OVARIAN CARCINOMA

National Standard Treatment Guideline

Ministry of Health
Republic of Maldives

ADB

JFPR
Japan Fund for Prosperous and Resilient Asia and the Pacific

From the People of Japan

World Health Organization
Maldives

National Standard Treatment Guidelines

- Acid Peptic Disease
- Acute Anxiety
- Acute Pancreatitis
- Acute Psychosis
- Acute kidney Injury
- Arrhythmia
- Chronic Liver Disease
- Chronic Pancreatitis
- Chronic kidney disease
- Congenital Heart Diseases
- Dementia
- Depression
- Diabetes Mellitus Type 1
- Diabetes Mellitus Type 2
- Gestational Diabetes
- Epilepsy
- Heart Failure
- Hyponatremia
- Hypernatremia
- Hypokalemia
- Hyperkalemia
- Interstitial Lung Disease
- Liver Failure
- Obesity
- Obstructive Sleep Apnoea
- Osteoarthritis
- Ovarian Cancer
- Pneumonia
- Stroke
- Upper Gastrointestinal bleed
- Unstable Angina

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GUIDELINES DEVELOPMENT METHODOLOGY

The development of the Maldives Standard Treatment Guidelines (STGs) followed a structured, evidence-informed, and consensus-driven methodology adapted from internationally accepted guideline-development standards and the Delhi Society for Promotion of Rational Use of Drugs (DSPRUD) model. The process combined systematic evidence retrieval, critical appraisal, contextual adaptation, and multidisciplinary expert review to ensure feasibility, clinical relevance, and national ownership.

1. Determining Scope and Priority Conditions

Priority clinical conditions were identified through consultation with national programme managers, specialty clinicians, and health-system stakeholders. Selection criteria included: (i) major causes of morbidity and mortality, (ii) observed variation in clinical practice or prescribing patterns, (iii) potential to improve patient outcomes, and (iv) the feasibility of implementation across health-facility levels in Maldives. The final list of diseases reflected national epidemiology, service-delivery capacity, and essential-medicine availability.

2. Identification of Existing Evidence and Source Guidelines

A targeted search strategy was used to identify high-quality existing clinical guidelines. Searches were conducted across international guideline repositories (e.g., WHO, NICE, SIGN and other intergovernmental bodies, international and national guideline repositories, specialty societies and professional associations.

3. Quality Appraisal of Source Guidelines

Retrieved guidelines were screened for transparency of development, methodological rigour, clarity of recommendations, applicability to health-system reality, editorial independence. Guidelines were included if they met the Institute of Medicine (IOM) definition of a clinical guideline and addressed treatment or management of priority conditions. Guidelines that did not meet minimum quality standards, review articles, diagnostic criteria, or technical standards were excluded.

4. Adoption, Adaptation, and Contextualization

The guideline-development team employed an adopt–adapt–contextualize model:

- **Adoption**: High-quality recommendations that aligned with Maldivian health-system realities were retained without modification.
- **Adaptation**: Recommendations were modified when local considerations such as diagnostic capacity, medicine availability, workforce skills, referral pathways, or cost constraints affected feasibility.

- **Contextualization**: Where evidence was absent or inconclusive, conditional recommendations were formulated based on expert consensus, with explicit consideration of pragmatism, safety, and local workflows.
  Medicines were selected in alignment with the Maldives National Essential Medicines List (NEML), based on suitability, efficacy, safety, and availability.

5. Expert Consensus and Multidisciplinary Input

Draft recommendations were initially prepared by experts from the DSPRUD, India, providing a strong methodological foundation for the process. Building on this, a collaborative and participatory process brought together clinicians from internal medicine, paediatrics, obstetrics-gynaecology, surgery, emergency medicine, endocrinology, cardiology, general practitioners, and public health representing different levels of healthcare. Consensus was achieved through moderated discussions, iterative revisions, and resolution of divergent views. For topics lacking strong evidence, recommendations were derived from expert clinical judgment grounded in extensive practice experience.

6. Drafting, Peer Review, and Validation

Each guideline section was organized in a standard format including key clinical features, essential investigations, non-pharmacological management, pharmacological therapy (with step-up/step-down options where relevant), referral criteria, paediatric considerations, and follow-up requirements. Drafts were peer-reviewed by senior clinicians and national experts. Reviewer comments were systematically integrated to strengthen clarity, accuracy, and applicability.

7. Addressing Conflicts of Interest

All contributors declared the absence of conflicts of interest. Individuals with potential or perceived conflicts were excluded from authorship or decision-making roles.

8. Updating and Future Revisions

The STGs were conceptualized as a living document. Future updates will incorporate new scientific evidence, changes in essential-medicine availability, national programme priorities, and user feedback from clinicians. Periodic review cycles will ensure the continued relevance and reliability of recommendations.

9. Distinctive Features of the Guidelines

Developed through a collaborative process involving a large group of multidisciplinary experts from different levels of healthcare, the guidelines incorporate the following distinctive features:

- **Diagnostic Assumption and Confirmation**: While assuming that an initial diagnosis has been established by the healthcare provider, the guidelines provide essential information for confirming diagnoses. This includes a comprehensive overview of major signs and symptoms, descriptions of confirmatory tests, and clear guidance on practices that are prohibited, discouraged, or unreliable—promoting evidence-based medicine supported by relevant references.
- **Comprehensive Treatment Approach**: The guidelines offer a systematic, up-to-date framework for managing medical conditions across the continuum of care. They begin at the primary care level and extend to secondary and tertiary care, incorporating protocols for treatment response assessment and referral criteria as integral components.
- **Diverse Treatment Modalities**: Recommendations encompass both non-pharmacological and pharmacological interventions and surgical intervention where applicable, providing flexibility for individualized treatment plans. Cautionary notes are included where necessary to ensure safe and effective use of therapies.
- **Assessment and Referral Criteria**: Clear criteria and goals for evaluating patient response to treatment are provided, along with guidance on when referral to higher levels of care is warranted ensuring continuity and comprehensiveness in patient management.

ACKNOWLEDGEMENTS

The Government of the Republic of Maldives is committed to ensuring universal access to quality health services for all citizens. The Constitution of Maldives mandates the progressive realization of rights, including the right to good standards of health care for the population. In line with this national commitment, standardized quality health services are regarded as the foundation of a strong and equitable healthcare system.

This important work would not have been possible without the cooperation and support of many individuals and institutions. We express our sincere appreciation to the Honourable Minister of Health, Abdullah Nazim Ibrahim, for his leadership, commitment, and continuous guidance throughout the development process. We are grateful to WHO and ADB for their significant contribution, support, and technical assistance.

Our heartfelt gratitude is extended to the technical lead and editor, Dr. Sangeeta Sharma, Professor, Neuropsychopharmacology, IHBAS and President, Delhi Society for Promotion of Rational Use of Drugs (DSPRUD), and her team. We express our deepest appreciation to the Maldivian and DSPRUD experts and contributors who played a pivotal role in this process. Their technical expertise and dedication to adapt the standards to the Maldivian context have been instrumental in the development and finalization of these guidelines. The time, experience, generous sharing of knowledge and insights contributed by all parties have not only enriched the work but also have been invaluable in making these standards practical, locally acceptable, and aligned with the needs of the resident population.

It is important to acknowledge the immense efforts, involvement, timely coordination, collaboration, and dedication of the Quality Assurance and Regulation Division team who made it possible for these Clinical Treatment Guidelines to come into existence.

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OVARIAN CARCINOMA

QUICK REFERENCE GUIDE

Definitions & different types

- Ovarian carcinoma refers to malignant tumors arising from the epithelial lining of the ovary, fallopian tube, or primary peritoneum.
- Epithelial ovarian cancer (EOC) account for around 85–90% of all ovarian malignancies, with the remaining cases comprising germ cell and sex-cord stromal tumors.
- Histological subtypes include high-grade serous carcinoma (the most prevalent), low-grade serous, endometrioid, clear cell, and mucinous carcinoma. Each subtype carries distinct molecular and clinical features, but all share an origin in the surface epithelium or its Müllerian derivatives.
- The term “epithelial ovarian cancer” therefore encompasses tumors that, despite varied morphology, follow common patterns of spread along peritoneal surfaces and lymphatic channels.

Causes, Risk factors & Triggers

- **Genetic:** BRCA1/2, Lynch (MLH1/MSH2/MSH6/PMS2).
- **Hormonal/gynecologic:** nulliparity, early menarche/late menopause, endometriosis (clear cell/endometrioid).
- **Metabolic/other**: age, obesity.
- **Protective:** combined oral contraceptive pills (OCPs), breastfeeding, parity, opportunistic salpingectomy.

Evaluation for Diagnosis

- **Clinical features:** abdominal/pelvic pain, bloating, early satiety, ↑abdominal girth, urinary urgency/frequency, abnormal bleeding, VTE, ascites.
- **Exam:** pelvic/adnexal mass, nodularity, ascites, pleural effusion.
- **Labs:** CA-125 (esp. in postmenopausal women), HE4 (Human Epididymis Protein 4) if available, β-hCG (beta human chorionic gonadotropin), AFP (alpha-fetoprotein), LDH (lactate dehydrogenase) in suspected germ cell tumors, CBC (complete blood count), CMP (comprehensive metabolic panel), pregnancy test in reproductive-age women.
- **Risk tools:** O-RADS (Ovarian-Adnexal Reporting and Data System (Ultrasound / MRI), RMI (Risk of Malignancy Index), ROMA (Risk of Ovarian Malignancy Algorithm: CA-125 + HE4).
- **Imaging:** Transvaginal ultrasound (with IOTA-International Ovarian Tumor Analysis-features), CT (computed tomography) chest/abdomen/pelvis for staging; CXR (chest X-ray)/US (ultrasound) if CT not available.
- **Confirmation:** histopathology after primary surgery or image-guided biopsy/paracentesis cytology if unresectable or neoadjuvant planned.

- **Molecular testing:** all epithelial cancers - BRCA germline and somatic, HRD (homologous recombination deficiency), MMR (mismatch repair)/ MSI (microsatellite instability) status.

Classification / severity assessment criteria

- FIGO (International Federation of Gynecology and Obstetrics) staging:
  - Stage I: confined to ovary/fallopian tube.
  - Stage II: pelvic extension.
  - Stage III: peritoneal spread/ retroperitoneal nodes.
  - Stage IV: distant metastasis.
- Histologic grade and subtype.
- Performance status and residual disease after cytoreduction guide prognosis.

Differential Diagnosis

Benign cysts, endometrioma, tubo-ovarian abscess, ectopic pregnancy, uterine fibroids, GI malignancy (Krukenberg), ascites from liver disease/ heart failure, Meigs syndrome.

Management Goals & principles

- Accurate staging and maximal cytoreduction (aim: no gross residual).
- Deliver effective systemic therapy; personalize maintenance by biology (BRCA/HRD).
- Control symptoms (ascites, pain, bowel dysfunction) and prevent complications; integrate palliative care early.
- Offer fertility counseling when relevant.

