff, ovaries, fallopian tubes or parametria. Further specimens may be submitted for pathological review including: omentum, sentinel lymph nodes, pelvic and periaortic lymph nodes, peritoneal washings, and peritoneal biopsies from various sites.  Inking of peritoneal and/or nonperitoneal surfaces is recommended in hysterectomy specimens and is essential in radical hysterectomy specimens in which a vaginal cuff is present. In addition, inking the peritoneal and nonperitoneal surfaces and extending the ink all the way to the vaginal cuff is useful to provide the status of the vaginal cuff margin.[1](#_ENREF_1) Reference 1 Malpica A, Euscher ED, Hecht JL, Ali-Fehmi R, Quick CM, Singh N, Horn LC, Alvarado-Cabrero I, Matias-Guiu X, Hirschowitz L, Duggan M, Ordi J, Parkash V, Mikami Y, Ruhul Quddus M, Zaino R, Staebler A, Zaloudek C, McCluggage WG and Oliva E (2019). Endometrial carcinoma, grossing and processing issues: recommendations of the international society of gynecologic pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S9-s24. |  |
| Non-core | TUMOUR SITE | * Isthmus/lower uterine segment * Fundus * Body * Other, *specify* | Anatomically, the lower uterine segment begins where the body funnels towards the cervix and ends at the internal os. The fundus is that part of the uterus above the origin of the fallopian tubes.  Endometrial carcinoma involving the lower uterine segment has several implications. Tumours originating in this location are more frequently associated with mismatch repair (MMR) protein deficiencies.[1](#_ENREF_1) Lower uterine segment involvement in early endometrial carcinoma is predictive of lymph node metastasis and is an independent poor prognostic factor for distant recurrence and death.[2](#_ENREF_2)  Endometrial carcinomas arising in the body of the uterus may extend to involve the lower uterine segment and this should also be recorded. Distinguishing lower uterine segment endometrial carcinoma from endocervical carcinoma is important for staging, prognosis and management, but this is not always straightforward.   References 1 Zhao S, Chen L, Zang Y, Liu W, Liu S, Teng F, Xue F and Wang Y (2022). Endometrial cancer in Lynch syndrome. *Int J Cancer* 150(1):7-17.  2 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113. |  |
| Non-core | MAXIMUM TUMOUR DIMENSION | \_\_\_ mm | Some studies have found that a larger tumour size is significantly associated with increased invasion of the lymphovascular space, lymph node metastasis, and/or risk of recurrence in endometrioid endometrial carcinoma (EEC). However, the threshold defining a larger tumour size varies from ≥20 to ≥50 millimetres (mm).[1](#_ENREF_1),[2](#_ENREF_2) Some studies have not found an association between a tumour size of ≥20 mm and prognosis.[3](#_ENREF_3),[4](#_ENREF_4)  It is recommended that the largest dimension of the tumour should be reported; other dimensions are not required. This may be determined by macroscopic or microscopic assessment or the combination of both. References 1 Sozzi G, Uccella S, Berretta R, Petrillo M, Fanfani F, Monterossi G, Ghizzoni V, Frusca T, Ghezzi F, Chiantera V and Scambia G (2018). Tumor size, an additional risk factor of local recurrence in low-risk endometrial cancer: a large multicentric retrospective study. *Int J Gynecol Cancer* 28(4):684-691.  2 Canlorbe G, Bendifallah S, Laas E, Raimond E, Graesslin O, Hudry D, Coutant C, Touboul C, Bleu G, Collinet P, Cortez A, Daraï E and Ballester M (2016). Tumor size, an additional prognostic factor to include in low-risk endometrial cancer: results of a French multicenter study. *Ann Surg Oncol* 23(1):171-177.  3 Oz M, Korkmaz V, Meydanli MM, Sari ME, Cuylan ZF and Gungor T (2017). Is tumor size really important for prediction of lymphatic dissemination in grade 1 endometrial carcinoma with superficial myometrial invasion? *Int J Gynecol Cancer* 27(7):1393-1398.  4 Euscher E, Fox P, Bassett R, Al-Ghawi H, Ali-Fehmi R, Barbuto D, Djordjevic B, Frauenhoffer E, Kim I, Hong SR, Montiel D, Moschiano E, Roma A, Silva E and Malpica A (2013). The pattern of myometrial invasion as a predictor of lymph node metastasis or extrauterine disease in low-grade endometrial carcinoma. *Am J Surg Pathol* 37(11):1728-1736. | . |
| Non-core | OMENTUM DIMENSIONS | \_\_\_mm x \_\_\_mm x \_\_\_mm | Omentectomy is currently undertaken in many, but not all, institutions for all high grade endometrial carcinomas, such as grade 3 endometrioid carcinoma, serous carcinoma, clear cell carcinoma, undifferentiated and dedifferentiated carcinoma and carcinosarcoma. Grade 1 and 2 endometrioid carcinomas are subject to omentectomy in some centres.  Thorough macroscopic examination of the omentum is essential.[1](#_ENREF_1) The omentum should be cut at 5 mm intervals to detect small lesions.[1](#_ENREF_1) Obvious lesions can be sampled in one or two blocks but if no lesion is seen then at least four blocks are recommended. Reference 1 Malpica A, Euscher ED, Hecht JL, Ali-Fehmi R, Quick CM, Singh N, Horn LC, Alvarado-Cabrero I, Matias-Guiu X, Hirschowitz L, Duggan M, Ordi J, Parkash V, Mikami Y, Ruhul Quddus M, Zaino R, Staebler A, Zaloudek C, McCluggage WG and Oliva E (2019). Endometrial carcinoma, grossing and processing issues: recommendations of the international society of gynecologic pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S9-s24. |  |
| Non-core | BLOCK IDENTIFICATION KEY | List overleaf or separately with an indication of the nature and origin of all tissue blocks. | The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks in some cases.  Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials. |  |
| Core and  Non-core | HISTOLOGICAL TUMOUR TYPE | * Endometrioid carcinoma * Serous carcinoma * Clear cell carcinoma * Carcinoma, undifferentiated * Mixed cell carcinoma * Mesonephric carcinoma * Squamous cell carcinoma * Mucinous carcinoma, gastrointestinal type * Mesonephric-like carcinoma * Neuroendocrine carcinomas Specify subtype \_\_\_\_\_\_ * Carcinosarcoma NOS   Epithelial \_\_\_%  AND  Sarcomatous \_\_\_ %  ↓   * Homologous * Heterologous * Other, *specify* | All endometrial carcinomas should be classified according to the World Health Organization (WHO) Classification of Tumours, Female Genital Tumours, 5th edition, 2020 (Table 1).[1](#_ENREF_1) The International Collaboration on Cancer Reporting (ICCR) dataset includes 5th edition Corrigenda, July 2024.[2](#_ENREF_2) It is beyond the scope of this dataset to provide detailed information about the microscopic features of each histologic type. However, some points are highlighted for clarification, particularly regarding the main modifications introduced in the 2020 WHO Classification.[1](#_ENREF_1)  Histological tumour type has consistently been demonstrated as an important biological predictor in endometrial carcinoma. Accurate histological typing is important both in biopsy and resection specimens. Moreover, assessment of histological type determines the extent of the initial surgical procedure, and subsequent use of adjuvant therapy.[3](#_ENREF_3)  Low grade (grade 1 and 2) endometrioid carcinomas are the most common tumours and are usually associated with favourable outcome. The prognosis for serous carcinoma is worse with recurrence occurring in about 50% of serous carcinomas compared with 20% recurrence in endometrioid carcinomas. Although there is moderate to excellent (κ=0.62-0.87) reproducibility in histological typing, inter-observer agreement is worse in high grade carcinomas.[4-6](#_ENREF_4)  Low grade endometrioid carcinoma is usually composed of cells arranged in a branching, maze-like glandular or complex papillary pattern of growth, while high grade endometrioid carcinoma has a predominant solid architecture, and serous carcinoma has a complex architectural pattern with papillae and cellular budding.[7](#_ENREF_7) However, serous carcinomas with a prominent glandular pattern can frequently be mistaken as low grade endometrioid carcinoma;[8](#_ENREF_8),[9](#_ENREF_9) and endometrioid carcinoma with papillary pattern can sometimes be misinterpreted as serous carcinoma.[10](#_ENREF_10)    High grade endometrioid carcinoma is characterised by a solid growth pattern associated with mostly moderate nuclear atypia and an increased number of mitoses. Application of the Cancer Genome Atlas (TCGA)-molecular surrogate has demonstrated that this is a heterogeneous group of tumours.[11](#_ENREF_11) This is one of the scenarios that shows the importance of integrating histologic typing with molecular classification.  Mixed carcinomas are composed of two or more discrete histological types of endometrial carcinoma, of which at least one component is either serous or clear cell.[12-15](#_ENREF_12) Rigorous criteria should be applied to make this diagnosis and a diagnosis of mixed carcinoma should only be used when both components exhibit a characteristic morphology and immunophenotype.[15](#_ENREF_15) There is no minimum percentage of one of the components to classify the tumour as a mixed endometrial carcinoma.  Several studies have shown that the presence of heterologous elements in carcinosarcomas is an important adverse prognostic feature particularly *in low stage* tumours.[16](#_ENREF_16),[17](#_ENREF_17) Reporting of the percentage of epithelial and sarcomatous elements and whether the sarcomatous component is homologous or heterologous is a non-core element. The rare instance of carcinoma arising in an adenosarcoma appears to be a distinct biologic process and should not be diagnosed as carcinosarcoma.[18](#_ENREF_18" \o "El Hallani S, 2021 #5924)  Neuroendocrine carcinomas of the endometrium are included in the section on neuroendocrine tumours of the female genital tract in the 2020 WHO Classification.[1](#_ENREF_1) Reporting of the neuroendocrine carcinoma subtype is a non-core feature.  For staging purposes, the 2023 International Federation of Gynaecology and Obstetrics (FIGO) staging system[19](#_ENREF_19) distinguishes two main groups of tumours regarding histological type:   1. Non-aggressive histological types are composed of low grade (G1, G2) endometrioid carcinomas. 2. Aggressive histological types are composed of high grade endometrioid carcinomas, serous, mixed, clear cell, undifferentiated, dedifferentiated, mesonephric-like and gastrointestinal type mucinous carcinomas and carcinosarcomas.   Endometrial carcinomas should be adequately sampled. The International Society of Gynecological Pathologists (ISGyP) 2019 guidelines recommend one section per 10 mm, considering the largest tumour dimension.[20](#_ENREF_20) An alternative, when dealing with large tumours, is to submit at least four blocks of tumour. However, the entire endometrium and underlying inner myometrium should be submitted for microscopic examination in the setting of a preoperative endometrial specimen demonstrating malignancy, when no gross lesion is seen in the hysterectomy specimen.[20](#_ENREF_20) Table 1 (See end of the document for Table)References 1 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  2 WHO Classification of Tumours Editorial Board (2024). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4 - Corrigenda July 2024*. Available from: https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Female-Genital-Tumours-2020 (Accessed 18th July 2024).  3 Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X (2021). ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch*:153-190.  4 Gilks CB, Oliva E and Soslow RA (2013). Poor interobserver reproducibility in the diagnosis of high-grade endometrial carcinoma. *Am J Surg Pathol* 37(6):874-881.  5 Hoang LN, McConechy MK, Köbel M, Han G, Rouzbahman M, Davidson B, Irving J, Ali RH, Leung S, McAlpine JN, Oliva E, Nucci MR, Soslow RA, Huntsman DG, Gilks CB and Lee CH (2013). Histotype-genotype correlation in 36 high-grade endometrial carcinomas. *Am J Surg Pathol* 37(9):1421-1432.  6 Murali R, Davidson B, Fadare O, Carlson JA, Crum CP, Gilks CB, Irving JA, Malpica A, Matias-Guiu X, McCluggage WG, Mittal K, Oliva E, Parkash V, Rutgers JKL, Staats PN, Stewart CJR, Tornos C and Soslow RA (2019). High-grade endometrial carcinomas: morphologic and immunohistochemical features, diagnostic challenges and recommendations. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S40-s63.  7 Gatius S and Matias-Guiu X (2016). Practical issues in the diagnosis of serous carcinoma of the endometrium. *Mod Pathol* 29 Suppl 1:S45-58.  8 Darvishian F, Hummer AJ, Thaler HT, Bhargava R, Linkov I, Asher M and Soslow RA (2004). Serous endometrial cancers that mimic endometrioid adenocarcinomas: a clinicopathologic and immunohistochemical study of a group of problematic cases. *Am J Surg Pathol* 28(12):1568-1578.  9 Garg K and Soslow RA (2012). Strategies for distinguishing low-grade endometrioid and serous carcinomas of endometrium. *Adv Anat Pathol* 19(1):1-10.  10 Bartosch C, Manuel Lopes J and Oliva E (2011). Endometrial carcinomas: a review emphasizing overlapping and distinctive morphological and immunohistochemical features. *Adv Anat Pathol* 18(6):415-437.  11 Bosse T, Nout RA, McAlpine JN, McConechy MK, Britton H, Hussein YR, Gonzalez C, Ganesan R, Steele JC, Harrison BT, Oliva E, Vidal A, Matias-Guiu X, Abu-Rustum NR, Levine DA, Gilks CB and Soslow RA (2018). Molecular classification of grade 3 endometrioid endometrial cancers identifies distinct prognostic subgroups. *Am J Surg Pathol* 42(5):561-568.  12 Matrai CE, Pirog EC and Ellenson LH (2018). Despite diagnostic morphology, many mixed endometrial carcinomas show unexpected immunohistochemical staining patterns. *Int J Gynecol Pathol* 37(5):405-413.  13 Coenegrachts L, Garcia-Dios DA, Depreeuw J, Santacana M, Gatius S, Zikan M, Moerman P, Verbist L, Lambrechts D, Matias-Guiu X and Amant F (2015). Mutation profile and clinical outcome of mixed endometrioid-serous endometrial carcinomas are different from that of pure endometrioid or serous carcinomas. *Virchows Arch* 466(4):415-422.  14 Köbel M, Meng B, Hoang LN, Almadani N, Li X, Soslow RA, Gilks CB and Lee CH (2016). Molecular analysis of mixed endometrial carcinomas shows clonality in most cases. *Am J Surg Pathol* 40(2):166-180.  15 Rabban JT, Gilks CB, Malpica A, Matias-Guiu X, Mittal K, Mutter GL, Oliva E, Parkash V, Ronnett BM, Staats P, Stewart CJR and McCluggage WG (2019). Issues in the differential diagnosis of uterine low-grade endometrioid carcinoma, including mixed endometrial carcinomas: recommendations from the international society of gynecological pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S25-s39.  16 Abdulfatah E, Lordello L, Khurram M, Van de Vijver K, Alosh B, Bandyopadhyay S, Oliva E and Ali-Fehmi R (2019). Predictive histologic factors in carcinosarcomas of the uterus: a multi-institutional study. *Int J Gynecol Pathol* 38(3):205-215.  17 Ferguson SE, Tornos C, Hummer A, Barakat R and Soslow R (2007). Prognostic features of surgical stage I uterine carcinosarcoma. *Am J Surg Pathol* 31(11):1653-1661.  18 El Hallani S, Arora R, Lin D, Måsbäc A, Mateoiu C, McCluggage WG, Nucci MR, Otis CN, Parkash V, Parra-Herran C and Longacre TA (2021). Mixed endometrioid adenocarcinoma and Müllerian adenosarcoma of the uterus and ovary clinicopathologic characterization with emphasis on its distinction from carcinosarcoma. *Am J Surg Pathol* 45:374-383.  19 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  20 Malpica A, Euscher ED, Hecht JL, Ali-Fehmi R, Quick CM, Singh N, Horn LC, Alvarado-Cabrero I, Matias-Guiu X, Hirschowitz L, Duggan M, Ordi J, Parkash V, Mikami Y, Ruhul Quddus M, Zaino R, Staebler A, Zaloudek C, McCluggage WG and Oliva E (2019). Endometrial carcinoma, grossing and processing issues: recommendations of the international society of gynecologic pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S9-s24.    21 Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin LH, Parkin DM, Whelan SL (eds) (2020). *International Classification of Diseases for Oncology, Third edition, Second revision ICD-O-3.2*. Available from: http://www.iacr.com.fr/index.php?option=com\_content&view=category&layout=blog&id=100&Itemid=577 (Accessed 10th July 2024). | Value list based on the WHO  Classification of Female Genital Tumours (2020).  Note that permission to publish the WHO Classification of Tumours may be needed in your implementation. It is advisable to check with the International Agency for Research on Cancer (IARC). |
