Epithelial ovarian cancer

➢ **Acknowledgments**

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➢ **Abbreviations**

ASIR	Age Standardized Incidence Rate
AUC	Area under the curve
CCC	Clear cell carcinoma
CT	Computed tomography
EC	Endometrioid carcinoma
EHC	Egyptian Health Council
EOC	Epithelial Ovarian Carcinoma
ESMO	European Society of Medical Oncology

HGSC	High grade serous carcinoma
HIPEC	Hyperthermic intraperitoneal chemotherapy
ICS	Interval cytoreductive surgery
KFTs,	Kidney function tests
LFTs	Liver function tests
LGSC	Low grade serous carcinoma
MC	Mucinous carcinoma
NACT	Neoadjuvant chemotherapy
NCCN	National Comprehensive Cancer Network
NICE	National Institute of Health and Care Excellence
PCS	Primary cytoreductive surgery
TFIp	Treatment-free interval from last platinum
US	Ultrasound
WHO	World Health Organization

- **Executive Summary**

Diagnostic and Staging Work up	
The standard work-up for patients suspected of having EOC (Epithelial Ovarian Carcinoma) should include detailed history and clinical examination, LFTs, KFTs, serum CA-125, serum CEA and CA 19-9 in case of mucinous carcinoma and endoscopy if either or both are elevated, as well as transabdominal and transvaginal US (should be done by an expert examiner), as well as CT of thorax, abdomen and pelvis**.**	**Strong**
Pathological examination of adequate tumor sample from diagnostic biopsy or surgical specimen should be done. In case of the presence of pleural effusion, cytological assessment should be done.	**Strong**
The revised 2017 FIGO staging system for EOC should be used.	**Strong**
Management of early EOC (FIGO STAGE I-II)	
Surgical staging is recommended in presumed early-stage ovarian cancer for classification and recommendation of optimal systemic therapy.	**Strong**
The aim of surgery for early EOC is complete resection of the tumour and to undertake adequate staging, which should be performed by midline laparotomy and should include: ○ Inspection and palpation of the whole abdominal cavity ○ Peritoneal washing with cytological examination ○ Biopsies from all visible lesions and all abdominal fields ○ Bilateral salpingo-oophorectomy ○ Hysterectomy ○ Omentectomy ○ Appendicectomy in MC ○ Systematic pelvic and para-aortic lymphadenectomy	**Strong**
Fertility-sparing surgery should be considered in young patients, but always after full discussion with the patient about potential risks.	**Strong**
Patients with any stage IA histotype or stage IC1-2 with unilateral ovarian involvement and favorable histology (i.e. low-grade tumors) would be amenable to contralateral ovary and uterus preservation, in combination with the other recommended surgical staging procedures.	**Strong**

Adjuvant chemotherapy in early-stage ovarian cancer is generally recommended for FIGO stage I-IIB (see exceptions below), either paclitaxel-carboplatin or carboplatin alone (six cycles).	**Strong**
The benefit of adjuvant chemotherapy is uncertain and can be considered as optional for: o Low grade serous carcinoma (LGSC) stage IB-IC o Clear cell carcinoma (CCC) stage IA-IC1 o Low-grade endometrioid carcinoma (EC) stage IB-IC o Expansile mucinous carcinoma (MC) stage IC o Infiltrative MC stage IA	**Conditional**
For patients receiving paclitaxel-carboplatin, a minimum of three cycles are recommended except for high grade serous carcinoma (HGSC) /high-grade endometrioid carcinoma (EC) or any stage IC-II regardless of histotype, for which six cycles should be administered.	**Strong**
Adjuvant chemotherapy is not recommended in completely staged patients with LGSC stage IA, low-grade EC stage IA or expansile MC stage IA-IB.	**Conditional**
Management of advanced EOC (FIGO STAGE III-IV)	
Patients with advanced EOC should be evaluated for primary cytoreductive surgery (PCS) by a specialized team, with the aim of achieving complete cytoreduction (absence of all visible residual disease).	**Strong**
When complete cytoreductive surgery is feasible, PCS is recommended; otherwise, obtaining adequate biopsy tissue for histology and molecular testing is recommended.	**Strong**
PCS should aim to maximal surgical effort and may require intestinal resection, diaphragmatic and peritoneal stripping, splenectomy and removal of bulky para-aortic lymph nodes and, in some cases, extra-abdominal disease.	**Strong**
We recommend against systematic lymphadenectomy in patients with macroscopic complete resection and clinically negative nodes as this may lead to unnecessarily increases the rate of post-operative complications and mortality and should not be done. .	**Strong**
PCS is also recommended in patients with less chemo-sensitive subtypes (e.g. MC or LGSC), even if uncertainty about achieving complete resection exists and a small residual tumour (<1 cm) is likely to remain.	**Strong**
When complete cytoreductive surgery is not feasible, neoadjuvant chemotherapy (NACT) for three cycles followed by interval cytoreductive surgery (ICS) and three cycles of paclitaxel-carboplatin are recommended, ± staging laparoscopy.	**Strong**
Consider the use of bevacizumab in the neoadjuvant setting, before interval cytoreductive surgery (ICS).	**Conditional**
When ICS is not possible, and in the absence of overt disease progression, three additional cycles of paclitaxel-carboplatin alone or with bevacizumab are recommended.	**Strong**