Approach to management

- Multidisciplinary triage (gynecologic oncology-led).
- Primary debulking surgery (PDS) if complete/near-complete cytoreduction feasible.
- Neoadjuvant chemotherapy (NACT) (carboplatin/paclitaxel ×3) followed by interval debulking surgery (IDS) and then complete 3 more cycles when bulky disease or poor surgical candidacy.
- Consider bevacizumab with chemo and as maintenance in selected epithelial cancers.
- Maintenance PARP inhibitor based on BRCA/HRD and response to platinum.

Non-Pharmacological interventions

- Early nutrition, VTE prevention, pain control, psychosocial support, management of ascites (paracentesis).
- In low-resource setting: prioritize pelvic US + CA-125/HE4; use RMI/ ROMA for referral decisions; CT if available; arrange tele-oncology; perform opportunistic salpingectomy during benign gynecologic surgery.

Pharmacological therapy (indications, dose, route, duration, cautions)

Setting	Regimen (examples)	Dose / Route / Duration	Key cautions
First-line epithelial carcinoma	Carboplatin + Paclitaxel (q3wk)	Carboplatin AUC 5–6 (Calvert formula) IV + Paclitaxel 175 mg/m² IV over 3 h × 6 cycles	Myelosuppression, neuropathy; antiemetics; hypersensitivity
	+/- Bevacizumab	15 mg/kg IV q3wk with chemo then maintenance up to 15–22 months	Hypertension (HTN), proteinuria, wound healing, GI perforation risk
Maintenance (post platinum response)	Olaparib (BRCA-mut)	300 mg PO BID up to 2 years	Anemia, fatigue; rare MDS/AML
	Niraparib (all-comers; best in HRD+)	200–300 mg PO daily (start 200 mg if weight <77 kg or platelets <150k)	Thrombocytopenia, HTN
	Olaparib + Bevacizumab (HRD+)	Olaparib 300 mg PO BID + Bevacizumab 15 mg/kg q3wk	As above + Bevacizumab risks
Recurrent-platinum-sensitive	Platinum doublet ± Bevacizumab; PARP maintenance if not used	As per first-line	Hypersensitivity to platinum; cumulative toxicity
Recurrent-platinum-resistant	Weekly paclitaxel, pegylated liposomal doxorubicin, topotecan, gemcitabine ± Bevacizumab	Standard doses per agent	Focus on QoL/toxicity; consider trials
MSI-H/dMMR	Pembrolizumab	Per label	Immune-related AEs
Germ cell tumors	BEP (Bleomycin, Etoposide, Cisplatin)	Bleomycin 30 U weekly + Etoposide 100 mg/m² D1–5 + Cisplatin 20 mg/m² D1–5 q3wk × 3–4	Pulmonary toxicity (bleomycin), nephro/ototoxicity
Sex cord–stromal	Surgery ± BEP or Carboplatin/Taxol; endocrine therapy in select	Letrozole 2.5 mg PO daily (selected)	Thromboembolic risk; menopausal symptoms

Assessment of response, review & follow-up

- **Response:** CA-125 trend (if elevated at baseline), exam, CT per RECIST (Response Evaluation Criteria in Solid Tumors) after 3 cycles and end of treatment.
- **Toxicity:** CBC/CMP each cycle; manage neuropathy, marrow suppression, HTN/proteinuria (bevacizumab), cytopenias (PARP).
- **Adjust/Step-up:** radiologic/biochemical progression, symptomatic ascites/obstruction - change regimen, consider trials, palliative procedures.
- **Step-down:** intolerable toxicity reduce dose or interrupt; stop maintenance at planned duration.

- **Follow-up:** every 3-4 months for 2 years, then every 6–12 months to 5 years; symptom-driven imaging; CA-125 if previously informative.

Referral (tiered)

- **Primary:** suspect ovarian cancer (fixed mass, ascites, high RMI) - urgent referral.
- **Secondary:** imaging, tumor markers, initial stabilization; refer to tertiary gynecologic oncology for PDS/IDS and comprehensive care.
- **Tertiary:** cytoreductive surgery, systemic therapy, genetics, fertility/ palliative services.

Complications

Bowel obstruction, malignant ascites, VTE, infection, neuropathy, platinum hypersensitivity, treatment-related cytopenias, renal/hepatic toxicity, fistula/ perforation (bevacizumab), fatigue, sexual dysfunction, menopausal symptoms.

Objectives of patient education & caregiver instructions

- Explain diagnosis, stage, and plan (surgery, chemo, maintenance).
- Genetic counseling/testing and implications for family.
- Treatment adherence; contraception and pregnancy avoidance during therapy.
- Manage side effects (fever, bleeding, shortness of breath, calf pain, severe abdominal pain-seek care).
- Nutrition, activity within tolerance; VTE warning signs; bowel regimen if opioids.
- Clear follow-up schedule and contacts; discuss advance care planning when appropriate.

OVARIAN CARCINOMA

INTRODUCTION

Ovarian carcinoma develops when ovarian surface, stromal or germ cells undergo malignant transformation. It ranks fifth in cancer-related mortality among women worldwide and carries the highest fatality of all gynecologic malignancies, as most cases remain asymptomatic until late stages-earning it the label "silent killer". In 2020, there were 314,000 new cases and 207,000 deaths worldwide (ASR 6.6 incidence, 3.9 mortality per 100,000). In South-East Asia (2022): 32,113 cases (5.3% of female cancers; ASR 6.7). Maldives (2022): 17 cases (7.4% of female cancers) and 12 deaths (5.0%). Most diagnoses are post-menopause; median age 63. SEER shows <2% under 20; the burden rises steeply after 55.

Five-year relative survival for invasive epithelial ovarian cancer varies sharply by extent of spread: 92% for localized disease, 71% for regional spread, 32% for distant metastases and 51% overall. Because about 75% of patients are diagnosed with advanced-stage disease, outcomes remain poor. Implementing standardized protocols-from early symptom awareness and CA-125 screening to prompt ultrasound evaluation, urgent referral and consistent cytoreductive surgery with platinum-taxane chemotherapy-can improve early detection and help narrow survival disparities across regions and levels of care.

SCOPE OF THE GUIDELINES

These guidelines include clinical approach to surgical management within the overall treatment plan, indications for referral, peri-diagnostic care, chemotherapy and radiotherapy indications, and follow-up schedules. The guidelines outline the clinical approach to surgical management within the broader treatment framework but do not elaborate on procedural details for diagnostic or therapeutic surgeries.

Intended users

General practitioners, medical officers, gynecologists, oncologists, radiologists, pathologists, nurses, allied health, educators, program managers, and policymakers.

Applicability by level of care

- **Primary care:** Recognize symptoms and red flags, take focused history and exam, order first-line tests (CBC, pregnancy test, ultrasound where available), start supportive care, and initiate referral.

- **Secondary care:** Confirm suspicion with imaging and tumor markers (e.g., transvaginal/pelvic ultrasound, CA-125 per protocol), stage clinically, manage complications, and coordinate timely referral to oncology.
- **Tertiary care:** Multidisciplinary assessment, definitive oncologic management (surgery, chemotherapy, radiotherapy, genetics), clinical trials, and survivorship planning.

These guidelines bridge gaps before tertiary access by setting standardized symptom checklists, minimum diagnostic panels, and clear referral thresholds; simplifying decisions with flowchart triage, stage-appropriate care bundles, and concise documentation; providing resource-aware alternatives when imaging, pathology, or markers are limited and clear advice on when to manage locally versus transfer; strengthening coordination through defined referral routes, contact points, and time targets; and building capacity with short training modules for non-specialists and patient information sheets to improve understanding and adherence.

DEFINITION

Ovarian carcinoma refers to malignant tumors arising from the epithelial lining of the ovary, fallopian tube, or primary peritoneum. These carcinomas account for around 85–90% of all ovarian malignancies, with the remaining cases comprising germ cell and sex-cord stromal tumors. Histologic subtypes include high-grade serous carcinoma (the most prevalent), low-grade serous, endometrioid, clear cell, and mucinous carcinoma. Each subtype carries distinct molecular and clinical features, but all share an origin in the surface epithelium or its Müllerian derivatives. The term “epithelial ovarian cancer” therefore encompasses tumors that, despite varied morphology, follow common patterns of spread along peritoneal surfaces and lymphatic channels.

CAUSES, RISK FACTORS, AND TRIGGERS

Ovarian carcinoma risk climbs with advancing age; half of all cases arise in women aged 63 or older, and incidence peaks among those in their sixth decade or beyond.

Category	Key Risk Factors	Notes / Mechanism
Age	Risk rises with age; median age at diagnosis ~63 years	Incidence peaks in 6th decade and beyond
Genetic	BRCA1 (up to 44% lifetime risk), BRCA2 (up to 17%); Lynch syndrome (MMR gene defects)	Strongest hereditary risks; indicate need for genetic counseling and surveillance
Molecular (HRD)	Homologous recombination deficiency (BRCA1/2 or other repair gene defects)	Present in ~50% of high-grade serous ovarian cancers; predicts response to platinum chemotherapy and PARP inhibitors

Reproductive History	Nulliparity, early menarche, late menopause	Prolonged lifetime ovulation → repeated epithelial injury and malignant transformation
Endometriosis	Severe/endometriosis increases risk (up to 4x overall; up to 19x for type I subtypes)	Strong association with clear cell and endometrioid carcinomas
Hormonal	Long-term unopposed estrogen therapy (without progesterone)	Drives epithelial proliferation; linked with increased risk
Lifestyle	Obesity; cigarette smoking	Obesity → higher estrogen, systemic inflammation. Smoking → oxidative stress and DNA damage
Pelvic Inflammatory Disease	Chronic inflammation may contribute, though evidence less consistent	Association weaker but biologically plausible
Family History	First-degree relatives with breast/ovarian cancer	Strong indicator of inherited predisposition; requires tailored screening

EVALUATION FOR DIAGNOSIS

Ovarian cancer is called a silent disease because symptoms are absent or unrecognized. Ovarian cancer symptoms may be vague and can be caused by more common, less serious conditions.

Domain	Key Components	Details / Purpose
History	Symptom inquiry	Bloating > few weeks, abdominal/pelvic pain or discomfort, early satiety after small meals, urinary urgency/frequency
Physical Examination	Bimanual pelvic exam	Palpation of adnexal mass, assessment of peritoneal cavity
	Signs of ascites	Shifting dullness, fluid wave → suggest peritoneal spread
Laboratory Tests	Tumor markers	CA-125 (>35 U/mL raises suspicion), HE4 (adjunct to improve specificity)
	Basic blood tests	CBC (look for anemia, thrombocytopenia), LFTs & renal panel (baseline function, guide chemotherapy dosing, imaging safety)
Imaging	First-line	Transvaginal ultrasound → characterizes adnexal masses (solid, cystic, complex) and estimates size
	Staging & mapping	Contrast-enhanced CT or MRI abdomen/pelvis → evaluate peritoneal implants, lymph nodes, ascites, guide surgical staging & planning

MALIGNANCY RISK STRATIFICATION TOOLS

Common risk stratifications tools that can be used include

1. The Ovarian-Adnexal Reporting and Data System (O-RADS) US/MRI provides a standardized lexicon for ovarian and adnexal lesions, enables stratification of these lesions with use of a numeric score based on morphologic features to indicate the risk of malignancy, and offers management guidance.

2. Risk malignancy index (RMI) is a simple scoring system based on three factors serum CA 125, USG score and menopausal status.