| Core | HISTOLOGICAL TUMOUR GRADE | * Not applicable * Cannot be assessed * Grade 1 (low) * Grade 2 (low) * Grade 3 (high) | Evaluation of histopathological grade in endometrioid carcinoma is very important in both the initial biopsy/curettage and the final hysterectomy specimen, as risk stratification and decisions on the extent of surgical treatment and administration of adjuvant therapy take into account information on grading.[1](#_ENREF_1)  Serous, clear cell, undifferentiated, dedifferentiated, mesonephric-like, gastrointestinal type mucinous and neuroendocrine carcinomas and carcinosarcomas are considered high grade by definition. Tumours that are high grade by definition should be recorded as ‘not applicable’ in the reporting guide. The value of the FIGO grading system was shown in a univariate analysis of more than 600 patients with clinical Stage I or occult Stage II endometrioid carcinomas.[2](#_ENREF_2) The 5-year relative survival was 94% for patients with grade 1 tumours, 84% for those with grade 2 tumours, and 72% for those with grade 3 tumours.[3](#_ENREF_3)  The 2023 FIGO grading criteria for endometrioid carcinoma is primarily based on architectural features.[3](#_ENREF_3) Grade 1, 2, and 3 tumours exhibit ≤5%, 6-50%, and >50% solid non-glandular growth, respectively.[3](#_ENREF_3) In endometrioid carcinomas with squamous differentiation, the grade of the tumour should be assessed in the non-squamous areas. The presence of severe cytological atypia in the majority of cells (>50%) increases the grade by one level.  The ISGyP guidelines and the 2020 WHO Classification, highlight the benefits of binary grading, whereby grade 1 and 2 tumours are categorised as low grade and grade 3 tumours as high grade.[4](#_ENREF_4),[5](#_ENREF_5) This recommendation has been endorsed in the 2023 FIGO staging criteria.[3](#_ENREF_3) It is based on the benefits of the binary grading system for easier clinical decision making and improved reproducibility. Classification and regression tree statistical analysis show that the distinction between low and high grade tumours was the second most informative predictor of survival after stage.[6](#_ENREF_6),[7](#_ENREF_7) However, some reports show a small, but statistically significant survival difference of around 5% between low stage, grade 1 and 2 tumours,[4](#_ENREF_4) and the distinction between grade 1 and 2 carcinomas may be still important in some institutions for patients desiring fertility-sparing treatments.[8-11](#_ENREF_8)  Agreement in histopathological grade between biopsy and hysterectomy specimens varies, with concordance of only 35% reported in some series.[12](#_ENREF_12),[13](#_ENREF_13) Tumour heterogeneity may explain some of this discrepancy, since biopsies may not be necessarily representative of the whole tumour.[14](#_ENREF_14) When there is discrepancy between the reported histological grade in the biopsy and the hysterectomy specimen, it is recommended to review the initial biopsy, and to take this into account when assigning the final histological grade, particularly in cases in which the amount of tumour in the hysterectomy specimen is very limited.  Histological grade may be difficult to apply for cases (especially hysterectomy specimens) in which the specimen was inappropriately fixed and/or the tumour is autolysed. The category of ‘cannot be assessed’ should be used sparingly and only in cases where there is genuine doubt. In such cases, it may be useful to state the reason for a response of ’cannot be assessed’ in the report and correlation with the preoperative biopsy may be valuable. The ‘cannot be assessed’ category may also be used in biopsy specimens containing extremely scant tissue. References 1 Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, Marth C, Nout R, Querleu D, Mirza MR and Sessa C (2016). ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. *Ann Oncol* 27(1):16-41.  2 Prat J (2004). Prognostic parameters of endometrial carcinoma. *Hum Pathol* 35(6):649-662.  3 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  4 Soslow RA, Tornos C, Park KJ, Malpica A, Matias-Guiu X, Oliva E, Parkash V, Carlson J, McCluggage WG and Gilks CB (2019). Endometrial carcinoma diagnosis: use of FIGO grading and genomic subcategories in clinical practice: recommendations of the International Society of Gynecological Pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S64-s74.  5 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  6 Barlin JN, Soslow RA, Lutz M, Zhou QC, St Clair CM, Leitao MM, Jr., Iasonos A, Hensley ML, Barakat RR, Matias-Guiu X and Abu-Rustum NR (2013). Redefining stage I endometrial cancer: incorporating histology, a binary grading system, myometrial invasion, and lymph node assessment. *Int J Gynecol Cancer* 23(9):1620-1628.  7 Barlin JN, Zhou Q, St Clair CM, Iasonos A, Soslow RA, Alektiar KM, Hensley ML, Leitao MM, Jr., Barakat RR and Abu-Rustum NR (2013). Classification and regression tree (CART) analysis of endometrial carcinoma: Seeing the forest for the trees. *Gynecol Oncol* 130(3):452-456.  8 Zhang Q, Qi G, Kanis MJ, Dong R, Cui B, Yang X and Kong B (2017). Comparison among fertility-sparing therapies for well differentiated early-stage endometrial carcinoma and complex atypical hyperplasia. *Oncotarget* 8(34):57642-57653.  9 Wei J, Zhang W, Feng L and Gao W (2017). Comparison of fertility-sparing treatments in patients with early endometrial cancer and atypical complex hyperplasia: A meta-analysis and systematic review. *Medicine (Baltimore)* 96(37):e8034.  10 Qin Y, Yu Z, Yang J, Cao D, Yu M, Wang Y and Shen K (2016). Oral progestin treatment for early-stage endometrial cancer: a systematic review and meta-analysis. *Int J Gynecol Cancer* 26(6):1081-1091.  11 Luo L, Luo B, Zheng Y, Zhang H, Li J and Sidell N (2018). Oral and intrauterine progestogens for atypical endometrial hyperplasia. *Cochrane Database Syst Rev* 12(12):Cd009458.  12 Leitao MM, Jr., Kehoe S, Barakat RR, Alektiar K, Gattoc LP, Rabbitt C, Chi DS, Soslow RA and Abu-Rustum NR (2009). Comparison of D&C and office endometrial biopsy accuracy in patients with FIGO grade 1 endometrial adenocarcinoma. *Gynecol Oncol* 113(1):105-108.  13 Visser NCM, Reijnen C, Massuger L, Nagtegaal ID, Bulten J and Pijnenborg JMA (2017). Accuracy of Endometrial Sampling in Endometrial Carcinoma: A Systematic Review and Meta-analysis. *Obstet Gynecol* 130(4):803-813.  14 Gatius S, Cuevas D, Fernández C, Roman-Canal B, Adamoli V, Piulats JM, Eritja N, Martin-Satue M, Moreno-Bueno G and Matias-Guiu X (2018). Tumor heterogeneity in endometrial carcinoma: practical consequences. *Pathobiology* 85(1-2):35-40. |  |
| Core and Non-core | MYOMETRIAL INVASION | * Not identified * <50% o ≥50%   ↓ ↓  Pattern of myometrial invasion, *specify* \_\_\_\_\_\_\_  Absolute percentage of myometrial wall thickness invaded by carcinoma \_\_\_%  Distance of myoinvasive tumour  to serosa \_\_\_mm | The extent of myometrial invasion has long been recognised to be an important risk factor for regional lymph node metastasis, and in some studies, for overall survival in low stage endometrioid cancer patients.[1](#_ENREF_1) Accordingly, the extent of myometrial invasion is a central component of most contemporary systems for prognostication, staging, intra- and post-operative risk stratification, and decision-making models for adjuvant therapy.[2-5](#_ENREF_2)  Various methods of determining the extent of myometrial invasion have previously been evaluated. These have included the absolute depth of invasion (DOI) from the endomyometrial junction to the deepest focus of invasive carcinoma, the tumour free distance (TFD) to serosa, and the percentage of myometrium involved, expressed either as the percentage of the overall myometrial thickness that is infiltrated by carcinoma, or as one of three categories: none, <50%, or ≥50%.[6-16](#_ENREF_6)  In the 2023 FIGO staging system, myometrial involvement is important in determining Stage I and II tumours.[5](#_ENREF_5) For cancer reporting, the absence or presence and depth of myometrial invasion should be recorded as none, <50%, or ≥50%; this is a core element. In addition, the absolute percentage of myometrial wall thickness that is invaded by carcinoma can be recorded as a non-core element.  Depth of invasion (DOI) as an individual variable has received less investigation. Nevertheless, higher DOI has been associated with an increased risk of lymphovascular invasion (LVI), lymph node involvement, high stage, recurrence and death of disease in some studies but not others. [1](#_ENREF_1)  Tumour free distance (TFD) is the distance between the deepest point of myometrial invasion of the cancer and the nearest serosal surface.[17](#_ENREF_17) TFD theoretically eliminates some of the difficulties that are inherent in determining the depth of myometrial invasion, and is reportedly more reproducibly diagnosed by pathologists.[18](#_ENREF_18) However, much like DOI, the prognostic significance of TFD is unclear, since the reported findings have been conflicting.[13-16](#_ENREF_13) Both DOI and TFD are non-core elements. Additional studies are needed to clarify the prognostic roles of DOI and TFD.  Assessment of tumour invasion from adenomyosis is a controversial issue without strong scientific evidence. ISGyP guidelines state that “it is preferable to use the standard method for determining DOI, based on the location of the deepest focus of invasive carcinoma in relation to the total myometrial thickness in this area, irrespective of its relationship to adenomyosis.”[19](#_ENREF_19) Thus, a tumour in which the only invasion arises from adenomyotic foci in the outer half of the myometrium, should be regarded as involving the outer half of the myometrium and accompanied by a comment that the clinical significance is unknown, and that this may be an overestimate of true DOI.[5](#_ENREF_5),[19](#_ENREF_19),[20](#_ENREF_20)  Several patterns of myometrial invasion are recognised, and more than one pattern may be present within the same case.[21-24](#_ENREF_21) The pattern of myometrial invasion may be documented in the pathology report to facilitate future study, but it is a non-core item.  In most cases, determining the depth of myometrial invasion does not pose a challenge. However, a variety of circumstances may be encountered that may potentially render making this determination problematic.[25](#_ENREF_25) The ICCR Endometrial Cancer Dataset Authoring Committee endorses the ISGyP recommendations for handling these diagnostic scenarios as summarised below:[19](#_ENREF_19)   1. Exophytic tumours and endometrial polyps: Exophytic carcinomas not uncommonly contain bundles of smooth muscle within the stroma that should not be mistaken for true myometrium for the purposes of measuring the depth of myometrial invasion. Tumour thickness, which encompasses the exophytic component of a myoinvasive tumour, is not synonymous with the depth of myometrial invasion, where measurement begins at the endomyometrial junction. The location of the true endomyometrial junction may be inferred by comparing the area in question with an adjacent section that is uninvolved by myoinvasive carcinoma. For tumours that infiltrate an endometrial polyp, the same approaches are applicable. In endometrial carcinomas in general, every attempt should be made to submit at least one section that depicts any exophytic component, the most myoinvasive component, and an adjacent non-involved endomyometrial junction. 2. Uterine cornu and lower uterine segment: Given that the uterine wall thickness is thinnest at the cornu, the ISGyP recommendations are that the depth of myometrial invasion should not be measured at this focus, unless the tumour is entirely localised to the cornu, and/or extends to the serosa at that point. In contrast, for tumours whose maximal depth of myometrial invasion is in the lower uterine segment, measurements should be taken as they would be at other non-cornual areas of the uterine corpus. 3. Leiomyoma: For tumours that infiltrate a leiomyoma, measurements should be taken as if the leiomyoma represents non-leiomyomatous myometrium. Specifically, the thickness of the myometrial wall at the focus of myoinvasion should include the thickness of the leiomyoma, and the measurements of the depth of myometrial invasion should include the portion of the tumour that is invasive of the leiomyoma.  References 1 Wang J, Xu P, Yang X, Yu Q, Xu X, Zou G and Zhang X (2021). Association of Myometrial Invasion With Lymphovascular Space Invasion, Lymph Node Metastasis, Recurrence, and Overall Survival in Endometrial Cancer: A Meta-Analysis of 79 Studies With 68,870 Patients. *Front Oncol* 11:762329.  2 Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, Marth C, Nout R, Querleu D, Mirza MR and Sessa C (2016). ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. *Ann Oncol* 27(1):16-41.  3 Koh WJ, Abu-Rustum NR, Bean S, Bradley K, Campos SM, Cho KR, Chon HS, Chu C, Cohn D, Crispens MA, Damast S, Dorigo O, Eifel PJ, Fisher CM, Frederick P, Gaffney DK, George S, Han E, Higgins S, Huh WK, Lurain JR, 3rd, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Fader AN, Remmenga SW, Reynolds RK, Tillmanns T, Ueda S, Wyse E, Yashar CM, McMillian NR and Scavone JL (2018). Uterine Neoplasms, Version 1.2018, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 16(2):170-199.  4 FIGO Committee on Gynecological Cancer (2009). Revised FIGO staging for carcinoma of the vulva, cervix and endometrium. *Int. J. Gynecol. Obstet.* 105:103-104.  5 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  6 Lutz MH, Underwood PB, Jr., Kreutner A, Jr. and Miller MC (1978). Endometrial carcinoma: a new method of classification of therapeutic and prognostic significance. *Gynecol Oncol* 6(1):83-94.  7 Templeton AC (1982). Reporting of myometrial invasion by endometrial cancer. *Histopathology* 6(6):733-737.  8 Kaku T, Tsuruchi N, Tsukamoto N, Hirakawa T, Kamura T and Nakano H (1994). Reassessment of myometrial invasion in endometrial carcinoma. *Obstet Gynecol* 84(6):979-982.  9 Lindauer J, Fowler JM, Manolitsas TP, Copeland LJ, Eaton LA, Ramirez NC and Cohn DE (2003). Is there a prognostic difference between depth of myometrial invasion and the tumor-free distance from the uterine serosa in endometrial cancer? *Gynecol Oncol* 91(3):547-551.  10 Schwab KV, O'Malley DM, Fowler JM, Copeland LJ and Cohn DE (2009). Prospective evaluation of prognostic significance of the tumor-free distance from uterine serosa in surgically staged endometrial adenocarcinoma. *Gynecol Oncol* 112(1):146-149.  11 Kondalsamy-Chennakesavan S, van Vugt S, Sanday K, Nicklin J, Land R, Perrin L, Crandon A and Obermair A (2010). Evaluation of tumor-free distance and depth of myometrial invasion as prognostic factors for lymph node metastases in endometrial cancer. *Int J Gynecol Cancer* 20(7):1217-1221.  12 Chattopadhyay S, Galaal KA, Patel A, Fisher A, Nayar A, Cross P and Naik R (2012). Tumour-free distance from serosa is a better prognostic indicator than depth of invasion and percentage myometrial invasion in endometrioid endometrial cancer. *Bjog* 119(10):1162-1170.  13 Geels YP, Pijnenborg JM, van den Berg-van Erp SH, Snijders MP, Bulten J and Massuger LF (2013). Absolute depth of myometrial invasion in endometrial cancer is superior to the currently used cut-off value of 50%. *Gynecol Oncol* 129(2):285-291.  14 Ozbilen O, Sakarya DK, Bezircioglu I, Kasap B, Yetimalar H and Yigit S (2015). Comparison of myometrial invasion and tumor free distance from uterine serosa in endometrial cancer. *Asian Pac J Cancer Prev* 16(2):519-522.  15 Doghri R, Chaabouni S, Houcine Y, Charfi L, Boujelbene N, Driss M and Mrad K (2018). Evaluation of tumor-free distance and depth of myometrial invasion as prognostic factors in endometrial cancer. *Mol Clin Oncol* 9(1):87-91.  16 Oge T, Comert DK, Cakmak Y and Arık D (2020). Is tumor-free distance an independent prognostic factor for early-stage endometrioid endometrial cancer? *J Oncol* 2020:1-5.  17 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  18 van der Putten LJ, van de Vijver K, Bartosch C, Davidson B, Gatius S, Matias-Guiu X, McCluggage WG, Toledo G, van der Wurff AA, Pijnenborg JM, Massuger LF and Bulten J (2017). Reproducibility of measurement of myometrial invasion in endometrial carcinoma. *Virchows Arch* 470(1):63-68.  19 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113.  20 Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X (2021). ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch*:153-190.  21 Park JY, Hong DG, Chong GO and Park JY (2019). Tumor budding is a valuable diagnostic parameter in prediction of disease progression of endometrial endometrioid carcinoma. *Pathol Oncol Res* 25(2):723-730.  22 Quick CM, May T, Horowitz NS and Nucci MR (2012). Low-grade, low-stage endometrioid endometrial adenocarcinoma: a clinicopathologic analysis of 324 cases focusing on frequency and pattern of myoinvasion. *Int J Gynecol Pathol* 31(4):337-343.  23 Murray SK, Young RH and Scully RE (2003). Unusual epithelial and stromal changes in myoinvasive endometrioid adenocarcinoma: a study of their frequency, associated diagnostic problems, and prognostic significance. *Int J Gynecol Pathol* 22(4):324-333.  24 Longacre TA and Hendrickson MR (1999). Diffusely infiltrative endometrial adenocarcinoma: an adenoma malignum pattern of myoinvasion. *Am J Surg Pathol* 23(1):69-78.  25 Ali A, Black D and Soslow RA (2007). Difficulties in assessing the depth of myometrial invasion in endometrial carcinoma. *Int J Gynecol Pathol* 26(2):115-123. |  |