Paclitaxel (175 mg/m2)-carboplatin (AUC 5-6) every 3 weeks for six cycles is the standard first-line chemotherapy in advanced ovarian cancer.	**Strong**
We recommend the schedule of weekly chemotherapy with paclitaxel (60 mg/m2)-carboplatin (AUC 2) as an alternative in frail patients.	**Strong**
Bevacizumab may be considered in addition to paclitaxel-carboplatin in high-risk patients, (defined as patients with stage III and macroscopic residual tumour >1 cm or stage IV).	**Conditional**
Bevacizumab dose, if given, should be 7.5 mg/kg and the duration of treatment is 12 months.	**Strong**
Intraperitoneal chemotherapy and hyperthermic intraperitoneal chemotherapy (HIPEC) are not considered a standard of care in first-line treatment.	**Conditional**
Maintenance with anti-estrogen therapy after first-line platinum-based chemotherapy can be considered in ER positive low grade serous carcinoma (LGSC) or grade I endometrioid carcinoma.	**Conditional**
Other recommended regimens (other than paclitaxel/carboplatin regime) such as docetaxel/carboplatin or 5FU/ calcium leucovorin/oxaliplatin or Capecitabin/Oxaliplatin specially in mucinous carcinoma may be used	**Conditional**
Management of recurrent EOC.	
The following should be assessed when selecting treatment for patients with recurrent disease: o Histotype o Number of prior lines of treatment o Exposure and response to prior treatment o TFIp (treatment-free interval from last platinum) o Possibility of achieving a complete secondary surgical cytoreduction o Residual chemotherapy toxicity o The patient's general condition and preferences	**Good Practice Statement**
Patients with first relapse of ovarian cancer after >6 months of last platinum administration should be evaluated by a team experienced in surgery for ovarian cancer to identify potential candidates for surgical cytoreduction.	**Strong**
Patients who have previously responded to platinum without early symptomatic relapses (after >6 months) should be treated with either a platinum-based doublet (paclitaxel or gemcitabine with bevacizumab) or single agent (liposomal doxorubicin). The selection should be based on safety and patient preference.	**Strong**
If combination therapy is contraindicated, carboplatin monotherapy remains an option.	**Strong**
Treatment is usually recommended for four to six cycles.	**Strong**