3. International Ovarian Tumor Analysis group (IOTA) Risk Assessment Models for Ovarian Tumor Diagnosis.

Tool	Inputs	Output / Risk categories	Cut-offs / How to use	Advantages	Limitations	Recommended setting / Management
O-RADS (US/ MRI) Ovarian-Adnexal Reporting and Data System (Ultrasound / MRI)	US: morphology (cystic/solid), papillary projections, septa, size, Doppler flow. MRI: T1/T2 signal, fat/ blood, enhancement, diffusion	0–5: 0 incomplete; 1 normal; 2 <1% benign; 3 1–<10% low risk; 4 10–<50% intermediate; 5 ≥50% high risk	1–2: routine/ none. 3: short-interval follow-up or surgery if symptomatic. 4–5: refer to gynecologic oncology for staging/ surgery	Standardized lexicon; aligns report → action; available for US and MRI	Requires trained imagers; MRI availability may be limited	Primary/ secondary/ tertiary. Use to standardize reports; triage 4–5 to oncology
RMI (Risk of Malignancy Index)	RMI = U × M × CA-125. U (US score: 0,1,3) using features: multilocularity, solid areas, bilateral, ascites, metastases. M (menopause): 1 pre, 3 post. CA-125 (U/mL)	Continuous score (higher = higher risk)	RMI ≥200 → high risk → refer to gynecologic oncology. <200 → consider conservative or benign surgery pathway	Simple; low cost; good for low-resource settings	Lower accuracy in early/ borderline tumors; depends on CA-125	Primary/ secondary. Use for first-line triage where expert US/MRI not available

IOTA models (International Ovarian Tumor Analysis models (Simple Rules, LR2, ADNEX)	Detailed US features (solid parts, papillae, shadows, ascites, blood flow), age; CA-125 optional (improves some models)	Simple Rules: benign / malignant / indeterminate. LR2: malignancy probability. ADNEX: probabilities for benign, borderline, stage I, stage II–IV, metastatic	Common thresholds: >10–20% malignancy risk → oncology referral; indeterminate on Simple Rules → expert scan or MRI	High diagnostic accuracy; ADNEX subtyping helps planning; guideline-endorsed	Needs skilled sonography; calculators/ apps; learning curve	Secondary/ tertiary with experienced sonographers. Use for precise risk estimates and surgical planning

Notes: If tools disagree, prioritize expert ultrasound/MRI review and multidisciplinary discussion. Always integrate clinical context (age, symptoms, family history/BRCA, rapid growth, ascites). Choose the tool by resources and expertise: RMI for broad triage; IOTA for expert US; O-RADS to standardize reports and downstream management.

If primary surgery unsuitable (unresectable disease, poor performance/comorbidities): obtain image-guided core biopsy (percutaneous preferred; laparoscopic if needed) for histology and molecular testing.

- Ascitic cytology alone is insufficient-use only in exceptional cases after MDT review.
- Prioritize histologic confirmation (surgery or image-guided) to distinguish mimics and plan definitive therapy.

CLASSIFICATION AND STAGING

Staging follows the 2014 FIGO (International Federation of Gynecology and Obstetrics) classification, which relies on surgical and pathologic findings.

Stage/Substage	Definition
IA	Tumor confined to one ovary; capsule intact, no tumor on surface, negative peritoneal washings.
IB	Tumor confined to both ovaries; capsules intact, no surface tumor, negative peritoneal washings.
IC1	Tumor in one or both ovaries with surgical spill.
IC2	Tumor in one or both ovaries with pre-surgical capsule rupture or tumor on ovarian surface.
IC3	Tumor in one or both ovaries with malignant cells in ascites or peritoneal washings.
IIA	Extension and/or implants involving the uterus and/or fallopian tubes.
IIB	Extension and/or implants on other pelvic tissues (e.g., bladder, bowel serosa).

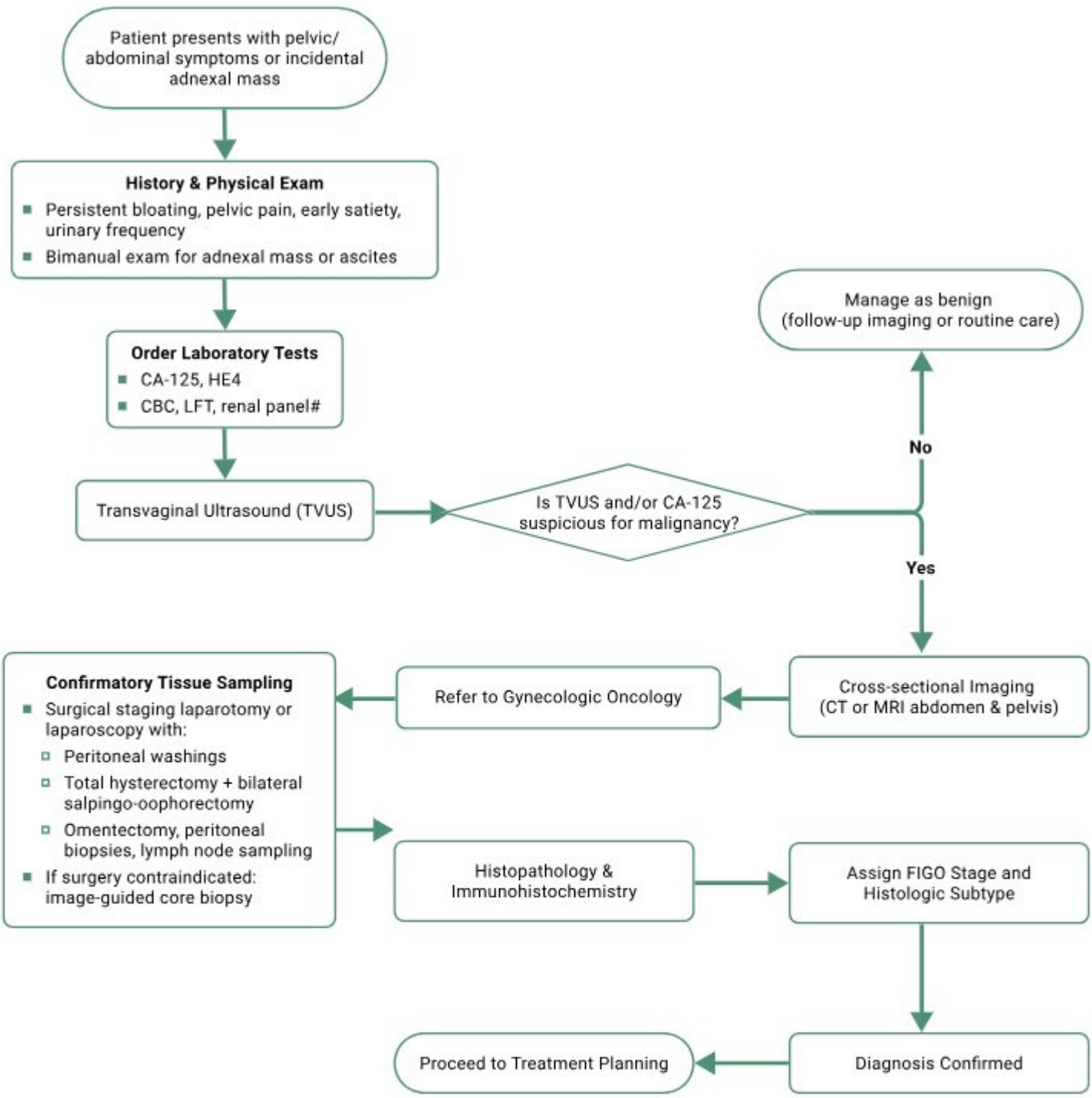
III A	Positive retroperitoneal lymph nodes and /or microscopic metastasis beyond the pelvis)
III A1	Positive retroperitoneal lymph nodes only
IIIA1(i)	Metastasis ≤ 10 mm
IIIA1(ii)	Metastasis > 10 mm
IIIA2	Microscopic peritoneal metastases beyond the pelvis, with or without positive retroperitoneal nodes.
IIIB	Macroscopic peritoneal metastases beyond the pelvis ≤ 2 cm in greatest dimension, with or without positive retroperitoneal nodes.
IIIC	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.
IV	Distant metastases, including pleural effusion with positive cytology or parenchymal liver or lung metastases.

Several additional recommendations refine ovarian cancer staging:

- Assign histologic type and grade at the time of staging to guide prognosis and treatment.
- Whenever feasible, specify the primary origin-ovary versus fallopian tube versus peritoneum-since site influences management.
- Lesions that appear confined to the ovary but are bound by dense adhesions should be upstaged to II if microscopic tumor is confirmed within those adhesions.

When chemotherapy precedes surgery, initial clinical staging applies. Still, imaging or diagnostic laparoscopy should be performed before starting chemo to approximate surgical staging. Patients whose first surgery did not include full staging must be counseled about its importance and offered a restaging laparotomy to complete peritoneal washings, biopsies, nodal assessment and other key steps for optimal treatment planning.

DIAGNOSTIC FLOWCHART



Perform beta human chorionic gonadotropin (β-hCG), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) in women under 40 if a suspicious mass is seen on pelvic ultrasound scan. Other ovarian tumor markers may include inhibin, carcinoembryonic

antigen (CEA), CA 19–9, and HE4). Serum levels can be elevated in patients with rarer ovarian cancer types (e.g., mucinous or endometrioid)

or secondary ovarian malignancies/other primary tumours (e.g., appendiceal, colorectal and upper gastrointestinal tumours). Measurement

of these markers prior to surgery can help avoid inappropriate

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for an adnexal mass mimicking ovarian carcinoma encompasses several benign and non-gynecologic conditions.

Condition	Clinical Features	Imaging Characteristics	Key Distinguishing Points
Simple ovarian cyst	Common in premenopausal women; often asymptomatic	TVUS: unilocular, thin-walled, anechoic, <10 cm	Usually benign; observe if CA-125 normal and no solid components
Endometrioma ("chocolate cyst")	Seen in women with endometriosis; pelvic pain, dysmenorrhea	US: cystic with low-level homogeneous echoes; MRI: T1 hyperintense with "shading" on T2	Contains old blood; chronic course
Tubo-ovarian abscess (TOA)	Pelvic pain, fever, leukocytosis; complication of PID	US/CT: complex multiloculated adnexal mass, thick enhancing walls, hydrosalpinx	Infective origin; systemic signs (fever, leukocytosis)
Subserosal or pedunculated uterine fibroid	May mimic adnexal mass if detached	US/MRI: solid whorled myometrial mass, contiguous with uterus, acoustic shadowing	Uterine origin; not ovarian
Krukenberg tumor (metastatic GI cancer)	Bilateral ovarian masses; often GI symptoms; elevated CEA	Bilateral solid-cystic masses; histology: mucin-laden signet-ring cells	Usually from gastric/colorectal primary; bilateral involvement typical

MANAGEMENT GOALS

Management goals in ovarian carcinoma center on maximizing survival while preserving function and quality of life. Manage within a multidisciplinary gynecologic oncology team; decisions tailored to stage, histology/biology, and fitness.