| Core | LYMPHOVASCULAR INVASION | * Indeterminate * Not identified * Present   **Extent of lymphovascular invasion**   * Focal * Extensive/Substantial | Lymphovascular invasion (LVI) is an important prognostic indicator in endometrial carcinoma and documenting the presence and extent of LVI or documenting if LVI is not identified is a core element.  Lymphovascular invasion (LVI) is diagnosed when there is a tumour embolus within an endothelial-lined channel.[1-4](#_ENREF_1) There are several morphological features that may simulate LVI: these include spreading artefact, artefactual pseudoinvasion secondary to tumour disruption; microcystic elongated and fragmented (MELF) pattern myometrial invasion; and retraction artefacts.[1](#_ENREF_1),[2](#_ENREF_2)  Artefactual pseudoinvasion secondary to tumour disruption is predominantly encountered in the setting of laparoscopic and/or robotic surgery.[5](#_ENREF_5) Clues to the presence of this type of artefact include fragments of tumour and, sometimes, normal constituents around the cut surfaces of the section, in tissue ‘cracks’, in large, medium-sized and small vessels, both adjacent to the invasive front and in distant locations.[1](#_ENREF_1),[2](#_ENREF_2) Often the amount of tumour within vessel appears disproportionate, for example in a tumour which is low grade and low stage. Adequate fixation before prosection, generally lessens the degree of artefact.  Microcystic elongated and fragmented (MELF) myometrial invasion may also mimic LVI. Adding to the complexity is that MELF myometrial invasion is also associated with LVI. The distinction between the two can usually be resolved by knowing about this type of artefact and careful examination to differentiate between endothelium on one hand (LVI) and tumour cells floating in a microcyst lined by flattened and attenuated epithelium (MELF myometrial invasion) on the other.  Immunohistochemical staining with endothelial markers can sometimes be used to confirm a suspicion of LVI, especially when there is extensive retraction artefact, although the literature is inconsistent on the added value of immunohistochemistry (IHC) after haematoxylin and eosin (H&E) evaluation.[4](#_ENREF_4)  The absence of LVI is defined as no tumour cells within vessels.[6](#_ENREF_6) There is controversial data regarding the cut off for ‘substantial (extensive)’ LVI. ‘Substantial LVI’ is defined as the presence of three or more vessels containing tumour, according to ISGyP recommendations,[6](#_ENREF_6) but five or more vessels in the 2020 WHO Classification[7](#_ENREF_7), the FIGO 2023 staging system, and in the 2020 ESGO-ESTRO-ESP guidelines.[8](#_ENREF_8) None of these recommendations explicitly state whether assessment of the number of involved vessels should be on the slide containing the greatest number of involved vessels or whether the number of involved vessels on all the slides should be added together. The WHO classification is expected to be updated in 2025 and it is hoped that this issue will be clarified.  For staging purposes, the 2023 FIGO staging system includes substantial LVI as an important parameter for non-aggressive histological types (low grade endometrioid carcinoma). By following the WHO rule of five or more vessels, cases with substantial LVI are categorised as Stage IIB tumours.[9](#_ENREF_9) However, in the FIGO 2023 system, and as previously stated, it is not clear as to whether the number of vessels is to be counted in a single section or across all the sections.  Some data indicate that ’substantial’ LVI is associated with adverse outcomes when compared to carcinomas with ‘focal’ or ‘no’ LVI.[10-12](#_ENREF_10) Recording the degree of LVI (focal or substantial/extensive) is regarded as a core element.  Lymphovascular invasion (LVI) should not be included in the assessment of depth of myometrial invasion.[4](#_ENREF_4) LVI features in many (but not all) multivariate clinical outcomes analyses and is associated with lymph node metastasis, local and distant recurrence and poor survival.[10](#_ENREF_10),[11](#_ENREF_11),[13](#_ENREF_13) Thus, the presence of substantial LVI may highlight the need for adjuvant treatment, such as recommended in the 2020 ESGO-ESTRO-ESP guidelines.[8](#_ENREF_8)  A value of ‘indeterminate’ should be used sparingly and only in cases where there is genuine doubt as to whether LVI is present or not. In such cases, it may be useful to report the reason for a response of ‘indeterminate’. References 1 McCluggage WG (2018). Pathologic staging of endometrial carcinomas: selected areas of difficulty. *Adv Anat Pathol* 25(2):71-84.  2 Soslow RA (2016). Practical issues related to uterine pathology: staging, frozen section, artifacts, and Lynch syndrome. *Mod Pathol* 29 Suppl 1(Suppl 1):S59-77.  3 Peters EEM, Bartosch C, McCluggage WG, Genestie C, Lax SF, Nout R, Oosting J, Singh N, Smit H, Smit V, Van de Vijver KK and Bosse T (2019). Reproducibility of lymphovascular space invasion (LVSI) assessment in endometrial cancer. *Histopathology* 75(1):128-136.  4 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113.  5 Delair D, Soslow RA, Gardner GJ, Barakat RR and Leitao MM, Jr. (2013). Tumoral displacement into fallopian tubes in patients undergoing robotically assisted hysterectomy for newly diagnosed endometrial cancer. *Int J Gynecol Pathol* 32(2):188-192.  6 Soslow RA, Tornos C, Park KJ, Malpica A, Matias-Guiu X, Oliva E, Parkash V, Carlson J, McCluggage WG and Gilks CB (2019). Endometrial carcinoma diagnosis: use of FIGO grading and genomic subcategories in clinical practice: recommendations of the International Society of Gynecological Pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S64-s74.  7 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  8 Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X (2021). ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch*:153-190.  9 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  10 Pifer PM, Bhargava R, Patel AK, Ling DC, Vargo JA, Orr BC, Sukumvanich P, Courtney-Brooks MB, Boisen MM, Berger JL, Taylor S, Olawaiye AB, Comerci JT, Lesnock JL, Edwards RP and Beriwal S (2020). Is the risk of substantial LVSI in stage I endometrial cancer similar to PORTEC in the North American population? - A single-institution study. *Gynecol Oncol* 159(1):23-29.  11 Bosse T, Peters EE, Creutzberg CL, Jürgenliemk-Schulz IM, Jobsen JJ, Mens JW, Lutgens LC, van der Steen-Banasik EM, Smit VT and Nout RA (2015). Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer--A pooled analysis of PORTEC 1 and 2 trials. *Eur J Cancer* 51(13):1742-1750.  12 Barnes EA, Martell K, Parra-Herran C, Taggar AS, Donovan E and Leung E (2021). Substantial lymphovascular space invasion predicts worse outcomes in early-stage endometrioid endometrial cancer. *Brachytherapy*:527-535.  13 Stålberg K, Bjurberg M, Borgfeldt C, Carlson J, Dahm-Kähler P, Flöter-Rådestad A, Hellman K, Hjerpe E, Holmberg E, Kjølhede P, Marcickiewicz J, Rosenberg P, Tholander B, Åvall-Lundqvist E and Högberg T (2019). Lymphovascular space invasion as a predictive factor for lymph node metastases and survival in endometrioid endometrial cancer - a Swedish Gynecologic Cancer Group (SweGCG) study. *Acta Oncol* 58(11):1628-1633. |  |
| Non-core | CERVICAL SURFACE OR CRYPT | * Not involved * Involved | Cervical surface mucosal or crypt epithelial involvement (without cervical stromal invasion) does not affect tumour stage in the 2009 or 2023 FIGO staging system and is regarded as a non-core element.[1](#_ENREF_1),[2](#_ENREF_2) However, it is a potential adverse risk factor for locoregional recurrence and may be taken into consideration for adjuvant radiotherapy.[3](#_ENREF_3) References 1 Pecorelli S (2009). Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet* 105(2):103-104.  2 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  3 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113. |  |
| Non-core | LOWER UTERINE SEGMENT | * Not involved * Involved | Anatomically, the lower uterine segment begins where the body funnels towards the cervix and ends at the internal os. As stated in **TUMOUR SITE**, lower uterine segment involvement is a potential adverse risk factor for locoregional and distant recurrence and may be taken into consideration for adjuvant radiotherapy, although it does not affect the FIGO tumour stage.[1](#_ENREF_1) It is regarded as a non-core element for reporting.  As tumours arising in the lower uterine segment also show frequent association with Lynch syndrome, documentation of origin in the lower uterine segment has important risk implications.[2](#_ENREF_2) References 1 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113.  2 Zhao S, Chen L, Zang Y, Liu W, Liu S, Teng F, Xue F and Wang Y (2022). Endometrial cancer in Lynch syndrome. *Int J Cancer* 150(1):7-17. |  |
| Core and Non-core | CERVICAL STROMA | * Indeterminate * Not involved * Involved   **Depth of cervical stromal**  **Invasion \_\_\_mm**  **Percentage of cervical**  **stromal invasion \_\_\_%** | Cervical stromal invasion indicates Stage IIA endometrial carcinoma according to the FIGO 2023 staging system for non-aggressive histological types (low grade endometrioid carcinomas) and is a core element for reporting.[1](#_ENREF_1)  Cervical stromal invasion is associated with a significant risk of recurrence and is a predictor of pelvic lymph node metastases.[2-4](#_ENREF_2) However, the role of cervical stromal involvement as an independent prognosticator per se has been questioned.[5](#_ENREF_5) Cervical stromal invasion often occurs in the presence of other adverse features such as high histologic grade, deep myometrial invasion and LVI. In one study, the presence of these factors conferred worse disease-free survival in patients with Stage II endometrial cancer.[6](#_ENREF_6)  Determination of cervical stromal invasion can be complicated by difficulties in demarcating the upper cervix from the lower uterine segment. By convention, the boundary is defined by the most proximal mucinous gland/crypt.[7](#_ENREF_7),[8](#_ENREF_8) Consequently, any invasion identified at the level of, or distal to, a benign mucinous gland should be considered cervical stromal invasion.  Significant interobserver variation in the assessment of cervical involvement by endometrial carcinoma has been documented. A study by McCluggage et al (2011) demonstrated fair to good agreement among six experienced gynaecologic pathologists in this exercise.[7](#_ENREF_7) While, a study by Zaino et al (2013) showed high agreement in determining whether the cervix is involved or not, but only slight agreement in the distinction between glandular and stromal involvement.[9](#_ENREF_9) Problematic scenarios include: determination of the junction between the lower uterine segment and upper endocervix; the distinction between ‘floaters’ and true cervical glandular involvement; the distinction between cervical glandular involvement and stromal involvement; and the distinction between cervical glandular involvement and reactive non-neoplastic glandular lesions such as tuboendometrial metaplasia or changes secondary to a recent biopsy.[7](#_ENREF_7)  A value of ‘indeterminate’ should be used sparingly and only in cases where there is genuine doubt; in such cases, it may be useful to state the reason for a response of indeterminate in the report. References 1 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  2 Fanning J, Alvarez PM, Tsukada Y and Piver MS (1991). Prognostic significance of the extent of cervical involvement by endometrial cancer. *Gynecol Oncol* 40(1):46-47.  3 Mariani A, Webb MJ, Keeney GL and Podratz KC (2001). Routes of lymphatic spread: a study of 112 consecutive patients with endometrial cancer. *Gynecol Oncol* 81(1):100-104.  4 Zhu J, Cao L, Wen H, Bi R, Wu X and Ke G (2020). The clinical and prognostic implication of deep stromal invasion in cervical cancer patients undergoing radical hysterectomy. *J Cancer* 11(24):7368-7377.  5 Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, Marth C, Nout R, Querleu D, Mirza MR and Sessa C (2016). ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. *Ann Oncol* 27(1):16-41.  6 Pitson G, Colgan T, Levin W, Lockwood G, Manchul L, Milosevic M, Murphy J and Fyles A (2002). Stage II endometrial carcinoma: prognostic factors and risk classification in 170 patients. *Int J Radiat Oncol Biol Phys* 53(4):862-867.  7 McCluggage WG, Hirschowitz L, Wilson GE, Oliva E, Soslow RA and Zaino RJ (2011). Significant variation in the assessment of cervical involvement in endometrial carcinoma: an interobserver variation study. *Am J Surg Pathol* 35(2):289-294.  8 McCluggage WG (2018). Pathologic staging of endometrial carcinomas: selected areas of difficulty. *Adv Anat Pathol* 25(2):71-84.  9 Zaino RJ, Abendroth C, Yemelyanova A, Oliva E, Lim D, Soslow R, DeLair D, Hagemann IS, Montone K and Zhu J (2013). Endocervical involvement in endometrial adenocarcinoma is not prognostically significant and the pathologic assessment of the pattern of involvement is not reproducible. *Gynecol Oncol* 128(1):83-87.  **Depth of cervical stromal invasion**  The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology Uterine Neoplasms lists deep cervical stromal invasion as an adverse risk factor in patients with Stage II endometrial carcinoma.[1](#_ENREF_1) Absolute depth of cervical stromal invasion and percentage of cervical stromal invasion are non-core elements. Reference 1 Abu-Rustum N, Yashar C, Bradley K, Campos SM, Chon HS, Chu C, Clinton L, Cohn D, Crispens MA, Damast S, Diver E, Fisher C, Frederick P, Gaffney DK, George S, Giuntoli R, Han E, Huh WK, Lea J, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Nickles Fader A, Remmenga SW, Reynolds RK, Salani R, Sisodi R, Soliman P, Tanner E, Tillmanns T, Ueda S, Urban R, Wyse E (2020). *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Uterine Neoplasms*. Available from: https://www.nccn.org/professionals/physician\_gls/pdf/uterine.pdf (Accessed 10th July 2024). |  |
| Core | PARAMETRIAa | * Not involved * Involved | Most hysterectomies for endometrial cancer are simple hysterectomies and do not have parametrial resections, although occasionally parametrial resection is undertaken when cervical stromal invasion is suspected preoperatively (radical or modified radical hysterectomy).  Endometrial carcinomas with parametrial invasion are staged as FIGO 2023 Stage IIIB1.[1](#_ENREF_1) Although not an independent prognostic indicator, parametrial involvement by direct extension is a poor prognostic factor.[2-4](#_ENREF_2) It is associated not only with cervical stromal invasion but also with outer half myometrial invasion, pelvic and/or paraaortic lymph node metastasis, ovarian metastasis, positive peritoneal cytology and lymphovascular invasion.[2-4](#_ENREF_2) Reporting of the presence or absence of parametrial involvement in hysterectomy specimens containing parametrial tissue is a core element. References 1 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  2 Sato R, Jobo T and Kuramoto H (2003). Parametrial spread is a prognostic factor in endometrial carcinoma. *Eur J Gynaecol Oncol* 24(3-4):241-245.  3 Watanabe Y, Satou T, Nakai H, Etoh T, Dote K, Fujinami N and Hoshiai H (2010). Evaluation of parametrial spread in endometrial carcinoma. *Obstet Gynecol* 116(5):1027-1034.  4 Yura Y, Tauchi K, Koshiyama M, Konishi I, Yura S, Mori T, Matsushita K, Hayashi M and Yoshida M (1996). Parametrial involvement in endometrial carcinomas: its incidence and correlation with other histological parameters. *Gynecol Oncol* 63(1):114-119. | a If submitted. |
| Core | VAGINAa | * Not involved * Involved | In endometrial carcinomas, vaginal involvement may occur in two different scenarios:   * Vaginal involvement at diagnosis (uncommon scenario) * Vaginal recurrence of endometrial carcinoma (common scenario).   Vaginal involvement at the time of diagnosis is uncommon and places the disease in FIGO 2023 Stage IIIB1.[1](#_ENREF_1) Vaginal involvement occurs either via direct extension from the corpus to the cervix and vagina or metastasis through lymphatic pathways. It is essential to report vaginal involvement for staging of disease and prognosis. Vaginal involvement at diagnosis is rare (less than 1% of cases) and it is very unusual that patients present with vaginal extension without lymph node metastasis or spread to other distant sites. The 5-year survival rate for these patients is approximately 25%, with a median survival of 1-2 years.[2](#_ENREF_2)  The vagina represents the most common site of recurrence of endometrial carcinoma.[3](#_ENREF_3),[4](#_ENREF_4) In the majority of cases, recurrence involves the upper vagina, while recurrence in the middle third or distal vagina is less common.[5](#_ENREF_5) In a study by Moschiano et al (2014) there were no disease-related deaths in patients with vaginal recurrence only, suggesting that vaginal recurrence is not a marker of aggressive tumour biology.[5](#_ENREF_5)  **References**  1 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  2 Hirschowitz L, Nucci M and Zaino RJ (2013). Problematic issues in the staging of endometrial, cervical and vulval carcinomas. *Histopathology* 62(1):176-202.  3 Ng TY, Perrin LC, Nicklin JL, Cheuk R and Crandon AJ (2000). Local recurrence in high-risk node-negative stage I endometrial carcinoma treated with postoperative vaginal vault brachytherapy. *Gynecol Oncol* 79(3):490-494.  4 Creutzberg CL, van Putten WL, Koper PC, Lybeert ML, Jobsen JJ, Wárlám-Rodenhuis CC, De Winter KA, Lutgens LC, van den Bergh AC, van de Steen-Banasik E, Beerman H and van Lent M (2000). Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. *Lancet* 355(9213):1404-1411.  5 Moschiano EJ, Barbuto DA, Walsh C, Singh K, Euscher ED, Roma AA, Ali-Fehmi R, Frauenhoffer EE, Montiel DP, Kim I, Djordjevic B, Malpica A, Hong SR and Silva EG (2014). Risk factors for recurrence and prognosis of low-grade endometrial adenocarcinoma; vaginal versus other sites. *Int J Gynecol Pathol* 33(3):268-273. | a If submitted. |
| Core | OMENTUMa | * Not involved * Involved | Omentectomy is part of the surgical staging procedure for some high grade endometrial cancers. Omental spread by endometrial carcinoma is associated with decreased overall survival.[1](#_ENREF_1) Omental metastases are associated with other adverse prognostic features such as high tumour grade, serous histology, deep myometrial invasion, LVI and adnexal involvement.[1](#_ENREF_1)  Spread of endometrial carcinoma to the omentum, either supracolic or infracolic, is regarded as a distant metastasis and places the disease in FIGO Stage IVB (pM1).[2](#_ENREF_2),[3](#_ENREF_3) References 1 Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann J, Bosse T, Chargari C, Fagotti A, Fotopoulou C, Gonzalez Martin A, Lax S, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell D, Querleu D, Raspollini MR, Sehouli J, Sturdza A, Taylor A, Westermann A, Wimberger P, Colombo N, Planchamp F and Creutzberg CL (2021). ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer* 31(1):12-39.  2 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1:S93-s113.  3 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394. | a If submitted. |
| Core and Non-core | PERITONEAL BIOPSIESa | * Not involved * Involved   **Site(s) of involvement**  (select all that apply)   * Pelvic * Abdominal   **Specify site \_\_\_\_\_\_\_\_\_\_\_** | Reporting of peritoneal involvement is core when biopsy specimens are submitted as part of staging of endometrial carcinoma. The site of the peritoneal biopsies and the presence or absence of tumour involvement should be documented. Taking of blind peritoneal biopsies is routine in some institutions.  It is important to distinguish between abdominal and pelvic peritoneal involvement since this denotes a different FIGO Stage (IIIB2 for pelvic peritoneal involvement and IVB for abdominal peritoneal involvement).[1](#_ENREF_1) Reference 1 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394. | a If submitted. |