Bevacizumab should be continued until disease progression (symptomatic) or the next line of treatment is started, as continuation of bevacizumab beyond progression has not been evaluated in the recurrent setting.	**Strong**
Platinum rechallenge following treatment with a platinum regimen (monotherapy or combination) should be considered if the tumour is not refractory or resistant.	**Strong**
Patients with relapsed EOC for whom platinum is not an option should be defined by: o Proven refractory (progression during platinum) o Expected resistance (early symptomatic progression post-platinum, response to rechallenge unlikely) o Platinum intolerance o Patient choice o QoL issues	**Good Practice Statement**
For patients who are not candidates to receive platinum, integrating palliative care early in the treatment pathway is strongly recommended.	**Good Practice Statement**
Single-agent non-platinum options that are recommended include weekly paclitaxel, a combination of gemcitabine and oral etoposide, navelbine, or metronomic cyclophosphamide.	**Strong**
Bevacizumab should be recommended in combination with weekly paclitaxel, or topotecan in patients without contraindications to bevacizumab (e.g. increased risk of intestinal fistulae, history of bowel obstruction or serosal invasion).	**Strong**
Hormonal therapy ((e.g. aromatase inhibitors, tamoxifen or luteinising hormone-releasing hormone agonists) is recommended for relapsed LGSC with ER and/or PgR expression.	**Strong**
Surveillance	
Surveillance of ovarian cancer patients can include CA-125 determination, physical examination and CT scan evaluation, first year: every three months, second year: every six months, and annually thereafter.	**Good Practice Statement**

- **Introduction**

In Egypt, there was an estimated 3070 new cases of ovarian cancer with an ASIR of 6.4/100 000 normal population and ranks the 4th most common cancer among females (4%). There were 1944 deaths because of this disease based on GLOBOCAN 2022.

- **Purpose and scope**

These guidelines are developed to improve the quality of care for ovarian

cancer via providing a uniform standard of care across the country to help in early diagnosis, treatment and follow up for epithelial ovarian cancer so more optimal treatment options and improved clinical outcomes.

- **Target audience**

Clinicians who are involved in the care and treatment of patients with Ovarian cancer, include medical oncologists, radiation oncologists, clinical oncologist, gynecologists, onco-surgeons, radiologists, pathologists, and palliative care specialists.

- **Methodology**

A comprehensive search for guidelines was undertaken to identify the most relevant guidelines to consider for adaptation. Inclusion/exclusion criteria followed in the search and retrieval of guidelines to be adapted:

- Selecting only evidence-based guidelines (guidelines must include a report on systematic literature searches and explicit links between individual recommendations and their supporting evidence). - Selecting only national and/or international guidelines.
- Specific range of dates for publication (using Guidelines published or updated 2015 and later).
- Selecting peer reviewed publications only.
- Selecting guidelines written in English language.
- Excluding guidelines written by a single author not on behalf of an organization to be valid and comprehensive, a guideline ideally requires multidisciplinary input.
- Excluding guidelines published without references as the panel needs to know whether a thorough literature review was conducted and whether current evidence was used in the preparation of the recommendations.

All retrieved Guidelines were screened and appraised using AGREE II instrument (www.agreetrust.org) by at least two members. the panel decided a cutoff point or rank the guidelines (any guideline scoring above 50% on the rigor dimension was retained)

The NCCN (National Comprehensive Cancer Network), ESMO (European Society of Medical Oncology), NICE (National Institute of Health and Care Excellence) guidelines are the main sources used while formulating the national guidelines for ovarian cancer (1-3).

- **Evidence assessment**

According to WHO handbook for Guidelines we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations. GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations. Detailed information on GRADE is available through the on the following sites:

. GRADE working group: http://www.gradeworkingroup.org

. GRADE online training modules: http://cebgrade.mcmaster.ca/

. GRADE profile software: http://ims.cochrane.org/revman/gradepro

Table 1: Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

Table 2: Significance of the four levels of evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Table 3: Factors that determine How to upgrade or downgrade the quality of evidence

Downgrade in presence of	Upgrade in presence of
Study limitations -1 Serious limitations -2 Very serious limitations	Dose-response gradient +1 Evidence of a dose-response gradient
Consistency -1 Important inconsistency	Direction of plausible bias +1 All plausible confounders would have reduced the effect
Directness -1 Some uncertainty -2 Major uncertainty	Magnitude of the effect +1 Strong, no plausible confounders, consistent and direct evidence
Precision -1 Imprecise data	+2 Very strong, no major threats to validity and direct evidence
Reporting bias -1 High probability of reporting bias	

- **The strength of the recommendation**

The strength of a recommendation communicates the importance of adherence to the recommendation:

Strong recommendations: With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional recommendations: These are made when there is greater uncertainty about the four factors above (Table 2) or if local adaptation must account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

When not to make recommendations; when there is lack of evidence on the effectiveness of an intervention, it may be appropriate not to make a recommendation.