Surgery

- Primary cytoreductive (debulking) surgery is preferred when feasible; aim for no visible residual disease (strongest survival predictor).
- Definitions: complete = no macroscopic disease; optimal = no residual >1 cm; suboptimal = any residual >1 cm.
- Interval cytoreduction after neoadjuvant platinum–taxane is appropriate if upfront complete resection is unlikely or risk is high (poor performance, major comorbidity, hypoalbuminemia).
- Fertility-sparing surgery may be offered to carefully selected young patients with early-stage, low-grade tumors.

Systemic therapy (first line)

- Carboplatin + paclitaxel every 3 weeks for ~6 cycles for most epithelial cancers.
- Consider bevacizumab in high-risk stage III–IV.
- PARP-inhibitor maintenance for BRCA-mutated or HRD-positive disease.

Recurrent disease

- Platinum-sensitive (≥6 mo): re-challenge with a platinum regimen ± maintenance per biomarkers.
- Platinum-resistant (<6 mo): non-platinum single agents (e.g., liposomal doxorubicin, weekly paclitaxel, topotecan).
- Secondary cytoreductive surgery only in highly selected patients at expert centers, followed by systemic therapy.

Supportive and adjunctive care

- Thromboprophylaxis, nutritional support, proactive toxicity management, and psychosocial care throughout.
- Genetic counseling/testing for all patients to guide therapy and family risk.
- Clinical trials should be offered whenever available.

a. Surgical Management

Surgical goals are complete removal of all visible diseases and accurate staging to guide adjuvant therapy.

Early-stage disease

- A midline laparotomy remains the standard approach to minimize capsule rupture.
- Cytoreductive surgery for ovarian cancer should generally be performed via open laparotomy, though minimally invasive surgery (MIS) may be appropriate in selected cases: presumed localized disease with low rupture risk, fertility-sparing procedures, staging laparoscopy for operability assessment, or isolated recurrence resections.
- After surgery, the extent of disease and completeness of cytoreduction must be documented: complete, optimal, or suboptimal, with sites and volume of residual disease specified.

- Comprehensive staging includes peritoneal inspection and palpation, washings, biopsies of suspicious or representative sites, bilateral salpingo-oophorectomy, hysterectomy, omentectomy, and appendectomy in mucinous tumors.
- Lymphadenectomy: performed systematically in stage I–II disease; in stage III–IV, only bulky nodes should be removed. Routine lymphadenectomy adds morbidity without survival benefit when nodes are clinically negative, and it may be omitted in low-grade or expansile mucinous subtypes with <1% risk of nodal metastasis.
- Intraoperative frozen section allows complete staging in one procedure, and upstaging occurs in up to 60% of cases.

Fertility-sparing surgery

- In young women with stage IA or IC1–2 tumors confined to one ovary and favorable histology (low-grade), preservation of the contralateral ovary and uterus may be offered after counseling regarding recurrence risk.

Advanced disease (FIGO III–IV)

- The primary goal is complete macroscopic cytoreduction, the strongest predictor of both progression-free and overall survival.
- Achieving this often requires extensive procedures such as bowel resection, diaphragmatic and peritoneal stripping, splenectomy, resection of bulky para-aortic nodes, partial hepatectomy, pancreatic tail excision, or even extra-abdominal resections. These are best performed in specialized high-volume centers.
- Routine lymphadenectomy again provides no survival benefit after complete resection in clinically node-negative disease.

Primary vs. neoadjuvant approach

- Primary cytoreductive surgery is preferred when complete clearance appears feasible and the patient can tolerate surgery.
- If complete resection seems unlikely upfront, neoadjuvant platinum–taxane chemotherapy followed by interval debulking is an accepted alternative.
- For less chemo-sensitive histologies (e.g., low-grade serous, mucinous carcinomas), primary surgery is recommended even if only minimal residual disease (<1 cm) is anticipated.

Complications of Surgical Management

Surgical management of ovarian carcinoma, while central to staging and cytoreduction, carries risks that must be anticipated and mitigated.

Table . Complications of Surgical Management in Ovarian Carcinoma

Category	Complication	Description / Risk	Management / Mitigation
Intra-operative	Hemorrhage	Bleeding during debulking or lymphadenectomy, especially with vascular invasion	Careful hemostasis, availability of blood products
Post-operative	Wound / Intra-abdominal infection	Cellulitis, pelvic abscess	Early recognition, antibiotics, drainage if needed
	Fistula formation	Enterocutaneous, vesicovaginal; due to extensive dissection or bowel injury	Imaging, nutritional support, re-operation or drainage
Chemotherapy-related	Myelosuppression	Neutropenia, anemia, thrombocytopenia from platinum/ taxanes	CBC monitoring, dose delays, G-CSF support
	Peripheral neuropathy	Tingling/numbness, cumulative with paclitaxel	Dose reduction, schedule modification
	Alopecia, mucositis	Hair loss, oral pain/inflammation	Scalp cooling, oral hygiene, topical anesthetics
	Hypersensitivity reactions	Flushing, dyspnea, hypotension (paclitaxel)	Premedication with steroids, antihistamines
Disease-related	Malignant ascites	Abdominal distension, respiratory compromise, protein loss	Paracentesis, tunneled catheter for palliation
	Bowel obstruction	Pain, vomiting, constipation due to tumor implants	NG decompression, corticosteroids, stenting or surgery if feasible
	Thromboembolism	DVT, pulmonary embolism from tumor hypercoagulability	LMWH prophylaxis, early mobilization, anticoagulation when indicated

b. Pharmacological therapy

Systemic chemotherapy after surgery is recommended for all advanced ovarian cancer. Before starting neoadjuvant chemotherapy, confirm invasive ovarian malignancy with a core-biopsy specimen. If biopsy isn't safe, positive cytology from ascitic or pleural fluid may suffice, provided the CA-125/CEA ratio is ≥25, which helps exclude a non-ovarian or non-primary peritoneal tumor. A ratio below 25 mandates gastroscopy and colonoscopy to rule out gastrointestinal cancer. Bear in mind that fluid cytology alone can't reliably distinguish borderline from invasive carcinoma.

Adjuvant therapy by stage and grade (Epithelial Ovarian Carcinoma)

- **IA–IB, grade 1:** Observation only in carefully selected early-stage, low-risk ovarian cancer patients, since surgery alone yields >90% survival. Indications include Stage IA low-grade serous or endometrioid carcinoma; Stage IA–IB expansile mucinous carcinoma, Borderline tumours after complete staging, Node-negative disease in subtypes with <1 % nodal spread; Patients too frail for chemotherapy
  In these scenarios, surveillance with periodic clinical exams, imaging and CA-125 monitoring replaces systemic therapy. Regular follow-up allows early detection of recurrence while sparing low-risk patients the toxicity of chemotherapy.
- **IA–IB, grade 2:** Either surveillance or 3–6 cycles of adjuvant chemotherapy; complete surgical staging is mandatory.
- **IA–IB, grade 3 or any IC:** 3–6 cycles of adjuvant chemotherapy.
- **Stage II (any grade):** Six cycles of adjuvant chemotherapy.

First-line treatment for epithelial ovarian carcinoma (I-IIB).

1. Carboplatin is dosed to achieve an area under the curve (AUC) of 5–6 mg·min/mL, calculated by the Calvert formula (Total dose = target AUC × [GFR + 25]) and infused intravenously over 30–60 minutes on day 1 of each cycle. In practice, this equates to approximately AUC 5–6 on day 1 every three weeks for six cycles

2. Paclitaxel 175 mg/m² IV day 1 as a three-hour IV infusion of the same cycle for six cycles (Every 21 days, 6 cycles)

Cautions: Carboplatin's dose-limiting toxicity is myelosuppression, chiefly thrombocytopenia and neutropenia; paclitaxel commonly causes peripheral neuropathy, myelosuppression and alopecia, and carries a risk of hypersensitivity reactions that mandate premedication with corticosteroids, H_1/H_2 antagonists and vigilance during infusion. Hematologic and neurologic parameters must be assessed prior to each cycle, with dose delays or reductions instituted for significant cytopenia (ANC < 1 × 10^9/L, platelets < 100 × 10^9/L) or grade ≥2 neuropathy.

Note: Extending beyond six cycles or adding a third agent offers no added benefit. Patients who cannot tolerate paclitaxel-because of allergy, neuropathy, or other contraindications-may receive carboplatin with docetaxel (60-75 mg/m2)-carboplatin, gemcitabine-carboplatin or pegylated liposomal doxorubicin (PLD 30 mg/sq m)-carboplatin AUC 5 to be given once in 4 weeks.

In certain low-risk subtypes-low-grade serous carcinoma stage IB–IC, clear cell carcinoma stage IA–IC1, low-grade endometrioid carcinoma stage IB–IC, expansile mucinous carcinoma stage IC and infiltrative mucinous carcinoma stage IA-the benefit of adjuvant chemotherapy is uncertain and may be considered optional.

Adjuvant chemotherapy is not recommended for fully staged patients with low-grade serous carcinoma stage IA, low-grade endometrioid carcinoma stage IA or expansile mucinous carcinoma stage IA–IB.

Role of Intra-peritoneal (IP) chemotherapy and hyperthermic intraperitoneal perioperative chemotherapy (HIPEC)

IP chemotherapy is not recommended as standard first-line treatment for epithelial ovarian cancer outside clinical trials. Although earlier studies suggested PFS and overall survival (OS) benefits over intravenous therapy, the GOG252 trial found no advantage when combined with bevacizumab, with higher rates of infection, catheter-related pain, and gastrointestinal toxicity.

Hyperthermic intraperitoneal chemotherapy (HIPEC) delivers heated chemotherapy at cytoreductive surgery. In stage III disease at interval cytoreductive surgery (ICRS) after neoadjuvant chemotherapy, the OVHIPEC trial showed improved PFS and OS with cisplatin (100 mg/m^2), while another trial found benefit only in the ICRS subgroup. HIPEC is not advised at primary cytoreductive surgery (PCRS) and should be performed only in specialized centres with trained teams under strict governance.

In relapsed ovarian cancer, HIPEC with carboplatin during secondary cytoreduction showed no survival benefit and is not recommended. Both IP chemotherapy and HIPEC remain restricted to selected cases within research or highly specialized settings.

BRCA-mutated:

PARP inhibitors - Olaparib, niraparib and rucaparib are approved for maintenance in high-grade tubo-ovarian carcinoma after platinum response, regardless of BRCA or HRD status.

Initial (BRCA mutated). In patients with germline BRCA1/2 mutations who achieve at least a partial response to first-line platinum-taxane therapy, maintenance olaparib extends progression-free survival.

Maintenance (BRCA-mutated):

In patients with germline BRCA1/2 mutations who respond to first-line platinum–taxane chemotherapy, continuing olaparib as maintenance prolongs progression-free survival.