| Non-core | PERITONEAL CYTOLOGY | * Positive * Negative * Atypical/suspicious | Positive peritoneal cytology is no longer part of the FIGO staging system, but the results of the peritoneal cytology may provide risk-stratification. As a consequence, consideration for adjuvant therapy may be discussed in multidisciplinary tumour board meeting. Positive peritoneal cytology has been shown to be an independent prognostic factor for serous carcinoma regardless of stage and it is important to report for other carcinomas.[1-4](#_ENREF_1)  There is lack of consensus in the literature regarding the prognostic significance of positive peritoneal washings in the absence of other evidence of extrauterine spread.[5](#_ENREF_5) It is also unclear whether the method of hysteroscopy or operative procedure may influence the likelihood of positive peritoneal washings.[5](#_ENREF_5) References 1 Abu-Rustum N, Yashar C, Bradley K, Campos SM, Chon HS, Chu C, Clinton L, Cohn D, Crispens MA, Damast S, Diver E, Fisher C, Frederick P, Gaffney DK, George S, Giuntoli R, Han E, Huh WK, Lea J, Mariani A, Mutch D, Nagel C, Nekhlyudov L, Nickles Fader A, Remmenga SW, Reynolds RK, Salani R, Sisodi R, Soliman P, Tanner E, Tillmanns T, Ueda S, Urban R, Wyse E (2020). *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Uterine Neoplasms*. Available from: https://www.nccn.org/professionals/physician\_gls/pdf/uterine.pdf (Accessed 10th July 2024).  2 Han KH, Park NH, Kim HS, Chung HH, Kim JW and Song YS (2014). Peritoneal cytology: a risk factor of recurrence for non-endometrioid endometrial cancer. *Gynecol Oncol* 134(2):293-296.  3 Hanley KZ, Fadare O, Fisher KE, Atkins KA and Mosunjac MB (2016). Clinical significance of positive pelvic washings in uterine papillary serous carcinoma confined to an endometrial polyp. *Int J Gynecol Pathol* 35(3):249-255.  4 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  5 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113. |  |
| Core | UTERINE SEROSA | * Not involved * Involved | Documentation of the presence or absence of serosal involvement is a core element. According to ESGO-ESTRO-ESP[1](#_ENREF_1) and ISGyP guidelines,[2](#_ENREF_2) tumour infiltrating the full myometrial thickness and reaching submesothelial fibroconnective tissue or the mesothelial layer should be reported as serosal involvement. This criteria has been endorsed in the 2023 FIGO staging system.[3](#_ENREF_3)  Involvement of the serosa (FIGO Stage IIIA2) carries a higher risk of locoregional recurrence than does adnexal involvement ( FIGO Stage IIIA1).[3](#_ENREF_3) References 1 Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X (2021). ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch*:153-190.  2 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113.  3 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394. |  |
| Core | ADNEXAa | * Not involved * Involved   **Site(s) of involvement**  (select all that apply)   * Ovary(ies) * Left * Right * Laterality not specified * Fallopian tube(s) * Left * Right * Laterality not specified   Describe involvement (e.g.,  mucosal) \_\_\_\_\_\_\_\_\_\_\_\_\_\_ | The presence or absence of adnexal involvement is a core element. Adnexal involvement has an impact on overall survival rate.[1-3](#_ENREF_1) The involved adnexa should be documented, particularly specifying which ovary and which fallopian tube is involved as well as the location of tubal involvement.  It is sometimes difficult to distinguish between endometrial carcinoma with ovarian metastasis and synchronous primary tumours of the endometrium and the ovary.[4](#_ENREF_4) For high grade tumours, including serous carcinoma, ovarian involvement is almost always categorised as metastatic. However, there is always the possibility of coincidental independent primary serous carcinomas in the endometrium and the tube/ovary, although this situation is exceedingly unusual. Furthermore, metastasis from the adnexa to the endometrium rarely occurs. 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.[5](#_ENREF_5)  Five percent of endometrioid carcinomas of the endometrium are associated with an endometrioid carcinoma of the ovary. Cases with simultaneous involvement of the endometrium and ovary by low grade endometrioid carcinomas are often associated with indolent outcome.  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.[6-9](#_ENREF_6) However, this clonal relationship should not be equated with the clinical outcomes expected of metastatic endometrial carcinoma.  In the 2020 WHO Classification,[10](#_ENREF_10) it is suggested that patients with synchronous endometrioid carcinomas in the endometrium and ovary be managed conservatively (as if they were two independent primaries) when the following criteria are met: 1) low grade endometrioid morphology at both sites, 2) no more than superficial myometrial invasion, 3) absence of LVI, and 4) absence of additional metastases.[10](#_ENREF_10),[11](#_ENREF_11)  This is an evolving field, and it is not clear at this time why a subset of metastatic low grade endometrioid carcinomas involving the endometrium and ovary are associated with good prognosis. Potential explanations are: 1) that clonal ovarian metastasis occurs early in the process of endometrial tumour development, thereby allowing tumours in each site to acquire additional, sometimes distinct molecular abnormalities; and 2) tumour cells follow retrograde transtubal spread, with ovarian implantation, rather than destructive invasion. It is recommended to discuss these cases in multidisciplinary tumour board meetings.  The 2023 FIGO staging system endorses criteria proposed by the WHO and ESGO-ESTRO-ESP for endometrial carcinomas with ovarian involvement.[3](#_ENREF_3) The system establishes the category of Stage IA3 when the following criteria are met in a low grade endometrioid carcinoma: 1) no more than superficial myometrial invasion is present (<50%), 2) absence of substantial LVI, 3) absence of additional metastases, and 4) the ovarian tumour is unilateral, limited to the ovary, without capsule invasion/breach. Cases which do not fulfill these criteria should be categorised as Stage IIIA1.  Although true independent simultaneous endometrial and ovarian carcinomas do exist, they are relatively infrequent, and may occur in the setting of Lynch syndrome.[9](#_ENREF_9) In this scenario, these may represent synchronous endometrioid carcinomas of the endometrium and ovary or an endometrioid carcinoma of the endometrium may coexist with ovarian clear cell carcinoma.[12](#_ENREF_12)  It is important to remember that the presence of LVI in ovarian hilar or parenchymal vessels or tubal vessels without stromal invasion does not affect stage.  Tumour involvement of the fallopian tube should also be recorded.[13](#_ENREF_13) It is important to stress that the presence of detached aggregates of tumour cells in the tubal lumen, without involvement of the wall, should not be considered tubal involvement,[14](#_ENREF_14) since this is thought to be an artefact related to the type of surgery performed and/or specimen fixation. However, the presence of serous carcinoma cells in the lumen of the fallopian tube may be associated with peritoneal metastasis.[15](#_ENREF_15) Floating tumour cells in the fallopian tube lumen should not lead to upstaging of the tumour, although this should prompt a careful review of the peritoneal/pelvic washings if performed.  Tubal involvement by endometrial carcinoma in the form of intramucosal spread has controversial prognostic significance. Tubal tumour is generally considered metastatic from the endometrium, rather than a coincidental low risk ‘synchronous’ endometrioid carcinoma of the fallopian tube. The approach to distinguishing between low- and high-risk carcinomas could theoretically follow the same paradigm used for tumours involving endometrium and ovary. The prognostic significance of tubal mucosal involvement by endometrioid carcinoma is unknown.[15](#_ENREF_15)  Tubal involvement by serous carcinoma, with or without stromal invasion is usually a manifestation of metastatic serous carcinoma. Studies have shown that endometrial serous carcinoma frequently extends to the fallopian tube, giving rise to a lesion that may be indistinguishable from serous tubal intraepithelial carcinoma (STIC); this is referred to as a STIC-like lesion.[16](#_ENREF_16) There is also the possibility that a *bona fide* STIC can be the nidus from which serous carcinoma cells detach and implant in the endometrium, simulating a primary endometrial serous carcinoma. There is also the possibility of the coincidental presence of an endometrial serous carcinoma and a primary STIC, but in these cases ancillary techniques are required. Assessment of WT1 expression may be helpful in these scenarios. WT1 immunoreactivity is negative in the majority of primary endometrial serous carcinomas, although a significant proportion are positive, but positive in almost all serous carcinomas arising from the ovary or the fallopian tube.[17](#_ENREF_17)  Endometrial carcinomas metastatic to the fallopian tube wall or its serosa should be interpreted as metastatic unless there is evidence of an origin in endometriosis. References 1 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th Edition*, Springer, New York.  2 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *UICC TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.  3 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  4 Heitz F, Amant F, Fotopoulou C, Battista MJ, Wimberger P, Traut A, Fisseler-Eckhoff A, Harter P, Vandenput I, Sehouli J, Schmidt M, Kimmig R, du Bois R and du Bois A (2014). Synchronous ovarian and endometrial cancer--an international multicenter case-control study. *Int J Gynecol Cancer* 24(1):54-60.  5 Malpica A, Euscher ED, Hecht JL, Ali-Fehmi R, Quick CM, Singh N, Horn LC, Alvarado-Cabrero I, Matias-Guiu X, Hirschowitz L, Duggan M, Ordi J, Parkash V, Mikami Y, Ruhul Quddus M, Zaino R, Staebler A, Zaloudek C, McCluggage WG and Oliva E (2019). Endometrial carcinoma, grossing and processing issues: recommendations of the international society of gynecologic pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S9-s24.  6 Reijnen C, Küsters-Vandevelde HVN, Ligtenberg MJL, Bulten J, Oosterwegel M, Snijders M, Sweegers S, de Hullu JA, Vos MC, van der Wurff AAM, van Altena AM, Eijkelenboom A and Pijnenborg JMA (2020). Molecular profiling identifies synchronous endometrial and ovarian cancers as metastatic endometrial cancer with favorable clinical outcome. *Int J Cancer* 147(2):478-489.  7 Chao A, Wu RC, Jung SM, Lee YS, Chen SJ, Lu YL, Tsai CL, Lin CY, Tang YH, Chen MY, Huang HJ, Chou HH, Huang KG, Chang TC, Wang TH and Lai CH (2016). Implication of genomic characterization in synchronous endometrial and ovarian cancers of endometrioid histology. *Gynecol Oncol* 143(1):60-67.  8 Anglesio MS, Wang YK, Maassen M, Horlings HM, Bashashati A, Senz J, Mackenzie R, Grewal DS, Li-Chang H, Karnezis AN, Sheffield BS, McConechy MK, Kommoss F, Taran FA, Staebler A, Shah SP, Wallwiener D, Brucker S, Gilks CB, Kommoss S and Huntsman DG (2016). Synchronous endometrial and ovarian carcinomas: evidence of clonality. *J Natl Cancer Inst* 108(6):djv428.  9 Schultheis AM, Ng CK, De Filippo MR, Piscuoglio S, Macedo GS, Gatius S, Perez Mies B, Soslow RA, Lim RS, Viale A, Huberman KH, Palacios JC, Reis-Filho JS, Matias-Guiu X and Weigelt B (2016). Massively parallel sequencing-based clonality analysis of synchronous endometrioid endometrial and ovarian carcinomas. *J Natl Cancer Inst* 108(6):djv427.  10 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  11 Turashvili G, Gómez-Hidalgo NR, Flynn J, Gonen M, Leitao MM, Jr., Soslow RA and Murali R (2019). Risk-based stratification of carcinomas concurrently involving the endometrium and ovary. *Gynecol Oncol* 152(1):38-45.  12 Zhou L, Yao L, Dai L, Zhu H, Ye X, Wang S, Cheng H, Ma R, Liu H, Cui H and Chang X (2021). Ovarian endometrioid carcinoma and clear cell carcinoma: A 21-year retrospective study. *J Ovarian Res* 14(1):63.  13 Stewart CJR, Crum CP, McCluggage WG, Park KJ, Rutgers JK, Oliva E, Malpica A, Parkash V, Matias-Guiu X and Ronnett BM (2019). Guidelines to aid in the distinction of endometrial and endocervical carcinomas, and the distinction of independent primary carcinomas of the endometrium and adnexa from metastatic spread between these and other sites. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S75-s92.  14 Delair D, Soslow RA, Gardner GJ, Barakat RR and Leitao MM, Jr. (2013). Tumoral displacement into fallopian tubes in patients undergoing robotically assisted hysterectomy for newly diagnosed endometrial cancer. *Int J Gynecol Pathol* 32(2):188-192.  15 Singh N, Hirschowitz L, Zaino R, Alvarado-Cabrero I, Duggan MA, Ali-Fehmi R, Euscher E, Hecht JL, Horn LC, Ioffe O, Matias-Guiu X, McCluggage WG, Mikami Y, Ordi J, Parkash V, Quddus MR, Quick CM, Staebler A, Zaloudek C, Nucci M, Malpica A and Oliva E (2019). Pathologic prognostic factors in endometrial carcinoma (other than tumor type and grade). *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S93-s113.  16 Kommoss F, Faruqi A, Gilks CB, Lamshang Leen S, Singh N, Wilkinson N and McCluggage WG (2017). Uterine serous carcinomas frequently metastasize to the fallopian tube and can mimic serous tubal intraepithelial carcinoma. *Am J Surg Pathol* 41(2):161-170.  17 Angelico G, Santoro A, Straccia P, Inzani F, Cianfrini F, Spadola S, Arciuolo D, Valente M, D'Alessandris N, Mulè A and Zannoni GF (2020). Diagnostic and prognostic role of WT1 immunohistochemical expression in uterine carcinoma: a systematic review and meta-analysis across all endometrial carcinoma histotypes. *Diagnostics (Basel)* 10(9):637. | a If submitted. |
| Core and Non-core | MARGIN STATUS | **Paracervical soft tissue margin**   * Cannot be assessed * Not involved   Distance of tumour to closest  margin \_\_\_ mm   * Involved   **Ectocervical/vaginal cuff margin**   * Cannot be assessed * Not involved   Distance of tumour to closest  margin \_\_\_ mm   * Involved | It is important to record the status of paracervical soft tissue and ectocervical/vaginal cuff margins, and this is a core reporting element. The term paracervical soft tissue refers to the small part of the parametrium that is included in simple hysterectomy specimens, which is the common surgical procedure for endometrial carcinoma.  Vaginal (direct extension or metastasis) or parametrial involvement by endometrial carcinoma is currently staged as IIIB.[1](#_ENREF_1),[2](#_ENREF_2) Positive margin status has been identified as a risk factor for local recurrence and mortality, and patients with positive margins are more likely to receive a vaginal vault brachytherapy boost.[3](#_ENREF_3),[4](#_ENREF_4) LVI at the cervical/parametrial/vaginal resection margin is not considered a positive margin.  Close cervical/parametrial/vaginal margins may indicate an increased risk of recurrence and may be taken into consideration for adjuvant radiotherapy.[5](#_ENREF_5) However, there are no criteria regarding the distance to margins that would be considered ‘close’. The distance to the margins is a non-core reporting element. When reported, the distance to margins should be stated in mm. References 1 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  2 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th Edition*, Springer, New York.  3 Martell K, Doll C, Barnes EA, Phan T, Leung E and Taggar A (2019). Radiotherapy practices in postoperative endometrial cancer: A survey of the ABS membership. *Brachytherapy* 18(6):741-746.  4 Bingham B, Orton A, Boothe D, Stoddard G, Huang YJ, Gaffney DK and Poppe MM (2017). Brachytherapy improves survival in stage III endometrial cancer with cervical involvement. *Int J Radiat Oncol Biol Phys* 97(5):1040-1050.  5 Mitra D, Klopp AH and Viswanathan AN (2016). Pros and cons of vaginal brachytherapy after external beam radiation therapy in endometrial cancer. *Gynecol Oncol* 140(1):167-175. | Applicable only if  appropriate anatomical structures submitted. |
| Non-core | BACKGROUND ENDOMETRIUM | * Cyclical * Atrophic/inactive * Hyperplasia without atypia * Atypical hyperplasia /endometrioid intraepithelial neoplasia * Other, *specify* | The background endometrium may provide useful information regarding tumour pathogenesis.[1](#_ENREF_1) The presence of stromal pseudodecidualisation may serve as evidence of preoperative hormonal therapy.[2](#_ENREF_2) These should be reported under ‘other’.  Atypical hyperplasia/endometrioid intraepithelial neoplasia is a manifestation of clonal expansion of neoplastic glands. This lesion predisposes to endometrioid carcinoma.[3-5](#_ENREF_3)  Serous carcinoma typically arises in a background of atrophic endometrium although it remains controversial as to what constitutes a precursor lesion. Serous endometrial intraepithelial carcinoma is regarded as a serous carcinoma which grows along pre-existing glands but still has the potential to metastasize to extrauterine sites. Therefore, it is considered a carcinoma rather than a precursor lesion.[6](#_ENREF_6) The literature on a precursor of clear cell carcinoma is limited.[7-9](#_ENREF_7)  Various types of carcinoma, including endometrioid and serous, may occasionally arise in an endometrial polyp.[10](#_ENREF_10) To prove that a carcinoma has arisen within an endometrial polyp rather than secondarily involving it, the tumour should be confined to the polyp. Usually this needs to be confirmed on a hysterectomy specimen. References 1 International Collaboration on Cancer Reporting (2021). *Endometrial Cancer Histopathology Reporting Guide. 4th edition*. Available from: http://www.iccr-cancer.org/datasets/published-datasets/female-reproductive/endometrial (Accessed 10th July 2024).  2 Yamani F and Fadare O (2016). Arias-Stella reaction in progestin-treated endometrioid adenocarcinoma: a potential diagnostic pitfall. *Int J Surg Pathol* 24(4):330-331.  3 Lacey JV, Jr., Sherman ME, Rush BB, Ronnett BM, Ioffe OB, Duggan MA, Glass AG, Richesson DA, Chatterjee N and Langholz B (2010). Absolute risk of endometrial carcinoma during 20-year follow-up among women with endometrial hyperplasia. *J Clin Oncol* 28(5):788-792.  4 Semere LG, Ko E, Johnson NR, Vitonis AF, Phang LJ, Cramer DW and Mutter GL (2011). Endometrial intraepithelial neoplasia: clinical correlates and outcomes. *Obstet Gynecol* 118(1):21-28.  5 Trimble CL, Kauderer J, Zaino R, Silverberg S, Lim PC, Burke JJ, 2nd, Alberts D and Curtin J (2006). Concurrent endometrial carcinoma in women with a biopsy diagnosis of atypical endometrial hyperplasia: a Gynecologic Oncology Group study. *Cancer* 106(4):812-819.  6 Chen H, Strickland AL and Castrillon DH (2022). Histopathologic diagnosis of endometrial precancers: Updates and future directions. *Semin Diagn Pathol* 39(3):137-147.  7 Fadare O, Liang SX, Ulukus EC, Chambers SK and Zheng W (2006). Precursors of endometrial clear cell carcinoma. *Am J Surg Pathol* 30(12):1519-1530.  8 Fadare O and Zheng W (2009). Insights into endometrial serous carcinogenesis and progression. *Int J Clin Exp Pathol* 2(5):411-432.  9 Talia KL, Arora R and McCluggage WG (2022). Precursor Lesions of Cervical Clear Cell Carcinoma: Evidence For Origin From Tubo-Endometrial Metaplasia. *Int J Gynecol Pathol* 41(2):105-112.  10 Trinh VQ, Pelletier MP, Echelard P, Warkus T, Sauthier P, Gougeon F, Mès-Masson AM, Provencher DM and Rahimi K (2020). Distinct histologic, immunohistochemical and clinical features associated with serous endometrial intraepithelial carcinoma involving polyps. *Int J Gynecol Pathol* 39(2):128-135. |  |