➢ **Recommendations**

Diagnostic and Staging Work up

- The standard work-up for patients suspected of having EOC (Epithelial Ovarian Carcinoma) should include detailed history and clinical examination, LFTs, KFTs, serum CA-125, serum CEA and CA 19-9 in case of mucinous carcinoma and endoscopy if either or both are elevated, as well as transabdominal and transvaginal US (should be done by an expert examiner), as well as CT of thorax, abdomen and pelvis**.**

Strong recommendation, low grade evidence (4,5).

- Pathological examination of adequate tumor sample from diagnostic biopsy or surgical specimen should be done. In case of the presence of pleural effusion, cytological assessment should be done.

Strong recommendation, low grade evidence (4).

- The revised 2017 FIGO staging system for EOC should be used.

Strong recommendation, high grade evidence (6).

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Management of early EOC (FIGO STAGE I-II)

- Surgical staging is recommended in presumed early-stage ovarian cancer for classification and recommendation of optimal systemic therapy.

Strong recommendation, moderate grade evidence (6).

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- The aim of surgery for early EOC is complete resection of the tumour and to undertake adequate staging, which should be performed by midline laparotomy and should include:
    - Inspection and palpation of the whole abdominal cavity
    - Peritoneal washing with cytological examination
    - Biopsies from all visible lesions and all abdominal fields
    - Bilateral salpingo-oophorectomy
    - Hysterectomy
    - Omentectomy
    - Appendicectomy in MC
    - Systematic pelvic and para-aortic lymphadenectomy

Strong recommendation, low grade evidence (7).

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- Fertility-sparing surgery should be considered in young patients, but always after full discussion with the patient about potential risks.

Strong recommendation, low grade evidence (8).

- Patients with any stage IA histotype or stage IC1-2 with unilateral ovarian involvement and favorable histology (i.e. low-grade tumors) would be amenable to contralateral ovary and uterus preservation, in combination with the other recommended surgical staging procedures.

Strong recommendation, low grade evidence (8).

- Adjuvant chemotherapy in early-stage ovarian cancer is generally recommended for FIGO stage I-IIB (see exceptions below), either paclitaxel-carboplatin or carboplatin alone (six cycles).

Strong recommendation, high grade evidence (9-11).

- The benefit of adjuvant chemotherapy is uncertain and can be considered as optional for:
    - o Low grade serous carcinoma (LGSC) stage IB-IC
    - o Clear cell carcinoma (CCC) stage IA-IC1
    - o Low-grade endometrioid carcinoma (EC) stage IB-IC
    - o Expansile mucinous carcinoma (MC) stage IC
    - o Infiltrative MC stage IA

Conditional recommendation, low grade evidence (12-14).

- For patients receiving paclitaxel-carboplatin, a minimum of three cycles are recommended except for high grade serous carcinoma (HGSC) /high-grade endometrioid carcinoma (EC) or any stage IC-II regardless of histotype, for which six cycles should be administered

Strong recommendation, high grade evidence (15,16).

- Adjuvant chemotherapy is not recommended in completely staged patients with LGSC stage IA, low-grade EC stage IA or expansile MC stage IA-IB.

Conditional recommendation, moderate grade evidence (10,12-14).

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Management of advanced EOC (FIGO STAGE III-IV)

- Patients with advanced EOC should be evaluated for primary cytoreductive surgery (PCS) by a specialized team, with the aim of achieving complete cytoreduction (absence of all visible residual disease).

Strong recommendation moderate grade evidence (7,17,18).

- When complete cytoreductive surgery is feasible, PCS is recommended; otherwise, obtaining adequate biopsy tissue for histology and molecular testing is recommended.

Strong recommendation, low grade evidence (19).

- PCS should aim to maximal surgical effort and may require intestinal resection, diaphragmatic and peritoneal stripping, splenectomy and removal of bulky para-aortic lymph nodes and, in some cases, extra-abdominal disease.

Strong recommendation, low grade evidence (17,18).