Olaparib 300 mg PO twice daily for up to 2 years (or until progression) beginning after completion of chemotherapy and continuing for up to two years or until disease progression

Note: Before each treatment cycle and periodically thereafter, monitor complete blood counts and liver function tests due to risks of anemia, neutropenia and hepatotoxicity. There's a slightly increased risk of acute myeloid leukemia and myelodysplastic syndromes, particularly in BRCA-mutated patients with prior platinum exposure. For persistent grade ≥ 3 hematologic or non-hematologic toxicities, interrupt or reduce dose, followed by close reassessment before resuming therapy. If toxicity persists despite modification, permanent discontinuation should be evaluated in accordance with risk-benefit considerations and clinical guidelines.

c. Non-pharmacological interventions

Intervention	Goal / Benefit	Key actions / What to do	When / Setting
Early nutrition assessment	Prevent weight loss; maintain muscle; manage chemo-related nausea/taste change	Dietitian review; calorie/protein targets; small frequent meals; antiemetic-compatible plans; oral supplements as needed	At diagnosis; each cycle; post-op
Supervised rehabilitation (aerobic + resistance + **lymphedema exercises)**	Reduce fatigue; preserve mobility; lower VTE risk via better circulation	Individualized program; step goals; resistance bands; arm care for lymphedema	Start during treatment; continue survivorship
Mechanical VTE prophylaxis	Prevent DVT/PE, especially peri-operative	Graduated compression stockings; intermittent pneumatic compression; **early ambulation**	Pre-/post-op and during reduced mobility
Ascites palliation	Relieve dyspnea/abdominal discomfort; improve function	**Therapeutic paracentesis;** consider tunneled peritoneal catheter for recurrent ascites; albumin per protocol	Symptomatic, between cycles or at clinic
Psychosocial support	Reduce anxiety/depression; address body-image, finances	One-to-one counseling; support groups; social work referral; caregiver education	From diagnosis; screen regularly
Integrative therapies	Ease pain, neuropathy, insomnia, mood symptoms without extra drugs	Acupuncture (neuropathy), mindfulness/CBT-i, gentle yoga/relaxation	Adjunct during chemo and survivorship
Genetic counseling & testing	Identify BRCA/Lynch; guide therapy and family risk	Pre-test counseling; germline ± tumor testing; cascade testing for relatives	As early as possible after diagnosis
Fertility preservation	Maintain future fertility options	Early referral for oocyte or ovarian tissue cryopreservation before gonadotoxic therapy	At diagnosis and throughout disease course
Early palliative care	Proactive symptom control; goal-concordant care; ACP	Pain/dyspnea/constipation plans; advance-care planning; home-based supports	At diagnosis and throughout disease course

VTE = venous thromboembolism; DVT = deep vein thrombosis; PE = pulmonary embolism; ACP = advance care planning.

d. Other interventions

Hormone/Non-Hormone Replacement Therapy

After bilateral salpingo-oophorectomy, both pre- and postmenopausal women often develop hot flashes and night sweats (vasomotor symptoms -VSM) because of the sudden loss of estrogen and androgens. Educate women on the potential risks and benefits of hormonal and nonhormonal treatments. When hormone therapy isn't an option, nonhormonal strategies can help.

Simple measures-paced breathing and avoiding triggers like caffeine, alcohol or tobacco-may ease mild symptoms. Regular exercise improves mood and quality of life, though its direct impact on hot flashes is inconsistent.

Herbal remedies such as black cohosh or phytoestrogens lack convincing evidence, and acupuncture's benefit appears no greater than placebo.

Among medications, certain antidepressants (venlafaxine, paroxetine) and the FDA-approved low-dose paroxetine 7.5 mg can modestly reduce vasomotor symptoms, while gabapentin (up to 900 mg daily) offers another nonhormonal option. Each approach carries its own side-effect profile, so treatment should be tailored to the patient's risks and preferences.

Bone Health

Ovarian cancer survivors often face accelerated bone loss after bilateral salpingo-oophorectomy or chemotherapy-induced menopause. In women who undergo BSO before age 50, studies show osteopenia in over 60 % and osteoporosis in nearly 10 %. To catch early bone density declines, experts recommend a baseline DXA scan of the spine and hip-especially in those under 45-with follow-up intervals guided by the T-score: no repeat testing if ≥ −1.0, a 24-month reassessment if between −1.0 and −2.5, and initiation of bisphosphonates plus a 24-month DXA if ≤ −2.0.

All survivors should optimize skeletal health through 1,200 mg of elemental calcium and 800–1,000 IU of vitamin D daily, weight-bearing exercise, smoking cessation and limited alcohol. For those with significant bone loss or fracture risk, antiresorptive therapy (bisphosphonates or denosumab) can preserve strength. Regular bone health monitoring and early intervention help maintain quality of life long after cancer treatment.

Cardiovascular health

Removing both ovaries before natural menopause elevates a woman's risk of dying from coronary heart disease-even up to age 55. Hysterectomy alone carries a smaller, age-dependent CHD mortality rise. Estrogen therapy appears to blunt this increased risk. Survivors should have personalized cardiovascular risk assessment and optimally manage blood pressure, lipids, diet, exercise and smoking to protect heart health.

Brain health

Early menopause after bilateral salpingo-oophorectomy raises women's risk of cognitive decline, dementia and parkinsonian symptoms, in addition to hot flashes, bone loss and heart disease. Estrogen-and androgen-loss likely contributes to these neurodegenerative changes. Offering hormone therapy until around the average age of natural menopause (≈51 years) may help preserve cognitive function and reduce parkinsonism risk. Personalized counseling and regular neurologic monitoring should be part of survivorship care.

Fertility preservation

Chemotherapy and surgery for gynecologic cancers can threaten future fertility. All newly diagnosed patients who wish to have children should be offered a reproductive-endocrinology consultation before treatment. Discussions should cover how surgery and chemotherapy affect ovarian reserve and outline preservation techniques-oocyte or embryo freezing and ovarian-tissue cryopreservation with later reimplantation. Legal planning for the disposition of stored gametes or embryos is also important. Outcomes are encouraging: gynecologic cancer survivors often match or exceed other cancer survivors in IVF success, and ovarian-tissue transplants can restore both hormone function and fertility without delaying care.

Contraception

Even after cancer treatment, contraception needs don't vanish. Women who keep their uterus and ovaries-or whose ovarian function returns-require tailored birth-control advice. Chemotherapy-induced amenorrhea may reverse in younger patients, so a contraception consult, ensures safe, effective choices. Survivors of estrogen-sensitive cancers should use estrogen-free methods (levonorgestrel IUS, copper IUD or implant), while those without hormone-dependent disease can select any suitable option. Assuming infertility risks unintended pregnancy; proactive counseling aligns care with each woman's goals and health.

Sexual health

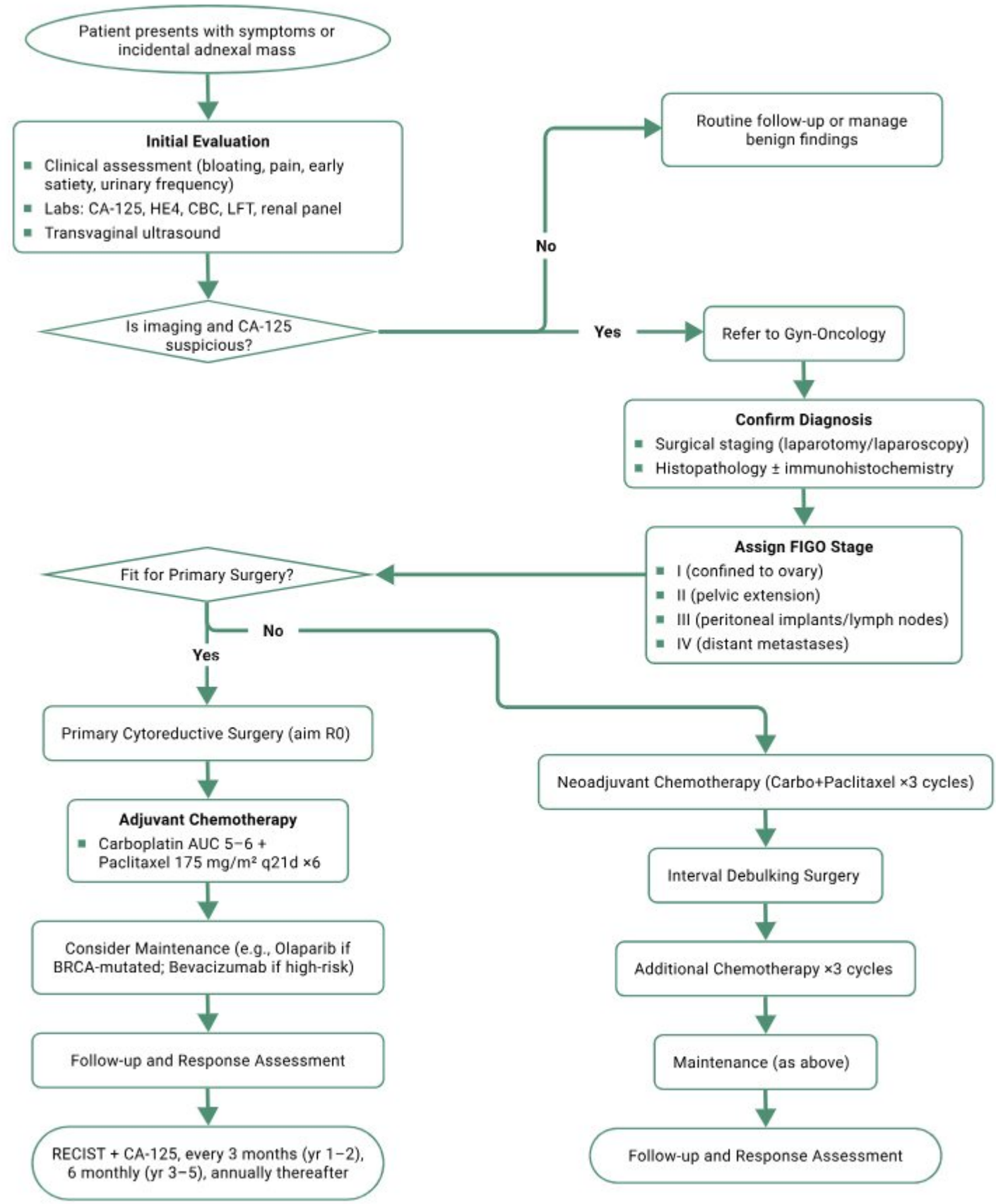
Gynecologic cancer and its treatment often disrupt sexual function through both hormonal and structural changes. Removing the ovaries-whether before or after natural menopause-cuts estrogen and androgen levels, undermining libido, arousal and lubrication. Radiation damages rapidly renewing vulvovaginal tissues, leading over time to dryness, thinning, fibrosis, adhesions and loss of elasticity, which can cause pain and shortening of the vaginal canal. Chemotherapy can trigger mucosal inflammation, and the stress of diagnosis and altered body image further erodes sexual wellbeing.

Yet fewer than half of gynecologic oncologists routinely raise sexual health, and most feel pressed for time. Addressing sexual concerns early i.e., tailored to tumor site, treatment plan and patient priorities are essential. Survivorship care should include proactive screening for dysfunction, referral to pelvic-floor or sexual-health specialists,

Genetic testing and counselling

Genetic counseling and testing are essential for women diagnosed with gynecologic cancer at a young age or those with multiple relatives affected by breast, ovarian, endometrial or related malignancies. A thorough pedigree-documenting first- and second-degree relatives and their ages at diagnosis-helps identify hereditary patterns. Referral to a certified genetic counselor ensures personalized risk assessment, discussion of gene-specific testing (for example, BRCA1/2 or Lynch-syndrome panels), and review of implications for surveillance, risk-reducing surgery and family planning. Testing decisions should balance clinical utility, psychological impact and insurance considerations, empowering patients with actionable information for themselves and at-risk relatives.