| Core and Non-core | LYMPH NODE STATUS | * Cannot be assessed * No nodes submitted or found   **Maximum dimension of**  **largest deposit in regional node**  **\_\_\_ mm**  **Extranodal spread**   * Not involved * Involved   **Other values are listed in Table 2.**  **Table 2 (See the end of the document for Tables)** | Lymph node status is an important prognostic factor for endometrial carcinoma and its assessment is crucial for determining both stage and appropriate adjuvant therapy. According to the FIGO staging system, metastatic involvement of lymph nodes increases tumour stage (IIIC1 and IIIC2 for pelvic and para-aortic nodes, respectively).[1](#_ENREF_1) A therapeutic benefit from lymph node resection has not been shown yet in randomised trials.[2-5](#_ENREF_2) Although a large retrospective study has shown benefit from extensive nodal dissection especially in serous tumours.[4](#_ENREF_4)  Resected lymph nodes are categorised as regional (paracervical, parametrial, various pelvic lymph node groups, including obturator, internal, common or external iliac, presacral and lateral sacral, and para-aortic) or non-regional nodes (inguinal and other nodes). It should be noted that non-regional lymph node involvement (including inguinal nodes) is considered to be distant metastases.  Core data elements regarding lymph node status include the number of lymph nodes identified from the various sites, the number of lymph nodes involved by metastatic tumour and the size of largest metastasis (maximum diameter in mm). Some other parameters which may be useful for future research may be recorded, such as extranodal spread. Extranodal spread is a non-core element. Occasionally, metastatic tumour is present in the specimen removed, but no lymph node tissue is identified.  The FIGO staging system includes lymph node status, and its structure is similar to that of the TNM system.[1](#_ENREF_1),[6-8](#_ENREF_6) Pelvic lymph node involvement is Stage IIIC1 and para-aortic nodal involvement Stage IIIC2. For TNM stage, regional lymph node metastases contribute to the N category, whereas metastases in non-regional nodes are regarded as distant metastasis and belong to the M category.[7](#_ENREF_7),[8](#_ENREF_8)  The 2023 FIGO staging system aligns with the TNM 8th edition staging systems.[1](#_ENREF_1),[6-8](#_ENREF_6) Stage IIIC is further divided into micrometastasis (0.2 to 2 mm and/or >200 cells) (IIIC1i, IIIC2i) and macrometastasis (>2 mm) (IIIC1ii, IIIC2ii), while isolated tumour cells (up to 0.2 mm and ≤200 cells) are not considered metastatic, are not included in FIGO 2023 and in TNM are regarded as pN0(i+).[1](#_ENREF_1)  Grossing of the lymph nodes is an important step for a thorough histologic evaluation. Lymph nodes up to 2 mm are embedded whole. If lymph nodes are larger than 2 mm, they should be sliced perpendicular to the long axis at 2 to 3 mm intervals and entirely submitted.  Multiple studies confirm the high sensitivity of the sentinel lymph node approach for determining the lymph node status in early-stage endometrial carcinoma and underscore the value of sentinel lymph node biopsy in selecting therapeutic approaches.[9-12](#_ENREF_9) One of the strengths of sentinel lymph node biopsy is the detection of a high percentage of lymph node positive cases by intense analysis (ultrastaging) of one or a few lymph nodes. Micrometastases and small macrometastases should be detected by ultrastaging of the lymph nodes. In addition, sentinel lymph node biopsy is associated with a substantially lower risk of post-operative morbidity, especially lower leg lymphoedema, since the dissection of other pelvic lymph nodes is avoided.[13](#_ENREF_13),[14](#_ENREF_14)  The presence of nodal micrometastases is associated with worse prognosis, particularly in patients not receiving adjuvant treatment.[15](#_ENREF_15) There is no evidence that the presence of isolated tumour cells has prognostic ramifications. Based on large randomised trials,[5](#_ENREF_5) lymph node staging does not impact survival, but provides information on extent of the disease and decisions about adjuvant treatment.  According to the 2020 ESGO-ESTRO-ESP guidelines,[16](#_ENREF_16) sentinel lymph node biopsy can be considered for staging purposes in patients with low/intermediate risk disease and can be omitted in cases without myometrial invasion. Systematic lymphadenectomy is not recommended for these carcinomas due to the morbidity associated with the procedure and low incidence of positive nodes. For high-intermediate/high-risk carcinomas in Stages I/II, surgical lymph node staging should be performed and sentinel lymph node biopsy is an acceptable alternative to systematic lymphadenectomy.[17](#_ENREF_17)  Ultrastaging is recommended for the analysis of sentinel nodes which are negative on examination of initial H&E stained slides.[18](#_ENREF_18),[19](#_ENREF_19) Notably, if sentinel nodes are negative by ultrastaging, the occurrence of isolated nodal paraaortic metastasis is very unlikely.[16](#_ENREF_16),[19](#_ENREF_19)  Several ultrastaging protocols have been published, but there is no preferred standardised technique. Ultrastaging consists of additional sections cut at defined intervals and stained by H&E and pankeratins. References 1 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  2 Kitchener H, Swart AM, Qian Q, Amos C and Parmar MK (2009). Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. *Lancet* 373(9658):125-136.  3 Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, Angioli R, Tateo S, Mangili G, Katsaros D, Garozzo G, Campagnutta E, Donadello N, Greggi S, Melpignano M, Raspagliesi F, Ragni N, Cormio G, Grassi R, Franchi M, Giannarelli D, Fossati R, Torri V, Amoroso M, Crocè C and Mangioni C (2008). Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. *J Natl Cancer Inst* 100(23):1707-1716.  4 Todo Y, Kato H, Kaneuchi M, Watari H, Takeda M and Sakuragi N (2010). Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis. *Lancet* 375(9721):1165-1172.  5 Frost JA, Webster KE, Bryant A and Morrison J (2015). Lymphadenectomy for the management of endometrial cancer. *Cochrane Database Syst Rev* 2015(9):Cd007585.  6 FIGO Committee on Gynecological Cancer (2009). Revised FIGO staging for carcinoma of the vulva, cervix and endometrium. *Int. J. Gynecol. Obstet.* 105:103-104.  7 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th Edition*, Springer, New York.  8 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *UICC TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.  9 Bodurtha Smith AJ, Fader AN and Tanner EJ (2017). Sentinel lymph node assessment in endometrial cancer: a systematic review and meta-analysis. *Am J Obstet Gynecol* 216(5):459-476.e410.  10 Bogani G, Murgia F, Ditto A and Raspagliesi F (2019). Sentinel node mapping vs. lymphadenectomy in endometrial cancer: A systematic review and meta-analysis. *Gynecol Oncol* 153(3):676-683.  11 Buda A, Di Martino G, Restaino S, De Ponti E, Monterossi G, Giuliani D, Ercoli A, Dell'Orto F, Dinoi G, Grassi T, Scambia G and Fanfani F (2017). The impact on survival of two different staging strategies in apparent early stage endometrial cancer comparing sentinel lymph nodes mapping algorithm and selective lymphadenectomy: An Italian retrospective analysis of two reference centers. *Gynecol Oncol* 147(3):528-534.  12 Tschernichovsky R, Diver EJ, Schorge JO and Goodman A (2016). The role of lymphadenectomy versus sentinel lymph node biopsy in early-stage endometrial cancer: a review of the literature. *Am J Clin Oncol* 39(5):516-521.  13 Accorsi GS, Paiva LL, Schmidt R, Vieira M, Reis R and Andrade C (2020). Sentinel lymph node mapping vs systematic lymphadenectomy for endometrial cancer: surgical morbidity and lymphatic complications. *J Minim Invasive Gynecol* 27(4):938-945.e932.  14 Helgers RJA, Winkens B, Slangen BFM and Werner HMJ (2020). Lymphedema and post-operative complications after sentinel lymph node biopsy versus lymphadenectomy in endometrial carcinomas- a systematic review and meta-analysis. *J Clin Med* 10(1):120.  15 Ignatov A, Lebius C, Ignatov T, Ivros S, Knueppel R, Papathemelis T, Ortmann O and Eggemann H (2019). Lymph node micrometastases and outcome of endometrial cancer. *Gynecol Oncol* 154(3):475-479.  16 Concin N, Creutzberg CL, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann JA, Bosse T, Chargari C, Fagotti A, Fotopoulou C, González-Martín A, Lax SF, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell DE, Querleu D, Raspollini MR, Sehouli J, Sturdza AE, Taylor A, Westermann AM, Wimberger P, Colombo N, Planchamp F and Matias-Guiu X (2021). ESGO/ESTRO/ESP Guidelines for the management of patients with endometrial carcinoma. *Virchows Arch*:153-190.  17 Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, Ledermann J, Bosse T, Chargari C, Fagotti A, Fotopoulou C, Gonzalez Martin A, Lax S, Lorusso D, Marth C, Morice P, Nout RA, O'Donnell D, Querleu D, Raspollini MR, Sehouli J, Sturdza A, Taylor A, Westermann A, Wimberger P, Colombo N, Planchamp F and Creutzberg CL (2021). ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer* 31(1):12-39.  18 Euscher E, Sui D, Soliman P, Westin S, Ramalingam P, Bassett R and Malpica A (2018). Ultrastaging of sentinel lymph nodes in endometrial carcinoma according to use of 2 different methods. *Int J Gynecol Pathol* 37(3):242-251.  19 Kim CH, Soslow RA, Park KJ, Barber EL, Khoury-Collado F, Barlin JN, Sonoda Y, Hensley ML, Barakat RR and Abu-Rustum NR (2013). Pathologic ultrastaging improves micrometastasis detection in sentinel lymph nodes during endometrial cancer staging. *Int J Gynecol Cancer* 23(5):964-970. |  |
| Core and Non-core | ANCILLARY STUDIES | * Not performed * Performed (select all that apply) * Mismatch repair testing, specify * Immunohistochemistry, specify test(s) and result(s) * Molecular findings, specify test(s) and result(s) * TCGA-based molecular classification, specify * Other, *specify test(s) and result(s)*   **Representative blocks for ancillary studies**, *specify those blocks best representing tumour and/or normal tissue for further study* | **Immunohistochemistry for mismatch repair (MMR) proteins and MLH1 promoter methylation (Core)**  Immunohistochemistry (IHC) for MMR proteins is recommended in addition to analysis for MLH1 promoter methylation when there is immunohistochemical loss of MLH1 or PMS2 as a core reporting parameter in all endometrial carcinomas.[1](#_ENREF_1)  Endometrial cancer is one of the most common tumours in patients with Lynch syndrome (also known as hereditary non-polyposis colorectal cancer).[2](#_ENREF_2),[3](#_ENREF_3) Around 3% of all endometrial carcinomas and approximately 10% of MMR deficient (MMRd)/microsatellite unstable endometrial carcinomas are causally related to germline mutations of one of the MMR genes MLH1, PMS2, MSH2 and MSH6 or a related gene, EPCAM.[4](#_ENREF_4) ‘Constitutive methylation’ is also a rare cause of Lynch syndrome.[5](#_ENREF_5)  Testing for MMR status/microsatellite instability (MSI) in endometrial carcinoma patients has been shown to be important for four key reasons:   1. Diagnostic, since MMRd/MSI is helpful to diagnose endometrioid carcinomas (as opposed to serous carcinoma or human papillomavirus (HPV)-associated cervical carcinoma); 2. It is part of the screening algorithm to identify potential patients with Lynch syndrome;[6](#_ENREF_6) 3. Prognostic, as part of the Cancer Genome Atlas (TCGA) molecular classification;[7](#_ENREF_7) 4. Therapeutically as a predictive biomarker for potential utility of immune checkpoint inhibitor therapy.[8](#_ENREF_8)   Systematic clinical screening of personal and family history misses a significant proportion of women with Lynch syndrome, since up to 75% of patients do not fulfill the revised Bethesda Guidelines criteria.[9](#_ENREF_9) ISGyP has recommended testing for MMR status/MSI in all endometrial carcinomas (preferably curettings or biopsy), irrespective of age.[1](#_ENREF_1) This has also been recommended whenever resources are available by other societies/groups, such as the Manchester International Consensus Group.[10](#_ENREF_10) The identification of Lynch syndrome in women with endometrial carcinoma can lead to the prevention of a second cancer in the patient and prevention of cancers in family members through risk reducing strategies and heightened surveillance.  Microsatellite instability (MSI) can be detected by different methods, including polymerase chain reaction (PCR)-based approaches[9](#_ENREF_9),[11](#_ENREF_11),[12](#_ENREF_12) and next generation sequencing (NGS).[13](#_ENREF_13)  Immunohistochemistry (IHC) is cost effective and is used in most pathology departments. ISGyP guidelines recommend IHC as the best test to identify MMR deficiency and, indirectly, for MSI.[1](#_ENREF_1) The IHC approach consists of staining with the four DNA MMR proteins: MLH1, PMS2, MSH2, and MSH6. An alternative is to use only PMS2 and MSH6, with addition of MLH1 when PMS2 is lost, and of MSH2 when MSH6 is lost.[14](#_ENREF_14) Carcinomas showing loss of MLH1 and PMS2 expression should be investigated for MLH1 promoter hypermethylation,[15](#_ENREF_15) as its presence essentially excludes Lynch syndrome. Endometrial cancer patients whose tumours are MMRd, but not methylated at the MLH1 promoter, should undergo genetic counselling with consideration for germline testing.  Immunohistochemistry (IHC) may be not informative when the specimen has been subjected to poor pre-analytical conditions, such as inappropriate or delayed fixation. Furthermore, occasionally there are germline genetic abnormalities that do not result in abnormal expression of MMR proteins. In these cases, PCR-based techniques to assess MSI may be appropriate, particularly when the family history is highly suspicious for Lynch syndrome. MSI detected by PCR-based methods usually requires testing both normal and tumour tissue, although there is an alternative method that only requires tumour tissue.[16](#_ENREF_16)  **The Cancer Genome Atlas (TCGA)-based molecular classification of endometrial carcinomas (Non-core)**  Reporting of TCGA-based molecular classification of endometrial carcinomas is a non-core parameter. Diagnosis and classification of endometrial carcinoma has up until now largely been based on the microscopic appearance of the tumours, often supplemented by IHC.[17](#_ENREF_17) The different histologic types have different molecular features, microscopic appearances, precursor lesions, and natural history, although in multivariate analyses,[18](#_ENREF_18) FIGO stage and grade have more prognostic significance than histotype. Unfortunately, histological typing engenders problems with interobserver reproducibility and prognostication. While diagnosis is quite reproducible in low grade (FIGO grades 1 and 2) endometrioid carcinomas, which account for 70% of endometrial carcinomas, there is less interobserver agreement in classifying high grade endometrial carcinomas.[19-21](#_ENREF_19)  The TCGA performed an integrated genomic, transcriptomic and proteomic characterisation of endometrial carcinomas.[22](#_ENREF_22) This revealed four groups of tumours.  One group (approximately 7% of endometrial carcinomas) have somatic inactivating hotspot mutations in the *POLE* exonuclease domain and a very high mutational burden (ultramutated). FIGO grade 3 endometrioid carcinomas are highly represented in this group, some of which resemble serous carcinomas. Irrespective of grade, this group of tumours have an excellent prognosis, although this is not confirmed in all of the literature.[22-25](#_ENREF_22)  There are also two groups which show similar progression-free survival rates that are intermediate between the other two groups. With additional research, it is becoming apparent that these groups are heterogeneous, each having genomically-defined subgroups of tumours, some of which are prognostically favourable and others that are unfavourable.[22](#_ENREF_22),[26-28](#_ENREF_26) One group (approximately 30% of tumours) comprises carcinomas with MSI (hypermutated), frequently with MLH1 promoter hypermethylation and high mutation rates.  The other ‘intermediate’ group (approximately 39% of endometrial carcinomas) includes endometrioid carcinomas with low copy number alterations, and low mutational burden, which lack *POLE* and *TP53* mutations and which are not MSI-high (MSI-H). These tumours are commonly referred to as ‘no specific molecular profile (NSMP)’.  The last group is referred to as serous-like or copy-number high (approximately26% of endometrial carcinomas). These exhibit a low mutation rate, nearly universal (95%) *TP53* mutations, and a highly unfavourable prognosis. Most of these tumours are serous carcinomas, but up to 25% of endometrioid (mostly high grade), some clear cell carcinomas, and most carcinosarcomas, are in this group.  In an attempt to bring TCGA molecular-based classification into clinical practice, different groups have proposed a surrogate (simplified) algorithm which does not include comprehensive tumour profiling.[7](#_ENREF_7),[27](#_ENREF_27),[28](#_ENREF_28) The algorithm includes three immunohistochemical markers (p53, MSH6 and PMS2) and one molecular test (mutation analysis of *POLE*). Several studies have demonstrated the prognostic value of this TCGA-surrogate approach, and ISGyP have recommended this scheme.[1](#_ENREF_1),[26](#_ENREF_26),[29](#_ENREF_29)  According to this simplified algorithm, tumours with pathogenic *POLE* mutation correspond to ultramutated tumours. MSH6 or PMS2 abnormal expression defines tumours in the hypermutated group. Abnormal expression of p53 (mutated pattern), characterises the copy number high group. Finally, NSMP is defined by the absence of *POLE* mutation, and a normal expression pattern of MSH6, PMS2 and p53.