- We recommend against systematic lymphadenectomy in patients with macroscopic complete resection and clinically negative nodes as this may lead to unnecessarily increases the rate of post-operative complications and mortality and should not be done.

Strong recommendation, low grade evidence (20).

- PCS is also recommended in patients with less chemo-sensitive subtypes (e.g. MC or LGSC), even if uncertainty about achieving complete resection exists and a small residual tumour (<1 cm) is likely to remain.

Strong recommendation, low grade evidence (19).

- When complete cytoreductive surgery is not feasible, neoadjuvant chemotherapy (NACT) for three cycles followed by interval cytoreductive surgery (ICS) and three cycles of paclitaxel-carboplatin are recommended, ± staging laparoscopy.

Strong recommendation, high grade evidence (21,22).

- Consider the use of bevacizumab in the neoadjuvant setting, before interval cytoreductive surgery (ICS).

Conditional recommendation, moderate grade evidence (23-27).

- When ICS is not possible, and in the absence of overt disease progression, three additional cycles of paclitaxel-carboplatin alone or with bevacizumab are recommended.

Strong recommendation, high grade evidence (21,22).

- Paclitaxel (175 mg/m2)-carboplatin (AUC 5-6) every 3 weeks for six cycles is the standard first-line chemotherapy in advanced ovarian cancer.

Strong recommendation, high grade evidence (28,29).

- We recommend the schedule of weekly chemotherapy with paclitaxel (60 mg/m2)-carboplatin (AUC 2) as an alternative in frail patients.

Strong recommendation, high grade evidence (30).

- Bevacizumab may be considered in addition to paclitaxel-carboplatin in high-risk patients, (defined as patients with stage III and macroscopic residual tumour >1 cm or stage IV).

Conditional recommendation, high grade evidence (31).

- Bevacizumab dose, if given, should be 7.5 mg/kg and the duration of treatment is 12 months.

Strong recommendation, high grade evidence (31).

- Intraperitoneal chemotherapy and hyperthermic intraperitoneal chemotherapy (HIPEC) are not considered a standard of care in first-line treatment.

Conditional recommendation, high grade evidence (32,33).

- Maintenance with anti-estrogen therapy after first-line platinum-based chemotherapy can be considered in ER positive low grade serous carcinoma (LGSC) or grade I endometrioid carcinoma.

Conditional recommendation, very low grade evidence (34).

- Other recommended regimens (other than paclitaxel/carboplatin regime) such as docetaxel/carboplatin or 5FU/ calcium leucovorin/oxaliplatin or Capecitabin/Oxaliplatin specially in mucinous carcinoma may be used.

Conditional recommendation, high grade evidence (35,36).

Management of recurrent EOC

- The following should be assessed when selecting treatment for patients with recurrent disease:
  - o Histotype
  - o Number of prior lines of treatment
  - o Exposure and response to prior treatment
  - o TFIp (treatment-free interval from last platinum)
  - o Possibility of achieving a complete secondary surgical cytoreduction
  - o Residual chemotherapy toxicity
  - o The patient's general condition and preferences

Good Practice Statement

- Patients with first relapse of ovarian cancer after >6 months of last platinum administration should be evaluated by a team experienced in surgery for ovarian cancer to identify potential candidates for surgical cytoreduction.

Strong recommendation, high grade evidence (37-40).

- Patients who have previously responded to platinum without early symptomatic relapses (after >6 months) should be treated with either a platinum-based doublet (paclitaxel or gemcitabine with bevacizumab) or single agent (liposomal doxorubicin)
  The selection should be based on safety and patient preference.

Strong recommendation, high grade evidence (41,42).

- If combination therapy is contraindicated, carboplatin monotherapy should be used. Treatment is usually recommended for four to six cycles.

Strong recommendation, high grade evidence (43).

- Bevacizumab should be continued until disease progression (symptomatic) or the next line of treatment is started, as continuation of bevacizumab beyond progression has not been evaluated in the recurrent setting.

Strong recommendation, high grade evidence (44).

- Platinum rechallenge following treatment with a platinum regimen (monotherapy or combination) should be considered if the tumour is not refractory or resistant.