MANAGEMENT ALGORITHM



At any point, if recurrence/progression confirmed by RECIST or GCIG CA-125:

- Platinum-sensitive relapse (≥6 months): Platinum-based rechallenge
- Platinum-resistant relapse (<6 months): Non-platinum single agents
- Platinum-refractory: Clinical trials or palliative focus

ASSESSMENT OF RESPONSE

Response Evaluation During First-Line Therapy

- **Biochemical Monitoring:** Serial CA-125 measurement alongside clinical evaluation; baseline and pre-cycle levels are essential. A ≥50% decline from pretreatment levels suggests response but must be correlated with imaging.
- **Radiological Assessment:** Contrast-enhanced CT or MRI after three chemotherapy cycles; apply **RECIST 1.1** criteria to quantify response:
  - Partial Response: ≥30% decrease in target lesion diameter sum
  - Stable Disease: <30% decrease or <20% increase
  - Progressive Disease: ≥20% increase or new lesions
- **Clinical Correlation:** Resolution of ascites, pain, and improved performance status should guide ongoing management.
- **Transition to Follow-Up:** Once therapy concludes, structured follow-up enables timely detection of recurrence and long-term effects.

Surveillance After Treatment Completion

- **Focus:** Clinical evaluation remains central; avoid routine imaging or cytology in asymptomatic women.
- **Follow-Up Schedule:**
  - Years 1–2: Every 3 months – history, pelvic exam, CA-125 (if initially elevated), imaging as needed
  - Year 3: Every 4 months – same assessments
  - Years 4 onward: Every 6 months until progression, then annually
- Imaging Triggers: Clinical concerns or rising CA-125 prompt CT or PET scan. Pelvic ultrasound may substitute when CA-125 and exam are normal.
- Note: Routine CA-125 monitoring can lead to early chemo initiation without survival benefit, possibly worsening quality of life-pros and cons should be discussed.

Serological vs. Clinical Relapse

- Serological Relapse: Rising CA-125 without radiologic/clinical evidence. No proven survival benefit from early therapy; monitoring and clinical trial enrollment encouraged. Hormonal therapy may be considered.

- Clinical Relapse: Symptoms or imaging-confirmed recurrence ≥6 months post-treatment. Diagnosis via history, exam, tumor markers (CA-125, HE4), and imaging. Biopsy rarely required.

Salvage Therapy Planning

- Confirm Progression: Use RECIST or GCIG CA-125 progression criteria. Consider performance status, comorbidities, and patient preferences.
- **Platinum Sensitivity Classification:**
  - Sensitive (>6 months): Platinum combinations (e.g., paclitaxel + carboplatin; Docetaxel + platinum; Liposomal doxorubicin + platinum; Gemcitabine + platinum)
  - Resistant (<6 months): Non-platinum agents (e.g., liposomal doxorubicin, topotecan)
  - Refractory (progression on platinum): Prioritize novel therapies or trials; introduce palliative care early.

Additional Treatment Options

- Targeted Therapy: Bevacizumab improves outcomes in select patients; PARP inhibitors (e.g., olaparib) benefit BRCA-mutated, platinum-sensitive relapses after ≥3 chemo lines.
- Hormonal Therapy: Tamoxifen or aromatase inhibitors may be effective for low-volume, indolent disease.

Other factors in planning salvage therapy to be considered include prior toxicities and cumulative organ function.

Response Evaluation Criteria in Solid Tumors (RECIST 1.1)

Response Evaluation Criteria in Solid Tumors (RECIST 1.1) provide an objective, imaging-based framework for categorizing tumor burden changes. Up to five target lesions (maximum two per organ) are selected at baseline-each ≥10 mm in longest diameter on CT with slice thickness ≤5 mm-and non-target lesions (e.g., ascites) are documented qualitatively. On follow-up imaging, the sum of longest diameters (SLD) of target lesions is compared with baseline:

- **Complete response (CR):** Disappearance of all target lesions, no new lesions, and normalization of tumor markers.
- **Partial response (PR):** ≥30 % decrease in SLD, taking baseline as reference.
- **Stable disease (SD):** Neither sufficient shrinkage for PR nor sufficient increase (see PD).

- **Progressive disease (PD):** ≥20 % increase in SLD (minimum 5 mm absolute increase), appearance of any new lesion, or unequivocal progression of non-target lesions.

The Gynecological Cancer InterGroup (GCIG) CA-125 progression criteria

The Gynecological Cancer InterGroup (GCIG) CA-125 progression criteria offer a serologic complement to RECIST, especially useful when lesions are non-measurable or for earlier biochemical detection of relapse. Progression by CA-125 is defined as one of the following, confirmed on two measurements at least one week apart:

- **If baseline CA-125 was within normal limits:** a rise to ≥2× the upper limit of normal (ULN).
- **If baseline CA-125 was elevated and later normalized:** a rise to ≥2× ULN.
- **If baseline CA-125 remained elevated:** a rise to ≥2× the nadir value.

RECURRENT EPITHELIAL OVARIAN CANCER

Up to 70% of patients with stage III–IV high-grade ovarian cancer relapse within three years. Chemotherapy remains the first-line treatment in recurrence, with the choice of regimen guided by the platinum-free interval. Patients with platinum-sensitive disease benefit from platinum-based combinations, while those with platinum-resistant relapse are managed with non-platinum agents aimed at palliation.

Secondly, cytoreductive surgery may be considered in selected patients after assessing response to chemotherapy or in cases where disease is platinum-sensitive, the patient has good performance status, and disease is localized to sites amenable to complete resection. The goal is maximal tumor reduction, which can improve survival when followed by systemic therapy. As most recurrences are intra-abdominal, surgical intervention can be feasible in appropriately chosen cases.

A. Platinum-Sensitive Recurrence

Preferred Platinum-Based Combination Regimens (Choose based on prior toxicity and residual side effects)

1. **Carboplatin + Paclitaxel**
   - Carboplatin AUC 5–6 IV Day 1 + Paclitaxel 175 mg/m² IV over 3h Day 1
   - q3 weeks × 6–8 cycles
2. **Carboplatin + Pegylated Liposomal Doxorubicin (PLD)**

- Carboplatin AUC 5 IV Day 1 + PLD 30–40 mg/m² IV Day 1
- Lower neuropathy risk, useful if taxane-induced neuropathy present

3. Carboplatin + Gemcitabine

- Carboplatin AUC 4 IV Day 1 + Gemcitabine 1000 mg/m² IV Days 1 & 8 q3 weeks
- Useful if alopecia avoidance desired

Maintenance Therapy after Response:

- **PARP inhibitors** (Olaparib, Niraparib) - especially for BRCA-mutated/HRD-positive
- **Bevacizumab if** used during induction

B. Platinum-Resistant Recurrence

The prognosis in platinum-resistant ovarian cancer is poor. Surgery is not curative in this setting, and platinum-based chemotherapy offers little benefit. Management relies on non-platinum agents, symptom control, and supportive care, with an emphasis on maintaining quality of life.

Principles

- Platinum rechallenge not beneficial
- Aim for symptom control with lower toxicity regimens
- Use single-agent chemotherapy ± targeted therapy

Preferred Single-Agent Regimens

1. **Pegylated Liposomal Doxorubicin (PLD)** 40 mg/m² IV Day 1 q4 weeks
2. **Weekly Paclitaxel** 80 mg/m² IV Days 1, 8, 15 q28 days
3. **Topotecan** 4 mg/m² IV Days 1, 8, 15 q28 days or 1.25 mg/m²/day × 5 days q21 days
4. **Gemcitabine** 800–1000 mg/m² IV Days 1 & 8 q21 days

Targeted Therapy:

- **Bevacizumab** with PLD, weekly paclitaxel, or topotecan if no contraindication

C. Supportive Measures

- Antiemetic prophylaxis per regimen's emetogenicity
- Dose adjustments for marrow suppression, neuropathy, or mucositis
- Growth factor support if recurrent grade ≥3 neutropenia
- Early palliative care involvement if progressive symptoms

Table – Chemotherapy Selection in Recurrent Ovarian Cancer

Recurrence Type	Preferred Chemotherapy	Alternatives / Notes	Maintenance Options
Platinum-sensitive	Carboplatin + Paclitaxel	Carboplatin + PLD; Carboplatin + Gemcitabine	PARP inhibitor; Bevacizumab
Platinum-resistant	PLD; Weekly Paclitaxel; Topotecan; Gemcitabine	± Bevacizumab with above regimens	Not routinely recommended

D. Surgical Management

Surgery in recurrent ovarian cancer is not routine for all patients - it is considered only in carefully selected cases where there is a high likelihood of achieving complete gross resection (no visible residual disease), as this is the strongest predictor of benefit. Retrospective data and meta-analyses suggest that achieving <1 cm residual disease after secondary cytoreduction may extend median survival from 8–27 months to 16–61 months. In AGO DESKTOP I, complete cytoreduction improved post-recurrence survival to 45.2 months compared to 19.7 months with residual disease.

Key Indications

- Isolated or Limited Disease Recurrence: Single-site recurrence (e.g., pelvis, localized peritoneal deposit, solitary lymph node); Oligometastatic disease confined to areas amenable to complete excision
- Good Performance Status: ECOG 0–1, fit for major surgery
- No significant comorbidities that would increase perioperative risk
- Favourable Platinum-Free Interval: Recurrence ≥6–12 months after completion of primary platinum-based chemotherapy. Best outcomes seen in platinum-sensitive patients
- No Diffuse Carcinomatosis or Extensive Bowel/Upper Abdominal Involvement. Disease distribution such that complete resection is technically feasible. No unresectable disease on preoperative imaging (CT/MRI/PET-CT)
- Absence of Massive Ascites: Large-volume ascites (>500 mL) is a poor prognostic indicator and suggests diffuse disease
- Initial Complete Cytoreduction Achieved at Primary Surgery: Patients who had optimal primary debulking and good response to initial chemotherapy are better candidates

Situations Where Surgery is Generally Not Indicated

- Platinum-resistant recurrence with diffuse peritoneal spread

- Poor performance status or major comorbidities
- Inability to achieve complete gross resection on preoperative assessment
- Symptomatic widespread disease where systemic therapy or palliative care is more appropriate.

Definitions

- Secondary cytoreduction: Debulking surgery for first recurrence following primary surgery and chemotherapy.
- Tertiary cytoreduction: Debulking surgery for second recurrence.
- Palliative surgery: Limited procedures (e.g., bowel diversion) to relieve symptoms and improve short-term quality of life.

Surgical Considerations

- Conduct procedures in high-volume centers by specialized gynecologic oncologists
- Possible interventions: omentectomy, lymphadenectomy, excision of visceral or nodal implants
- Laparoscopic assessment may support patient selection but could increase complication risk

Tertiary and Palliative Surgery

Tertiary cytoreduction: Considered in highly selected cases with long disease-free intervals and resectable lesions.

Palliative surgery: Indicated when symptoms (e.g., obstruction) can be safely alleviated; requires multidisciplinary input and informed consent.