[7](#_ENREF_7),[28](#_ENREF_28)  The Cancer Genome Atlas (TCGA) surrogate approach has been shown to be particularly helpful in the group of high grade endometrioid carcinomas, including cases in the grey zone between endometrioid and serous carcinomas. High grade endometrioid carcinoma has been regarded as an aggressive tumour type with some similarities to serous carcinoma. However, application of the TCGA surrogate shows that there is a group of high grade endometrioid carcinomas with an improved prognosis (tumours with pathogenic *POLE* mutations), and a group with a very poor prognosis (p53-abnormal tumours (p53abn)). MSI-H and NSMP grade 3 endometrioid carcinomas have an intermediate prognosis.[30](#_ENREF_30) Application of this algorithm for clear cell carcinoma,[31](#_ENREF_31) undifferentiated/dedifferentiated carcinoma,[32](#_ENREF_32) neuroendocrine carcinoma,[33](#_ENREF_33) and carcinosarcoma[34](#_ENREF_34) is possible, although there has been limited study regarding these tumours and they were not included in the original TCGA paper.[22](#_ENREF_22) The vast majority of low grade endometrioid carcinomas are NSMP or MSI, with *POLE*-mutated, or p53abn tumours accounting for less than 10%. Moreover, the vast majority (95%) of serous carcinoma are p53abn.  There is still discussion about whether to apply the molecular classifier to all endometrial carcinomas or just in diagnostically challenging high grade tumours. An important factor in the decision to base therapy selection on genomic subgrouping, includes that most evidence is still retrospective. Prospective studies are awaited and ongoing (e.g., RAINBO trial).[35](#_ENREF_35) [36](#_ENREF_36) The availability of resources, particularly for *POLE* mutation analysis, is inconsistent.[7](#_ENREF_7) Also, most evidence in support of the TCGA classification is based on two large but retrospective cohorts.[7](#_ENREF_7),[28](#_ENREF_28) There are two additional complexities to *POLE* testing: distinguishing between pathogenic and non-pathogenic mutations,[37](#_ENREF_37) and coexistence of ultramutation (i.e., pathogenic *POLE* mutation) with secondary mutations in *TP53* and/or one or more of the MMR genes.[38](#_ENREF_38) These ‘multiple classifier’ cases are currently thought to retain the favourable prognosis of *POLE* mutated tumours, regardless of MMR or p53 status but this is still an evolving field.  The 2023 FIGO staging system encourages performance of the complete molecular classification in all endometrial carcinomas for prognostic risk-group stratification and as potential influencing factors for adjuvant and systemic treatment decisions.[39](#_ENREF_39) Although not mandatory for appropriate staging, identification of *POLE* mutations and p53abnormalities result in upstaging or downstaging the disease when molecular classification is performed in stage I and II tumours.[39](#_ENREF_39) For FIGO Stages I and II, based on surgical/anatomical and histological findings, the FIGO stage is modified when molecular classification reveals either POLEmut or p53abn. This is depicted in the FIGO stage by the addition of ‘m’ for molecular classification, and a subscript is added to denote POLEmut or p53abn status. MMRd or NSMP status do not modify early FIGO stages; however, these molecular classifications should be recorded for the purpose of data collection. No changes occur through the molecular features in stages III and IV, but cases for which the molecular classification is known should be recorded as Stage IIIm and Stage IVm with specification of the molecular class for purposes of data collection.  **Other markers (Non-core)**  Immunohistochemistry (IHC) may be helpful for diagnosis of endometrial carcinomas. With a differential diagnosis involving endometrioid and serous carcinomas, loss of expression of MMR proteins, PTEN and/or ARID1A would favour endometrioid carcinoma. Both serous and endometrioid carcinomas can show aberrant p53 staining and p16 overexpression (both more common in serous carcinoma).[40](#_ENREF_40) Napsin A, HNF1-beta and AMACR (together with negative estrogen receptor (ER))[41](#_ENREF_41),[42](#_ENREF_42) may be helpful in diagnosing clear cell carcinoma. A combination of broad spectrum cytokeratin, EMA, PAX8, ER and E-cadherin may be useful in distinguishing between undifferentiated carcinomas and high grade endometrioid carcinomas since the former generally shows markedly reduced staining with these markers compared to the latter. Neuroendocrine markers (INSM1, chromogranin, synaptophysin) can help in recognition of neuroendocrine tumours,[43](#_ENREF_43) and GATA3, TTF1 and CD10 may help in diagnosing mesonephric-like carcinoma.[44](#_ENREF_44),[45](#_ENREF_45) Finally, a panel including p16, ER, progesterone receptor (PR), and high risk *HPV* in situ hybridisation may be useful in ruling out an HPV-associated endocervical adenocarcinoma.[46](#_ENREF_46)  There are also immunohistochemical markers of prognostic and predictive value. HER2 protein overexpression and/or *HER2* gene amplification is present in approximately 25-30% of endometrial serous carcinomas,[47-49](#_ENREF_47) and 14% of endometrial carcinosarcomas.[50](#_ENREF_50) Intratumoural heterogeneity of HER2 expression and gene amplification are common in these tumours and this should be taken into consideration when evaluating their HER2 status.[47](#_ENREF_47),[51](#_ENREF_51) HER2 positivity in endometrial serous carcinomas is associated with worse progression free and overall survival,[52](#_ENREF_52) but can be therapeutically targeted by adding trastuzumab to the standard chemotherapy regimen.[53](#_ENREF_53),[54](#_ENREF_54) It has been shown that *HER2* amplification is characteristic of p53abn endometrial carcinomas as defined in the molecular classification, and is not restricted to the serous carcinoma category.[55](#_ENREF_55) Although currently no official endometrial cancer-specific pathology HER2 scoring guidelines exist, a new set of criteria have been proposed based on successful clinical trial experience.[56](#_ENREF_56)  L1CAM expression has been touted as a marker of aggressive behaviour amongst the NSMP carcinomas and is associated with non-endometrioid histology, distant metastasis and poor survival.[57-59](#_ENREF_57) Mutations in *CTNNB1* (often, but not always, associated with nuclear expression of beta-catenin with IHC) have been some in some studies to be associated with diminished survival in low grade endometrioid carcinomas, but this is not universally accepted.[28](#_ENREF_28),[60](#_ENREF_60),[61](#_ENREF_61)  Estrogen receptor (ER) expression has been associated with tumour behaviour and survival in endometrioid carcinomas.[62](#_ENREF_62),[63](#_ENREF_63) ER/PR may assist with tumour classification and may be important to clinicians for treatment planning. A systematic review by van Weeldon et al (2019) confirmed improved response rates to endocrine therapy in ER and PR positive tumours, especially when determined in the metastatic tissue.[64](#_ENREF_64)  WT1 expression may be helpful to distinguish between a primary endometrial serous carcinoma and a tubo-ovarian high grade serous carcinoma since the latter is more likely to be positive. However, up to 30-40% of endometrial serous carcinomas may exhibit some degree of WT1 positivity.[65](#_ENREF_65) References 1 Cho KR, Cooper K, Croce S, Djordevic B, Herrington S, Howitt B, Hui P, Ip P, Koebel M, Lax S, Quade BJ, Shaw P, Vidal A, Yemelyanova A, Clarke B, Hedrick Ellenson L, Longacre TA, Shih IM, McCluggage WG, Malpica A, Oliva E, Parkash V and Matias-Guiu X (2019). International Society of Gynecological Pathologists (ISGyP) Endometrial Cancer Project: Guidelines From the Special Techniques and Ancillary Studies Group. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S114-s122.  2 Egoavil C, Alenda C, Castillejo A, Paya A, Peiro G, Sánchez-Heras AB, Castillejo MI, Rojas E, Barberá VM, Cigüenza S, Lopez JA, Piñero O, Román MJ, Martínez-Escoriza JC, Guarinos C, Perez-Carbonell L, Aranda FI and Soto JL (2013). Prevalence of Lynch syndrome among patients with newly diagnosed endometrial cancers. *PLoS One* 8(11):e79737.  3 Zhao S, Chen L, Zang Y, Liu W, Liu S, Teng F, Xue F and Wang Y (2022). Endometrial cancer in Lynch syndrome. *Int J Cancer* 150(1):7-17.  4 Cuatrecasas M, Gorostiaga I, Riera C, Saperas E, Llort G, Costa I, Matias-Guiu X, Carrato C, Navarro M, Pineda M, Dueñas N, Brunet J, Marco V, Trias I, Busteros JI, Mateu G, Balaguer F, Fernández-Figueras MT, Esteller M and Musulén E (2020). Complete loss of EPCAM immunoexpression identifies EPCAM deletion carriers in MSH2-negative colorectal neoplasia. *Cancers (Basel)* 12(10):2803.  5 Dámaso E, González-Acosta M, Vargas-Parra G, Navarro M, Balmaña J, Ramon YCT, Tuset N, Thompson BA, Marín F, Fernández A, Gómez C, Velasco À, Solanes A, Iglesias S, Urgel G, López C, Del Valle J, Campos O, Santacana M, Matias-Guiu X, Lázaro C, Valle L, Brunet J, Pineda M and Capellá G (2020). Comprehensive constitutional genetic and epigenetic characterization of Lynch-like individuals. *Cancers (Basel)* 12(7):1799.  6 Frolova AI, Babb SA, Zantow E, Hagemann AR, Powell MA, Thaker PH, Gao F and Mutch DG (2015). Impact of an immunohistochemistry-based universal screening protocol for Lynch syndrome in endometrial cancer on genetic counseling and testing. *Gynecol Oncol* 137(1):7-13.  7 Talhouk A, McConechy MK, Leung S, Li-Chang HH, Kwon JS, Melnyk N, Yang W, Senz J, Boyd N, Karnezis AN, Huntsman DG, Gilks CB and McAlpine JN (2015). A clinically applicable molecular-based classification for endometrial cancers. *Br J Cancer* 113(2):299-310.  8 Green AK, Feinberg J and Makker V (2020). A review of immune checkpoint blockade therapy in endometrial cancer. *Am Soc Clin Oncol Educ Book* 40:1-7.  9 Umar A, Boland CR, Terdiman JP, Syngal S, de la Chapelle A, Rüschoff J, Fishel R, Lindor NM, Burgart LJ, Hamelin R, Hamilton SR, Hiatt RA, Jass J, Lindblom A, Lynch HT, Peltomaki P, Ramsey SD, Rodriguez-Bigas MA, Vasen HF, Hawk ET, Barrett JC, Freedman AN and Srivastava S (2004). Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. *J Natl Cancer Inst* 96(4):261-268.  10 Crosbie EJ, Ryan NAJ, Arends MJ, Bosse T, Burn J, Cornes JM, Crawford R, Eccles D, Frayling IM, Ghaem-Maghami S, Hampel H, Kauff ND, Kitchener HC, Kitson SJ, Manchanda R, McMahon RFT, Monahan KJ, Menon U, Møller P, Möslein G, Rosenthal A, Sasieni P, Seif MW, Singh N, Skarrott P, Snowsill TM, Steele R, Tischkowitz M and Evans DG (2019). The Manchester International Consensus Group recommendations for the management of gynecological cancers in Lynch syndrome. *Genet Med* 21(10):2390-2400.  11 Hissong E, Crowe EP, Yantiss RK and Chen YT (2018). Assessing colorectal cancer mismatch repair status in the modern era: a survey of current practices and re-evaluation of the role of microsatellite instability testing. *Mod Pathol* 31(11):1756-1766.  12 Pécriaux A, Favre L, Calderaro J, Charpy C, Derman J and Pujals A (2021). Detection of microsatellite instability in a panel of solid tumours with the Idylla MSI Test using extracted DNA. *J Clin Pathol* 74(1):36-42.  13 Middha S, Zhang L, Nafa K, Jayakumaran G, Wong D, Kim HR, Sadowska J, Berger MF, Delair DF, Shia J, Stadler Z, Klimstra DS, Ladanyi M, Zehir A and Hechtman JF (2017). Reliable pan-cancer microsatellite instability assessment by using targeted next-generation sequencing data. *JCO Precis Oncol* 2017:e1-17.  14 Mojtahed A, Schrijver I, Ford JM, Longacre TA and Pai RK (2011). A two-antibody mismatch repair protein immunohistochemistry screening approach for colorectal carcinomas, skin sebaceous tumors, and gynecologic tract carcinomas. *Mod Pathol* 24(7):1004-1014.  15 Ryan NAJ, Glaire MA, Blake D, Cabrera-Dandy M, Evans DG and Crosbie EJ (2019). The proportion of endometrial cancers associated with Lynch syndrome: a systematic review of the literature and meta-analysis. *Genet Med* 21(10):2167-2180.  16 Samaison L, Grall M, Staroz F and Uguen A (2019). Microsatellite instability diagnosis using the fully automated Idylla platform: feasibility study of an in-house rapid molecular testing ancillary to immunohistochemistry in pathology laboratories. *J Clin Pathol* 72(12):830-835.  17 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.  18 Piulats JM, Guerra E, Gil-Martín M, Roman-Canal B, Gatius S, Sanz-Pamplona R, Velasco A, Vidal A and Matias-Guiu X (2017). Molecular approaches for classifying endometrial carcinoma. *Gynecol Oncol* 145(1):200-207.  19 Gilks CB, Oliva E and Soslow RA (2013). Poor interobserver reproducibility in the diagnosis of high-grade endometrial carcinoma. *Am J Surg Pathol* 37(6):874-881.  20 Hoang LN, McConechy MK, Köbel M, Han G, Rouzbahman M, Davidson B, Irving J, Ali RH, Leung S, McAlpine JN, Oliva E, Nucci MR, Soslow RA, Huntsman DG, Gilks CB and Lee CH (2013). Histotype-genotype correlation in 36 high-grade endometrial carcinomas. *Am J Surg Pathol* 37(9):1421-1432.  21 Murali R, Davidson B, Fadare O, Carlson JA, Crum CP, Gilks CB, Irving JA, Malpica A, Matias-Guiu X, McCluggage WG, Mittal K, Oliva E, Parkash V, Rutgers JKL, Staats PN, Stewart CJR, Tornos C and Soslow RA (2019). High-grade Endometrial Carcinomas: Morphologic and Immunohistochemical Features, Diagnostic Challenges and Recommendations. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S40-s63.  22 Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, Robertson AG, Pashtan I, Shen R, Benz CC, Yau C, Laird PW, Ding L, Zhang W, Mills GB, Kucherlapati R, Mardis ER and Levine DA (2013). Integrated genomic characterization of endometrial carcinoma. *Nature* 497(7447):67-73.  23 Billingsley CC, Cohn DE, Mutch DG, Hade EM and Goodfellow PJ (2016). Prognostic significance of POLE exonuclease domain mutations in high-grade endometrioid endometrial cancer on survival and recurrence: a subanalysis. *Int J Gynecol Cancer* 26(5):933-938.  24 Church DN, Stelloo E, Nout RA, Valtcheva N, Depreeuw J, ter Haar N, Noske A, Amant F, Tomlinson IP, Wild PJ, Lambrechts D, Jürgenliemk-Schulz IM, Jobsen JJ, Smit VT, Creutzberg CL and Bosse T (2015). Prognostic significance of POLE proofreading mutations in endometrial cancer. *J Natl Cancer Inst* 107(1):402.  25 Stasenko M, Tunnage I, Ashley CW, Rubinstein MM, Latham AJ, Da Cruz Paula A, Mueller JJ, Leitao MM, Jr., Friedman CF, Makker V, Soslow RA, DeLair DF, Hyman DM, Zamarin D, Alektiar KM, Aghajanian CA, Abu-Rustum NR, Weigelt B and Cadoo KA (2020). Clinical outcomes of patients with POLE mutated endometrioid endometrial cancer. *Gynecol Oncol* 156(1):194-202.  26 Kommoss S, McConechy MK, Kommoss F, Leung S, Bunz A, Magrill J, Britton H, Kommoss F, Grevenkamp F, Karnezis A, Yang W, Lum A, Krämer B, Taran F, Staebler A, Lax S, Brucker SY, Huntsman DG, Gilks CB, McAlpine JN and Talhouk A (2018). Final validation of the ProMisE molecular classifier for endometrial carcinoma in a large population-based case series. *Ann Oncol* 29(5):1180-1188.  27 McAlpine J, Leon-Castillo A and Bosse T (2018). The rise of a novel classification system for endometrial carcinoma; integration of molecular subclasses. *J Pathol* 244(5):538-549.  28 Stelloo E, Nout RA, Osse EM, Jürgenliemk-Schulz IJ, Jobsen JJ, Lutgens LC, van der Steen-Banasik EM, Nijman HW, Putter H, Bosse T, Creutzberg CL and Smit VT (2016). Improved risk assessment by integrating molecular and clinicopathological factors in early-stage endometrial cancer-combined analysis of the PORTEC cohorts. *Clin Cancer Res* 22(16):4215-4224.  29 Soslow RA, Tornos C, Park KJ, Malpica A, Matias-Guiu X, Oliva E, Parkash V, Carlson J, McCluggage WG and Gilks CB (2019). Endometrial carcinoma diagnosis: Use of FIGO grading and genomic subcategories in clinical practice: Recommendations of the International Society of Gynecological Pathologists. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S64-s74.  30 Bosse T, Nout RA, McAlpine JN, McConechy MK, Britton H, Hussein YR, Gonzalez C, Ganesan R, Steele JC, Harrison BT, Oliva E, Vidal A, Matias-Guiu X, Abu-Rustum NR, Levine DA, Gilks CB and Soslow RA (2018). Molecular classification of grade 3 endometrioid endometrial cancers identifies distinct prognostic subgroups. *Am J Surg Pathol* 42(5):561-568.  31 DeLair DF, Burke KA, Selenica P, Lim RS, Scott SN, Middha S, Mohanty AS, Cheng DT, Berger MF, Soslow RA and Weigelt B (2017). The genetic landscape of endometrial clear cell carcinomas. *J Pathol* 243(2):230-241.  32 Rosa-Rosa JM, Leskelä S, Cristóbal-Lana E, Santón A, López-García M, Muñoz G, Pérez-Mies B, Biscuola M, Prat J, Esther O, Soslow RA, Matias-Guiu X and Palacios J (2016). Molecular genetic heterogeneity in undifferentiated endometrial carcinomas. *Mod Pathol* 29(11):1390-1398.  33 Howitt BE, Dong F, Vivero M, Shah V, Lindeman N, Schoolmeester JK, Baltay M, MacConaill L, Sholl LM, Nucci MR and McCluggage WG (2020). Molecular characterization of neuroendocrine carcinomas of the endometrium: representation in all 4 TCGA groups. *Am J Surg Pathol* 44(11):1541-1548.  34 Travaglino A, Raffone A, Gencarelli A, Mollo A, Guida M, Insabato L, Santoro A, Zannoni GF and Zullo F (2020). TCGA classification of endometrial cancer: the place of carcinosarcoma. *Pathol Oncol Res* 26(4):2067-2073.  35 RAINBO Research Consortium (2022). Refining adjuvant treatment in endometrial cancer based on molecular features: the RAINBO clinical trial program. *Int J Gynecol Cancer* 33(1):109-117.  36 van den Heerik A, Horeweg N, Nout RA, Lutgens L, van der Steen-Banasik EM, Westerveld GH, van den Berg HA, Slot A, Koppe FLA, Kommoss S, Mens JWM, Nowee ME, Bijmolt S, Cibula D, Stam TC, Jurgenliemk-Schulz IM, Snyers A, Hamann M, Zwanenburg AG, Coen V, Vandecasteele K, Gillham C, Chargari C, Verhoeven-Adema KW, Putter H, van den Hout WB, Wortman BG, Nijman HW, Bosse T and Creutzberg CL (2020). PORTEC-4a: international randomized trial of molecular profile-based adjuvant treatment for women with high-intermediate risk endometrial cancer. *Int J Gynecol Cancer* 30(12):2002-2007.  37 León-Castillo A, Britton H, McConechy MK, McAlpine JN, Nout R, Kommoss S, Brucker SY, Carlson JW, Epstein E, Rau TT, Bosse T, Church DN and Gilks CB (2020). Interpretation of somatic POLE mutations in endometrial carcinoma. *J Pathol* 250(3):323-335.  