Strong recommendation, low grade evidence (45).

- Patients with relapsed EOC for whom platinum is not an option should be defined by:
  - o Proven refractory (progression during platinum)
  - o Expected resistance (early symptomatic progression post-platinum, response to rechallenge unlikely)
  - o Platinum intolerance
  - o Patient choice

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o QoL issues

Good Practice Statement

- For patients who are not candidates to receive platinum, integrating palliative care early in the treatment pathway is strongly recommended.

Good Practice Statement

- Single-agent non-platinum options that are recommended include weekly paclitaxel, a combination of gemcitabine and oral etoposide, navelbine, or metronomic cyclophosphamide.

Strong recommendation, high grade evidence (46-51).

- Bevacizumab should be recommended in combination with weekly paclitaxel, or topotecan in patients without contraindications to bevacizumab (e.g. increased risk of intestinal fistulae, history of bowel obstruction or serosal invasion).

Strong recommendation, high grade evidence (49).

- Hormonal therapy ((e.g. aromatase inhibitors, tamoxifen or luteinising hormone-releasing hormone agonists) is recommended for relapsed LGSC with ER and/or PgR expression.

Strong recommendation, high grade evidence (52).

Surveillance

Surveillance of ovarian cancer patients can include CA-125 determination, physical examination and CT scan evaluation, first year: every three months, second year: every six months, and annually thereafter.

Good Practice Statement

- **Clinical Indicators**
  - Visits every 2–4 months for 2 years, then 3–6 months for 3 years, then annually after 5 years
  - Physical exam including pelvic exam as clinically indicated
  - C/A/P CT, MRI, PET/CT, or PET (skull base to mid-thigh) as clinically indicated
  - CBC and chemistry profile as indicated
  - CA-125 or other tumor markers if initially elevated
- **Update of this guideline**

  This guideline will be updated whenever there is new evidence.

- **Research gaps**
  - Systematic inclusion of cost-benefit analyses in clinical trials with collection of health economic analysis such as incremental cost effectiveness ratio in order to facilitate clinical decision-making.
  - Predictive biomarkers: response to specific systemic targeted therapies and immunotherapy.
  - Improve models for pre-clinical testing of novel drugs.
  - Search for tools to assess quality of life and in clinical trials.
  - Dietary supplements, nutritional counselling, physical activity recommendations and psychological support as part of an integrative healthcare approach to care for people with ovarian cancer.

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- **Annex.**

Table 1. FIGO staging system for EOC

Stage I: Tumour confined to ovaries or fallopian tube(s)	
IA	Tumour limited to one ovary (capsule intact) or fallopian tube, without tumour on ovarian or fallopian tube surface and without malignant cells in the ascites or peritoneal washings
IB	Tumour limited to both ovaries (capsules intact) or fallopian tubes, without tumour on ovarian or fallopian tube surface and without malignant cells in the ascites or peritoneal washings
IC	Tumour limited to one or both ovaries or fallopian tubes, with any of the following:
IC1	Surgical spill
IC2	Capsule ruptured before surgery or tumour on ovarian or fallopian tube surface
IC3	Malignant cells in the ascites or peritoneal washings
Stage II: Tumour involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer	
IIA	Extension and/or implants on uterus and/or fallopian tubes and/or ovaries
IIB	Extension to other pelvic intraperitoneal tissues
Stage III: Tumour involves one or both ovaries or fallopian tubes or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	
IIIA1	Positive retroperitoneal lymph nodes only (cytologically or histologically proven):
IIIA1(i)	Metastasis ≤10 mm in greatest dimension
IIIA1(ii)	Metastasis >10 mm in greatest dimension
IIIA2	Microscopic extra-pelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
IIIB	Macroscopic peritoneal metastasis beyond the pelvis ≤2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
IIIC	Macroscopic peritoneal metastasis beyond the pelvis >2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumour to capsule of liver and spleen without parenchymal involvement of either organ)
Stage IV: Distant metastasis excluding peritoneal metastases	
IVA	Pleural effusion with positive cytology
IVB	Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

EOC, epithelial ovarian cancer; FIGO, International Federation of Gynecology and Obstetrics.