Ongoing Research

DESKTOP III and GOG 213 Phase III trials are evaluating survival benefits of secondary cytoreduction combined with chemotherapy vs. chemotherapy alone in platinum-sensitive recurrence. Results may refine surgical indications and patient selection.

Role of Radiotherapy

Radiotherapy has no role as adjuvant or consolidation treatment in epithelial ovarian cancer except in rare cases where chemotherapy is not feasible, or for selected histological subtypes such as early-stage clear cell carcinoma or small cell carcinoma of hypercalcaemic type.

- For recurrent disease, definitive treatment with intensity-modulated radiotherapy (IMRT) or stereotactic radiotherapy may be considered for loco-regional recurrence or oligometastatic disease when surgery is not possible, particularly in patients with small-volume, platinum-sensitive disease and good performance status.
- Stereotactic radiosurgery (SRS) is effective for brain metastases, and stereotactic body radiotherapy (SBRT) offers high local control for extra-cranial oligometastases with minimal toxicity.
- Palliative radiotherapy should be used for symptom control, including vaginal bleeding, pain, and brain metastases, using short-course regimens or whole brain radiotherapy where appropriate.
- Cases requiring radiotherapy must be referred abroad (in advance cases/palliative radiotherapy.

OVARIAN CARCINOMA IN PREGNANCY

Ovarian malignancy in pregnancy is rare, occurring in approximately 0.2–2% of pregnancies, with an incidence of 1:10,000 to 1:100,0001 deliveries. It poses unique challenges due to the need to balance maternal treatment with fetal safety.

DIAGNOSIS OF OVARIAN MALIGNANCY IN PREGNANCY (ACOG)

Diagnosis involves identifying adnexal masses and distinguishing benign from malignant etiologies while considering pregnancy-related changes (e.g., corpus luteum cysts).

- Presentation: Often asymptomatic, detected incidentally during routine ultrasound (e.g., first-trimester dating scan).
- Symptoms: similar to pregnancy related symptoms when present, include pelvic pain, abdominal distention, or mass effect (e.g., pressure on bladder). Persistent symptoms e.g., bloating, early satiety or fast-growing masses raise malignancy suspicion.
- Evaluation:
  - **History and Physical:** Assess symptoms suggestive of malignancy e.g., persistent pain, weight loss. Risk factors include BRCA 1&2 mutations and family history. Perform gentle pelvic exam to avoid uterine stimulation.

- **Imaging:** Transvaginal ultrasound (TVUS) is first-line, safe in pregnancy, with high sensitivity (88–93%) for malignancy. Look for features like irregular borders, solid components, septations >2 mm, or ascites. MRI is second-line if US is inconclusive, avoiding gadolinium due to fetal risks. CT is avoided unless critical (e.g., staging suspected metastasis).
- **Tumor Markers:** CA 125 is less reliable in pregnancy (elevated in normal pregnancy, especially first trimester), but levels >35 U/mL in second/third trimester or rising trends are concerning. Other markers (e.g., AFP, hCG, LDH) may help differentiate germ cell tumors. Inhibin B or AMH may support granulosa cell tumor diagnosis.
- **Risk Stratification:** Use tools like the International Ovarian Tumor Analysis (IOTA) simple rules or Risk of Malignancy Index (RMI). Masses >7 cm, persistent beyond 16 weeks, or with malignant features, e.g., Doppler flow in solid areas warrant referral to a gynecologic oncologist.
- **Diagnostic Confirmation:** Surgical exploration (laparoscopy preferred if feasible) with biopsy or mass removal for histopathology. Avoid fine-needle aspiration due to risk of tumor seeding.

Notes: Most adnexal masses in pregnancy are benign (e.g., functional cysts, 70–80%). Malignant types include epithelial (e.g., serous carcinoma), germ cell (e.g., dysgerminoma), or sex cord-stromal tumors.

Differential diagnosis

Differential includes benign cysts, endometriomas, or ectopic pregnancy. The histopathological classification critical for confirming ovarian malignancy (IARC/WHO):

- Epithelial Tumors: Serous, mucinous, endometrioid, clear cell, Brenner (e.g., low-grade serous carcinoma, common in pregnancy).
- Germ Cell Tumors: Dysgerminoma, yolk sac tumor, teratoma (malignant forms rare but more common in younger pregnant women).
- Sex Cord-Stromal Tumors: Granulosa cell tumors, Sertoli-Leydig cell tumors.
- Other: Metastatic tumors (e.g., Krukenberg from GI primaries).

Significance: Accurate classification guides treatment (e.g., chemotherapy regimens differ for germ cell vs. epithelial tumors). Molecular markers (e.g., BRCA1/2, TP53 mutations) are noted for targeted therapies like PARP inhibitors.

Application: Pathology from surgical specimens (e.g., during staging laparotomy) is classified per WHO criteria, ensuring standardized reporting for multidisciplinary teams.

MANAGEMENT OF OVARIAN MALIGNANCY IN PREGNANCY

Management balances maternal oncologic needs with fetal safety, guided by histology type, stage, gestational age, obstetric complications and patient preferences concerning continuation versus termination of pregnancy, and discussed in multidisciplinary team. Multidisciplinary team includes gynecologic oncologist / obstetrician, medical oncologist, radiologist, neonatologist.

General Principles:

- Individualize case based on FIGO staging, histology, and trimester. Early-stage (I-II) may allow conservative surgery and delayed treatment; advanced (III-IV) requires urgent intervention.
- Prioritize maternal survival while optimizing fetal outcomes. Involve hospital ethics committees for complex decisions such as termination.
- Refer to gynecologic oncologist for suspected malignancy to improve survival (5-year survival for stage I: 90%, stage III-IV: 20–30%).:

Management by Trimester

First Trimester:

- **Surgery:** Laparoscopy preferred for masses >5–10 cm or suspicious features (e.g., solid components). Perform at 14–16 weeks to minimize miscarriage risk (10–15% in first trimester). Unilateral salpingo-oophorectomy or cystectomy for early-stage. Staging laparotomy omentectomy, lymphadenectomy if malignancy confirmed.
- **Chemotherapy:** Avoid unless life-threatening (e.g., stage IV); teratogenic risks highest in weeks 2–8.
- Consider termination counseling for advanced cases, respecting patient autonomy.

Second Trimester

- **Surgery:** Safest window (16–20 weeks); laparoscopy or laparotomy for staging. Fertility-sparing surgery (unilateral salpingo-oophorectomy) feasible for early-stage germ cell or low-grade epithelial tumors in young women.
- **Chemotherapy:** Safe after 12 weeks (e.g., carboplatin + paclitaxel for epithelial tumors, BEP for germ cell tumors). Minimal fetal risk (malformation rate <3% post-first trimester).

Third Trimester:

- **Surgery:** Delay until delivery if possible (e.g., stage I, asymptomatic). Perform cesarean with concurrent staging/debulking if needed.
- **Chemotherapy:** Administer if urgent; plan delivery at 34–37 weeks to minimize fetal exposure. Avoid PARP inhibitors (e.g., olaparib) due to limited pregnancy data.

Delivery Considerations:

- Vaginal delivery preferred for early-stage, and stable cases. Cesarean for obstetric indications or concurrent debulking.
- Timing: Aim for 37–39 weeks if maternal/fetal condition allows; earlier (34–36 weeks) for advanced disease or fetal compromise.
- Neonatal care: NICU readiness for preterm births; monitor for chemotherapy effects (e.g., transient neutropenia in neonate).

Postpartum: Resume or initiate adjuvant therapy (e.g., chemotherapy, PARP inhibitors for BRCA-positive cases). Breastfeeding contraindicated during chemotherapy.

Specific Considerations:

- Germ Cell Tumors: Often early-stage, highly responsive to BEP (bleomycin, etoposide, cisplatin). Fertility-sparing surgery successful in 80–90% of cases.
- Epithelial Tumors: Low-grade serous/mucinous may allow conservative management; high-grade require aggressive debulking.
- Genetic Testing: Offer to all patients post-diagnosis to identify BRCA/HRD mutations for targeted therapies.
- Counseling: Discuss fertility preservation (e.g., oocyte cryopreservation pre-treatment), recurrence risks, and psychological support.

Notes:

1. Risks in Pregnancy: Maternal risks include tumor rupture, torsion, or hemorrhage; fetal risks include preterm delivery (20–30% in treated cases) or IUGR from chemotherapy.
2. Multidisciplinary Approach: Essential for balancing oncologic and obstetric needs. Include patient preferences in shared decision-making.
3. Postpartum Follow-Up: Regular surveillance (CA 125, imaging) and long-term management for recurrence (20–50% in advanced stages).

PROGNOSIS AND PROGRESSION

Prognosis in ovarian carcinoma hinges on the extent of disease at diagnosis, tumor biology and surgical outcomes. Continuous improvements in early detection, surgical technique and adjuvant therapies aim to shift more patients into the favorable survival brackets defined by early-stage diagnosis and optimal cytoreduction.

- Five-year relative survival rates by FIGO stage fall steeply from 90–95% for stage I to 70–80% for stage II, 20–50% for stage III and a dismal 1–5% for stage IV.
- Histologic grade further stratifies risk: low-grade tumors carry a roughly 88% five-year survival, intermediate-grade about 58% and high-grade around 27%.
- Among surgical factors, the volume of residual disease left after cytoreductive surgery is the strongest predictor of outcome. In one meta-analysis, women with residual tumor nodules ≤ 2 cm experienced a 78% five-year survival compared to just 29.2% for those with residual disease exceeding 2 cm.
- Achieving no gross residual disease (R0 resection) yields the best prognosis and remains a primary goal of initial management.

Referral for specialist consultation/higher level

- **Primary care providers** should immediately refer to higher level whenever ovarian carcinoma is suspected. Any woman over 50 (or younger with significant family history) presenting with persistent bloating, pelvic pain or urinary frequency plus a CA-125 level ≥35 IU/mL or an abnormal transvaginal ultrasound should trigger a “two-week wait” referral to a gynae-oncology service to expedite diagnosis and staging.

  Before referral, basic evaluation-including pelvic examination, CA-125, and ultrasound-helps prioritize cases, but should not delay specialist review when malignancy is in the differential.

- **At secondary care level,** once histopathologic confirmation of ovarian carcinoma is obtained, all patients must be transferred without delay to a tertiary oncology center staffed by a gynecologic oncologist and multidisciplinary team. These centers provide comprehensive surgical staging, optimal cytoreduction and protocol-driven chemotherapy, interventions shown to improve overall survival when compared to non-specialist care. Referral processes should include forwarding operative reports, imaging, pathology slides and baseline lab results to the receiving team. Ideally, surgical consultation occurs within four weeks of diagnosis and chemotherapy begins within eight weeks, minimizing progression risk.
- Clear, timely communication between primary, secondary and tertiary teams ensures patients access the highest-standard care pathways that standardization aims to guarantee, reducing variability and improving outcomes.

PREVENTION AND HEALTH PROMOTION

In the absence of a proven screening test for average-risk women, ovarian cancer prevention hinges on targeted risk-reduction measures. By weaving risk-reduction strategies into everyday care and community programs, we can shift diagnoses earlier and drive down ovarian cancer mortality.