38 León-Castillo A, Gilvazquez E, Nout R, Smit VT, McAlpine JN, McConechy M, Kommoss S, Brucker SY, Carlson JW, Epstein E, Rau TT, Soslow RA, Ganesan R, Matias-Guiu X, Oliva E, Harrison BT, Church DN, Gilks CB and Bosse T (2020). Clinicopathological and molecular characterisation of 'multiple-classifier' endometrial carcinomas. *J Pathol* 250(3):312-322.  39 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  40 Soslow RA (2013). High-grade endometrial carcinomas - strategies for typing. *Histopathology* 62(1):89-110.  41 Fadare O, Parkash V, Gwin K, Hanley KZ, Jarboe EA, Liang SX, Quick CM, Zheng W, Rawish KR, Hecht JL and Desouki MM (2013). Utility of α-methylacyl-coenzyme-A racemase (p504s) immunohistochemistry in distinguishing endometrial clear cell carcinomas from serous and endometrioid carcinomas. *Hum Pathol* 44(12):2814-2821.  42 Fadare O, Desouki MM, Gwin K, Hanley KZ, Jarboe EA, Liang SX, Quick CM, Zheng W, Parkash V and Hecht JL (2014). Frequent expression of napsin A in clear cell carcinoma of the endometrium: potential diagnostic utility. *Am J Surg Pathol* 38(2):189-196.  43 Pocrnich CE, Ramalingam P, Euscher ED and Malpica A (2016). Neuroendocrine Carcinoma of the Endometrium: A Clinicopathologic Study of 25 Cases. *Am J Surg Pathol* 40(5):577-586.  44 Euscher ED, Bassett R, Duose DY, Lan C, Wistuba I, Ramondetta L, Ramalingam P and Malpica A (2020). Mesonephric-like carcinoma of the endometrium: a subset of endometrial carcinoma with an aggressive behavior. *Am J Surg Pathol* 44(4):429-443.  45 Horn LC, Höhn AK, Krücken I, Stiller M, Obeck U and Brambs CE (2020). Mesonephric-like adenocarcinomas of the uterine corpus: report of a case series and review of the literature indicating poor prognosis for this subtype of endometrial adenocarcinoma. *J Cancer Res Clin Oncol* 146(4):971-983.  46 Stewart CJR, Crum CP, McCluggage WG, Park KJ, Rutgers JK, Oliva E, Malpica A, Parkash V, Matias-Guiu X and Ronnett BM (2019). Guidelines to aid in the distinction of endometrial and endocervical carcinomas, and the distinction of independent primary carcinomas of the endometrium and adnexa from metastatic spread between these and other sites. *Int J Gynecol Pathol* 38 Suppl 1(Iss 1 Suppl 1):S75-s92.  47 Buza N, English DP, Santin AD and Hui P (2013). Toward standard HER2 testing of endometrial serous carcinoma: 4-year experience at a large academic center and recommendations for clinical practice. *Mod Pathol* 26(12):1605-1612.  48 Halle MK, Tangen IL, Berg HF, Hoivik EA, Mauland KK, Kusonmano K, Berg A, Hurtado A, Kalland KH, Øyan AM, Stefansson I, Vintermyr OK, Werner HM, Haldorsen IS, Trovik J, Salvesen HB and Krakstad C (2018). HER2 expression patterns in paired primary and metastatic endometrial cancer lesions. *Br J Cancer* 118(3):378-387.  49 Zhao S, Choi M, Overton JD, Bellone S, Roque DM, Cocco E, Guzzo F, English DP, Varughese J, Gasparrini S, Bortolomai I, Buza N, Hui P, Abu-Khalaf M, Ravaggi A, Bignotti E, Bandiera E, Romani C, Todeschini P, Tassi R, Zanotti L, Carrara L, Pecorelli S, Silasi DA, Ratner E, Azodi M, Schwartz PE, Rutherford TJ, Stiegler AL, Mane S, Boggon TJ, Schlessinger J, Lifton RP and Santin AD (2013). Landscape of somatic single-nucleotide and copy-number mutations in uterine serous carcinoma. *Proc Natl Acad Sci U S A* 110(8):2916-2921.  50 Rottmann D, Snir OL, Wu X, Wong S, Hui P, Santin AD and Buza N (2020). HER2 testing of gynecologic carcinosarcomas: tumor stratification for potential targeted therapy. *Mod Pathol* 33(1):118-127.  51 Buza N and Hui P (2013). Marked heterogeneity of HER2/NEU gene amplification in endometrial serous carcinoma. *Genes Chromosomes Cancer* 52(12):1178-1186.  52 Erickson BK, Najjar O, Damast S, Blakaj A, Tymon-Rosario J, Shahi M, Santin A, Klein M, Dolan M, Cimino-Mathews A, Buza N, Ferriss JS, Stone RL, Khalifa M and Fader AN (2020). Human epidermal growth factor 2 (HER2) in early stage uterine serous carcinoma: A multi-institutional cohort study. *Gynecol Oncol* 159(1):17-22.  53 Fader AN, Roque DM, Siegel E, Buza N, Hui P, Abdelghany O, Chambers S, Secord AA, Havrilesky L, O'Malley DM, Backes FJ, Nevadunsky N, Edraki B, Pikaart D, Lowery W, ElSahwi K, Celano P, Bellone S, Azodi M, Litkouhi B, Ratner E, Silasi DA, Schwartz PE and Santin AD (2020). Randomized phase II trial of carboplatin-paclitaxel compared with carboplatin-paclitaxel-trastuzumab in advanced (stage III-IV) or recurrent uterine serous carcinomas that overexpress Her2/Neu (NCT01367002): updated overall survival analysis. *Clin Cancer Res* 26(15):3928-3935.  54 Fader AN, Roque DM, Siegel E, Buza N, Hui P, Abdelghany O, Chambers SK, Secord AA, Havrilesky L, O'Malley DM, Backes F, Nevadunsky N, Edraki B, Pikaart D, Lowery W, ElSahwi KS, Celano P, Bellone S, Azodi M, Litkouhi B, Ratner E, Silasi DA, Schwartz PE and Santin AD (2018). Randomized phase II trial of carboplatin-paclitaxel versus carboplatin-paclitaxel-trastuzumab in uterine serous carcinomas that overexpress human epidermal growth factor receptor 2/neu. *J Clin Oncol* 36(20):2044-2051.  55 Vermij L, Horeweg N, Leon-Castillo A, Rutten TA, Mileshkin LR, Mackay HJ, Leary A, Powell ME, Singh N, Crosbie EJ, Smit V, Creutzberg CL and Bosse T (2020). HER2 Status in high-risk endometrial cancers (PORTEC-3): relationship with histotype, molecular classification, and clinical outcomes. *Cancers (Basel)* 13(1):44.  56 Buza N (2020). HER2 testing in endometrial serous carcinoma. *Arch Pathol Lab Med* 145(6):687-691.  57 van der Putten LJ, Visser NC, van de Vijver K, Santacana M, Bronsert P, Bulten J, Hirschfeld M, Colas E, Gil-Moreno A, Garcia A, Mancebo G, Alameda F, Trovik J, Kopperud RK, Huvila J, Schrauwen S, Koskas M, Walker F, Weinberger V, Minar L, Jandakova E, Snijders MP, van den Berg-van Erp S, Matias-Guiu X, Salvesen HB, Amant F, Massuger LF and Pijnenborg JM (2016). L1CAM expression in endometrial carcinomas: an ENITEC collaboration study. *Br J Cancer* 115(6):716-724.  58 Van Gool IC, Stelloo E, Nout RA, Nijman HW, Edmondson RJ, Church DN, MacKay HJ, Leary A, Powell ME, Mileshkin L, Creutzberg CL, Smit VT and Bosse T (2016). Prognostic significance of L1CAM expression and its association with mutant p53 expression in high-risk endometrial cancer. *Mod Pathol* 29(2):174-181.    59 Zeimet AG, Reimer D, Huszar M, Winterhoff B, Puistola U, Azim SA, Müller-Holzner E, Ben-Arie A, van Kempen LC, Petru E, Jahn S, Geels YP, Massuger LF, Amant F, Polterauer S, Lappi-Blanco E, Bulten J, Meuter A, Tanouye S, Oppelt P, Stroh-Weigert M, Reinthaller A, Mariani A, Hackl W, Netzer M, Schirmer U, Vergote I, Altevogt P, Marth C and Fogel M (2013). L1CAM in early-stage type I endometrial cancer: results of a large multicenter evaluation. *J Natl Cancer Inst* 105(15):1142-1150.  60 Myers A, Barry WT, Hirsch MS, Matulonis U and Lee L (2014). β-Catenin mutations in recurrent FIGO IA grade I endometrioid endometrial cancers. *Gynecol Oncol* 134(2):426-427.  61 Kurnit KC, Kim GN, Fellman BM, Urbauer DL, Mills GB, Zhang W and Broaddus RR (2017). CTNNB1 (beta-catenin) mutation identifies low grade, early stage endometrial cancer patients at increased risk of recurrence. *Mod Pathol* 30(7):1032-1041.  62 Backes FJ, Walker CJ, Goodfellow PJ, Hade EM, Agarwal G, Mutch D, Cohn DE and Suarez AA (2016). Estrogen receptor-alpha as a predictive biomarker in endometrioid endometrial cancer. *Gynecol Oncol* 141(2):312-317.  63 Trovik J, Wik E, Werner HM, Krakstad C, Helland H, Vandenput I, Njolstad TS, Stefansson IM, Marcickiewicz J, Tingulstad S, Staff AC, Amant F, Akslen LA and Salvesen HB (2013). Hormone receptor loss in endometrial carcinoma curettage predicts lymph node metastasis and poor outcome in prospective multicentre trial. *Eur J Cancer* 49(16):3431-3441.  64 van Weelden WJ, Massuger L, Pijnenborg JMA and Romano A (2019). Anti-estrogen treatment in endometrial cancer: a systematic review. *Front Oncol* 9:359.  65 Hedley C, Sriraksa R, Showeil R, Van Noorden S and El-Bahrawy M (2014). The frequency and significance of WT-1 expression in serous endometrial carcinoma. *Hum Pathol* 45(9):1879-1884. |  |
| Core | PATHOLOGICALLY CONFIRMED DISTANT METASTASES | * Not identified * Present, *specify site(s)* | Documentation of known metastatic disease is an important part of the pathology report. Such information, if available, should be recorded with as much detail as is available including the site, whether the specimen is a histopathology or cytopathology specimen and with reference to any relevant previous surgical pathology or cytopathology specimens. | Report when tissue submitted for evaluation |
| Core | PROVISIONAL PATHOLOGICAL STAGING | **FIGO (2023 edition) c,d,e**   * I Confined to the uterine corpus and ovaryf * IA Disease limited to the endometrium OR non-aggressive histological type, i.e., low grade endometrioid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease * IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium * IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI * IA3 Low grade endometrioid carcinomas limited to the uterus and ovaryf * IB Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSIg * IC Aggressive histological typesh limited to a polyp or confined to the endometrium * II Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion * IIA Invasion of the cervical stroma of non-aggressive histological types * IIB Substantial LVSIg of non-aggressive histological types * IIC Aggressive histological typesh with any myometrial involvement * III Local and/or regional spread of the tumour of any histological subtype * IIIA Invasion of uterine serosa, adnexa, or both by direct extension or metastasis * IIIA1 Spread to ovary or fallopian tube (except when   meeting stage IA3 criteria)f   * IIIA2 Involvement of submesothelial fibroconnective tissue or the mesothelial layeri or spread through the uterine serosa * IIIB Metastasis or direct spread to the vagina and/or to the   parametria or pelvic peritoneum   * IIIB1 Metastasis or direct spread to the vagina and/or * the parametria * IIIB2 Metastasis to the pelvic peritoneum * IIIC Metastasis to the pelvic or para-aortic lymph nodes or bothj * IIIC1 Metastasis to the pelvic lymph nodes * IIIC1i Micrometastasis * IIIC1ii Macrometastasis * IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes * IIIC2i Micrometastasis * IIIC2ii Macrometastasis * IV Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastsis * IVA Invasion of the bladder mucosa and/or the intestinal/ bowel mucosa * IVB Abdominal peritoneal metastasis beyond the pelvis * IVC Distant metastasis, including metastasis to any extra-or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone   **TNM Staging (UICC TNM 8th edition 2016)k**  **TNM Descriptors**  (only if applicable)   * m - multiple primary tumours * r - recurrent * y - post-therapy   **Primary tumour (pT)**   * TXl Primary tumour can not be assessed * T0 No evidence of primary tumour * T1 Tumour confined to the corpus uterim * T1a Tumour limited to endometrium or invading less than half of myometrium * T1b Tumour invades one half or more of myometrium * T2 Tumour invades cervical stroma, but does not extend beyond the uterus * T3 Local and/or regional spread as specified here: * T3a Tumour invades the serosa of the corpus uteri or adnexae (direct extension or metastasis) * T3b Vaginal or parametrial involvement (direct extension   or metastasis)   * T4 Tumour invades bladder/bowel mucosan   **Regional lymph nodes (pN)**   * NXl Regional lymph nodes cannot be assessed * N0 No regional lymph node metastasis * N1 Metastasis to pelvic lymph nodeso * N2 Metastasis to para-aortic lymph nodes with or * without metastasis to pelvic lymph nodeso | The pathological staging must be provided on the pathology report and is therefore a core element. The term ‘provisional pathological staging’ is used in this dataset to indicate that the stage that is provided may not represent the final tumour stage which should be determined at the multidisciplinary tumour board meeting where all the pathological, clinical and radiological features are available.[1-4](#_ENREF_1)  Either FIGO (2009 or 2023) *or* TNM staging, *or* both, can be used depending on local preferences.[1-4](#_ENREF_1) The FIGO staging system is used internationally and is the system used in most clinical trials and research studies. However, the revised 2023 FIGO staging system[4](#_ENREF_4) is currently in the process of being incorporated and is not yet in widespread use, with many jurisdictions still using the FIGO 2009 staging system. The Union for International Cancer Control (UICC) or American Joint Committee on Cancer (AJCC) versions of TNM are used or required in many parts of the world.[2](#_ENREF_2),[3](#_ENREF_3)  A tumour should be staged following diagnosis using various appropriate modalities (clinical, radiological, pathological). While the original tumour stage should not be altered following treatment, TNM systems allow staging to be performed on a resection specimen following non-surgical treatment (for example chemotherapy, radiotherapy); in such cases, if a stage is being provided on the pathology report (this is optional), it should be prefixed by ‘y’ to indicate that this is a post-therapy stage.  The revised 2023 FIGO staging system[4](#_ENREF_4) incorporates many of the core elements of the ICCR Endometrial cancer dataset 5th Edition. The reference document TNM Supplement: A commentary on uniform use, 5th edition (C Wittekind et al. editors) may be of assistance when staging.[5](#_ENREF_5)References 1 Amant F, Mirza MR, Koskas M and Creutzberg CL (2018). Cancer of the corpus uteri. *Int J Gynaecol Obstet* 143 Suppl 2:37-50.  2 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th Edition*, Springer, New York.  3 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *UICC TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.  4 Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N (2023). FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 162(2):383-394.  5 Wittekind C, Brierley JD, Lee A and van Eycken E (eds) (2019). *TNM Supplement: A Commentary on Uniform Use, 5th Edition*, Wiley, USA. | Note that permission to publish the FIGO cancer staging tables may be needed in your implementation. It is advisable to check with FIGO.  Note that permission to publish the TNM cancer staging tables may be needed in your implementation. It is advisable to check.  c Reprinted from Int J Gynaecol Obstet., DOI: 10.1002/ijgo.14923), Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, Lindemann K, Mutch D and Concin N, FIGO staging of endometrial cancer:2023, pages 1-12, 2023, with permission from Wiley.  Endometrial cancer is surgically staged and pathologically examined. In all stages, the grade of the lesion, the histological type and LVSI must be recorded. If available and feasible, molecular classification testing (POLEmut, MMRd, NSMP, p53abn) is encouraged in all patients with endometrial cancer for prognostic risk-group stratification and as factors  that might influence adjuvant and systemic treatment decisions.  e In early endometrial cancer, the standard surgery is a total hysterectomy  with bilateral salpingo-oophorectomy via a minimally invasive laparoscopic approach. Staging procedures include infracolic omentectomy in specific histological subtypes, such as serous and undifferentiated endometrial  carcinoma, as well as carcinosarcoma, due to the high risk of microscopic  omental metastases. Lymph node staging should be performed in patients  with intermediate-high/high-risk patients. Sentinel lymph node (SLN) biopsy is an adequate alternative to systematic lymphadenectomy for staging proposes. SLN biopsy can also be considered in low-/low-intermediate-risk  patients to rule out occult lymph node metastases and to identify disease truly confined to the uterus. Thus, the ESGO-ESTRO-ESP guidelines allow an approach of SLN in all patients with endometrial carcinoma, which is  endorsed by FIGO. In assumed early endometrial cancer, an SLN biopsy  in an adequate alternative to systematic lymphadenectomy in high-intermediate  and high-risk cases for the purpose of lymph node staging and can also be considered in low-/intermediate-risk disease to rule out occult  lymph node metastases. An SLN biopsy should be done in association with  thorough (ultrastaging) staging as it will increase the detection of low-volume  disease in lymph nodes.  Low grade EECs involving both the endometrium and the ovary are considered to have a good prognosis, and no adjuvant treatment is recommended if all the below criteria are met. Disease limited to low grade endometrioid carcinomas involving the endometrium and ovaries (Stage IA3) must be distinguished from extensive spread of the endometrial carcinoma to the ovary (Stage IIIA1), by the following criteria: (1) no  more than superficial myometrial invasion is present (<50%); (2) absence  of extensive/substantial LVSI; (3) absence of additional metastases; and  (4) the ovarian tumour is unilateral, limited to the ovary, without capsule  invasion/rupture (equivalent to pT1a).  g LVSI as defined in WHO 2021: extensive/substantial, ≥5 vessels involved.  h Grade and histological type.  i The consensus of the dataset authors was to replace ‘uterine subserosa’  with ‘submesothelial fibroconnective tissue or the mesothelial layer’.  j Micrometastases are considered to be metastatic involvement (pN1 (mi)).  The prognostic significance of isolated tumour cells (ITCs) is unclear. The presence of ITCs should be documented and is regarded as pN0(i+).  According to TNM8, macrometastases are >2 mm in size, micrometastases  are >0.2–2 mm and/or >200 cells, and isolated tumour cells are <0.2 mm and ≤200 cells.(Ref: Blakely et al, 2019) Based on staging established by FIGO and the American Joint Committee on Cancer (AJCC). AJCC Cancer Staging Manual. 8th ed. New York: Springer, 2017.  k Reproduced with permission. Source: UICC TNM Classification of  Malignant Tumours, 8th Edition, eds by James D. Brierley, Mary K.  Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley (incorporating any errata published up until 8th July 2024).  l TX and NX should be used only if absolutely necessary.  m Endocervical glandular involvement only should be considered as Stage I.  n The presence of bullous oedema is not sufficient evidence to classify as T4.  o Positive cytology has to be reported separately without changing the stage. |