- Chemoprevention: Use of combined oral contraceptives for five or more years lowers ovarian cancer risk by roughly half, even among BRCA carriers. Tubal ligation and opportunistic salpingectomy during pelvic surgery reduce risk by up to two-thirds, owing to the fallopian tube's role in tumor origin.
- High-risk monitoring: Women with BRCA1/2 or Lynch syndrome mutations should consider risk-reducing bilateral salpingo-oophorectomy, between 35–40 years for BRCA1 and 40–45 for BRCA2 carriers-once childbearing is complete.
- Genetic counseling and testing identify high-risk individuals, enabling personalized prevention plans and surveillance.
- Lifestyle modifications-maintaining a healthy weight through balanced nutrition and regular exercise, avoiding tobacco and limiting alcohol-further decrease risk by reducing chronic inflammation and hormonal imbalances.

Note: Ovarian cancer is the "silent killer" because early signs - bloating, pelvic discomfort or changes in appetite, are easy to overlook. By the time it's detected, the disease often has already spread. Therefore, routine screening is not recommended for average-risk women due to the limitations of current tools: transvaginal ultrasound and CA-125 testing yield high false-positive rates and lack evidence for mortality reduction.

For women with a strong family history or known BRCA1/2 mutations, a different approach is warranted. In these high-risk individuals, tailored surveillance may be offered, involving serial CA-125 measurements and transvaginal ultrasound. However, it's critical to emphasize that no standardized surveillance protocol exists.

CA-125 must be interpreted with caution since levels may rise due to benign conditions (e.g., endometriosis, fibroids, pelvic infections) and some ovarian cancers do not elevate CA-125 at all.

Each consultation should prioritize a transparent discussion of risks, benefits, and limitations, supporting informed decisions about prevention and monitoring that align with the woman's risk profile and reproductive goals.

- Effective health promotion combines provider-led education, community outreach and opportunistic prevention. Primary care clinicians should teach women that persistent bloating, pelvic pain or urinary changes lasting more than 2-3 weeks warrant evaluation, even when no mass is palpable.

- Focused awareness-and-screening drives can cut diagnostic delays and shift cancers to earlier stages. Mysuru's End-O Check - launched at Apollo BGS Hospitals for women 45+ - pairs symptom education with targeted evaluation (e.g., transvaginal ultrasound, CA-125), aiming to catch endometrial/ovarian cancers sooner and improve outcomes. Early reports from the launch stress that awareness gaps drive late diagnoses and that earlier detection markedly raises survival, underscoring the value of such campaigns.
- Public health messaging must emphasize the lack of routine screening for average-risk women while promoting symptom vigilance, family-history review and discussion of risk-reducing options - especially opportunistic salpingectomy during hysterectomy or sterilization procedures.

PATIENT EDUCATION

Patient education aims to empower women and their families to participate actively in care, recognize warning signs, adhere to treatment, and maintain well-being throughout the ovarian cancer journey.

- Patients should understand the nature of ovarian carcinoma - its origin, staging and expected course - to make informed decisions about surgery, chemotherapy and maintenance therapies.
- Education clarifies the purpose, schedule and potential side effects of each treatment, teaching self-monitoring for fever, neuropathy or bleeding and when to contact the care team.
- Emphasis on symptom awareness - new or worsening bloating, pain or gastrointestinal changes - facilitates early detection of recurrence.
- Instruction on lifestyle measures, including balanced nutrition, exercise and smoking cessation, supports recovery and reduces complication risks such as thromboembolism.
- Genetic counseling discussions ensure patients grasp the implications of BRCA or Lynch mutations for relatives and the value of risk-reducing surgery or family testing. Practical guidance on fertility preservation, use of port-a-cath devices and management of ascites or lymphedema addresses daily challenges.
- Psychosocial support resources (counseling, support groups and palliative care) are introduced to help patients cope with anxiety, fatigue and treatment-related changes in body image, reinforcing that care extends beyond tumor control to quality of life.
- Referral to pain management clinics.

Instructions to the patient/caregiver

Patients and caregivers play a vital role in successful treatment and recovery. Follow these instructions closely:

Topic	Do	Don't	When to call your team
Symptom monitoring	Track new/worsening bloating, pelvic/abdominal pain, bowel/bladder change, fatigue, weight change; check wounds/ports	Ignore "mild" new symptoms	Immediately for fever ≥38°C, severe nausea/vomiting, uncontrolled pain, redness/ swelling/discharge at surgical or port sites
Treatment adherence	Take meds on time; use a pillbox/phone reminders (e.g., olaparib); attend every infusion and follow-up	Skip or change doses on your own	If a dose is missed or vomiting occurs after dosing-call for advice
Nausea control	Small, frequent meals; take prescribed antiemetics before/after chemo	Rely only on home remedies	Persistent vomiting or inability to keep fluids down
Neuropathy	Daily hand/foot stretches; report tingling/numbness early	Wait for symptoms to "settle"	New numbness, burning pain, or balance issues
Hair/scalp care	Gentle scalp hygiene; consider scalp cooling or wigs	Use harsh chemicals/heat styling	If scalp is painful or infected
Mouth care (mucositis)	Brush gently; saline/ bicarbonate rinses after meals	Alcohol mouthwashes; rough brushing	Painful sores that prevent eating/drinking
Nutrition & hydration	High-protein, nutrient-dense foods; small frequent servings; sip water/ electrolytes through the day; see dietitian if >5% weight loss or swallowing issues	Skip meals; rely on supplements alone	Rapid weight loss, dehydration, or trouble swallowing
Activity & clot prevention	Light walking/cycling; gentle strength work; use compression stockings as prescribed; move every hour when awake	Prolonged bed rest or long immobility	New calf pain/swelling, sudden chest pain, or breathlessness
Port-a-cath care	Keep site clean/dry; follow flush protocol	Submerge the site or skip flushes	Redness, warmth, swelling, leakage, or fever
Paracentesis care	Rest after procedure; monitor for bleeding, fever, increasing pain	Heavy lifting the same day	Fever, severe pain, or persistent fluid leakage
Genetics & family	Arrange BRCA/Lynch counseling/testing; inform at-risk relatives	Delay discussions until after treatment ends	Questions on family risk or testing logistics

Fertility	If desired, complete oocyte/ ovarian tissue cryopreservation before chemo	Start chemo without discussing options (when time allows)	If periods stop or fertility concerns arise
Support & tracking	Name a primary caregiver; join a support group; keep a treatment journal (side effects, questions, milestones)	Go it alone	Caregiver burnout or difficulty managing meds/symptoms
Emergency planning	Carry a treatment summary (diagnosis, surgeries, regimens, allergies); list contacts (oncologist, PCP, nearest hospital, key family)	Travel without your info	Any urgent symptom while away from home
Substances	Stay smoke-free; avoid alcohol and recreational drugs	Smoke, vape, or drink alcohol during treatment	Cravings or withdrawal-ask for support to quit
Over-the-counter/herbals	Check all OTC/herbal products with your oncologist/pharmacist	Start supplements without approval	If you already took something-call to verify safety

Keep this table with your medication list and emergency contacts.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49. doi:10.3322/caac.21660.

2. International Agency for Research on Cancer. Global Cancer Observatory. South-Eastern Asia fact sheet 2022. Lyon: IARC; 2024 [cited 2025 Aug 15]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/920-south-eastern-asia-fact-sheet.pdf

3. International Agency for Research on Cancer. Cancer incidence and mortality: Maldives fact sheet 2022. Lyon: IARC; 2022 [cited 2025 Aug 15]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/462-maldives-fact-sheet.pdf

4. Cabasag CJ, Fagan PJ, Ferlay J, Vignat J, Laversanne M, Liu L, et al. Ovarian cancer today and tomorrow: A global assessment by world region and Human Development Index using GLOBOCAN 2020. Int J Cancer. 2022;151(9):1535-41. doi:10.1002/ijc.34002.

5. National Cancer Institute. Cancer stat facts: ovarian cancer. SEER 21 (2018–2022). Bethesda (MD): NCI; [cited 2025 Aug 15]. Available from: https://seer.cancer.gov/statfacts/html/ovary.html

6. American Cancer Society. Survival rates for ovarian cancer. Atlanta: ACS; 2025 Jun 30 [cited 2025 Aug 15]. Available from: https://www.cancer.org/cancer/types/ovarian-cancer/detection-diagnosis-staging/survival-rates.html

7. Ali AT, Al-Ani O, Al-Ani F. Epidemiology and risk factors for ovarian cancer. Prz Menopauzalny. 2023;22(2):93-104. doi:10.5114/pm.2023.128661.

8. Ovarian Cancer Research Alliance. Ovarian cancer prevention and risk. New York: OCRA; [cited 2025 Aug 15]. Available from: https://ocrahope.org/for-patients/prevention-risk/

9. Paavonen J, Fortner RT, Lehtinen M, Idahl A. Chlamydia trachomatis, pelvic inflammatory disease, and epithelial ovarian cancer. J Infect Dis. 2021;224(Suppl 2):S121-7. doi:10.1093/infdis/jiab017.

10. National Comprehensive Cancer Network. NCCN guidelines version 5.2022: Poland edition. Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer. Warsaw: NCCN; 2022. Available from: https://onkologia.org.pl/wp-content/uploads/2022/10/Wytyczne-postepowania-diagnostyczno-terapeutycznego-u-chorych-na-raka-jajnika-adaptacja-NCCN.pdf

11. González-Martín A, Lorusso D, Colombo N, Sessa C, Ray-Coquard I, Vergote I, et al. Newly diagnosed and relapsed epithelial ovarian cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol. 2023;34(10):833-48. doi:10.1016/j.annonc.2023.08.008.

12. Faubion SS, MacLaughlin KL, Long ME, Pruthi S, Casey PM. Surveillance and care of the gynecologic cancer survivor. J Womens Health (Larchmt). 2015;24(11):899-906. doi:10.1089/jwh.2014.5127.

13. Indian Council of Medical Research. Consensus document for management of epithelial ovarian cancer. New Delhi: ICMR; 2019 [cited 2025 Aug 15]. Available from: https://www.icmr.gov.in/icmrobject/custom_data/pdf/resource-guidelines/Ovarian_Cancer.pdf

14. Moss E, Taylor A, Andreou A, Ang C, Arora R, Attygalle A, et al. British Gynaecological Cancer Society (BGCS) ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024. Eur J Obstet Gynecol Reprod Biol. 2024;300:69-123. doi:10.1016/j.ejogrb.2024.06.025.

15. Royal College of Obstetricians and Gynaecologists; British Society for Gynaecological Endoscopy. Management of suspected ovarian masses in premenopausal women. Green-top guideline No. 62. London: RCOG/BSGE; 2011 Nov [cited 2025 Aug 15]. Available from: https://www.rcog.org.uk/media/yhujmdvr/gtg_62-1.pdf

16. ACOG Guidelines (Practice Bulletin No. 174, 2016, reaffirmed 2023). Evaluation and Management of Adnexal Masses, 2016, reaffirmed 2023

17. IARC/WHO Contribution (WHO Classification of Tumours, 5th edition, 2020)

18. Early detection program for endometrial, ovarian, cancer in women. https://timesofindia.indiatimes.com/city/mysuru/early-detection-prog-for-endometrial-ovarian-cancer-in-women-launched/articleshow/123003405.cms?utm_source=chatgpt.com