**Tables**

**Table 1: World Health Organization classification of tumours of the uterine corpus.**[**1**](#_ENREF_1)

| **Descriptor** | **ICD-O codesa** |
| --- | --- |
| **Endometrial epithelial tumours and precursors** |  |
| Endometrial hyperplasia without atypia |  |
| Atypical hyperplasia of the endometrium | 8380/2 |
| Endometrioid adenocarcinoma NOS | 8380/3 |
| *POLE*-ultramutated endometrioid carcinomab |  |
| Mismatch repair-deficient endometrioid carcinomab |  |
| P53-mutant endometrioid carcinomab |  |
| No specific molecular profile (NSMP) endometrioid carcinomab |  |
| Serous carcinoma NOS | 8441/3 |
| Clear cell adenocarcinoma NOS | 8310/3 |
| Carcinoma, undifferentiated, NOS | 8020/3 |
| Mixed cell adenocarcinoma | 8323/3 |
| Mesonephric adenocarcinoma | 9110/3 |
| Squamous cell carcinoma NOS | 8070/3 |
| Mucinous carcinoma, gastric (gastrointestinal)-type | 8144/3 |
| Mesonephric-like adenocarcinoma | 9113/3 |
| Carcinosarcoma NOS | 8980/3 |
| Neuroendocrine tumour NOS | 8240/3 |

a These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).[21](#_ENREF_21) Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Subtype labels are indented.

Incorporates all relevant changes from the 5th edition Corrigenda July 2024.[2](#_ENREF_2)

b These molecular types apply to all endometrial carcinomas (not just endometrioid carcinomas).

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# References

1 WHO Classification of Tumours Editorial Board (2020). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4*. IARC Press, Lyon.

2 WHO Classification of Tumours Editorial Board (2024). *Female Genital Tumours, WHO Classification of Tumours, 5th Edition, Volume 4 - Corrigenda July 2024*. Available from: https://publications.iarc.fr/Book-And-Report-Series/Who-Classification-Of-Tumours/Female-Genital-Tumours-2020 (Accessed 18th July 2024).

21 Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin LH, Parkin DM, Whelan SL (eds) (2020). *International Classification of Diseases for Oncology, Third edition, Second revision ICD-O-3.2*. Available from: http://www.iacr.com.fr/index.php?option=com\_content&view=category&layout=blog&id=100&Itemid=577 (Accessed 10th July 2024).

**Table 2**

A white sheet with black lines

Description automatically generated

b If the actual number of lymph nodes examined or the number of positive nodes cannot be determined due, for example, to fragmentation, then this should be indicated in the response.

c Isolated tumour cells (≤0.2 mm and ≤200 cells).

d Micrometastasis (>0.2 mm and ≤2 mm); Macrometastasis (>2 mm).