



# Ovarian cancer: recognition and initial management

Clinical guideline

Published: 27 April 2011

Last updated: 2 October 2023

www.nice.org.uk/guidance/cg122

## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the <u>Yellow Card Scheme</u>.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

### **Contents**

Overview	4
Who is it for?	4
Recommendations	5
1.1 Detection in primary care	5
1.2 Establishing the diagnosis in secondary care	7
1.3 Information and support for women with newly diagnosed ovarian cancer	8
1.4 Management of suspected early (stage 1) ovarian cancer	9
1.5 Management of advanced (stage 2 to 4) ovarian cancer	11
1.6 Systemic anti-cancer therapy for recurrent or relapsed ovarian cancer	13
Terms used in this guideline	15
Recommendations for research	16
1 Relationship between duration of symptoms of ovarian cancer and stage at diagnosis	16
2 Imaging in the diagnostic pathway for women with ovarian cancer	16
3 The value of primary surgery for women with advanced ovarian cancer	17
Appendix: Risk of malignancy index (RMI I)	18
Finding more information and committee details	19
Update information	20

This guideline partially replaces CG61.

This guideline is partially replaced by NG12.

This guideline is the basis of QS18.

### Overview

This guideline covers detecting, diagnosing and treating women (aged 18 and over) who have, or are suspected of having, epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer or borderline ovarian cancer. It aims to enable earlier detection of ovarian cancer and improve initial treatment.

NICE has also produced a guideline on identifying and managing familial and genetic risk associated with ovarian cancer.

#### Who is it for?

- Healthcare professionals
- Commissioners and providers
- People who provide palliative and hospice care for the NHS
- Women with ovarian cancer and their families and carers

### Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in <u>NICE's information on making decisions about your care</u>.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

### 1.1 Detection in primary care

Recommendations in this section have been incorporated into NICE's guideline on suspected cancer.

#### 1.1.1 Awareness of symptoms and signs

- 1.1.1.1 Refer the woman using a <u>suspected cancer pathway referral</u> if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously uterine fibroids).
- 1.1.1.2 Carry out tests in primary care (see the <u>section on asking the right question first tests</u>) if a woman (especially if 50 or over) reports having any of the following symptoms on a persistent or frequent basis particularly more than 12 times per month:
  - persistent abdominal distension (women often refer to this as 'bloating')
  - feeling full (early satiety) and/or loss of appetite
  - pelvic or abdominal pain
  - increased urinary urgency and/or frequency.

See also NICE's guideline on suspected cancer: recognition and referral.

- 1.1.1.3 Consider carrying out tests in primary care (see the <u>section on asking the right question first tests</u>) if a woman reports unexplained weight loss, fatigue or changes in bowel habit.
- 1.1.1.4 Advise any woman who is not suspected of having ovarian cancer to return to her GP if her symptoms become more frequent and/or persistent.
- 1.1.1.5 Carry out appropriate tests for ovarian cancer (see the <u>section on asking the right question first tests</u>) in any woman of 50 or over who has experienced symptoms within the last 12 months that suggest irritable bowel syndrome (IBS), because IBS rarely presents for the first time in women of this age.

See NICE's guideline on irritable bowel syndrome in adults.

#### 1.1.2 Asking the right question – first tests

- 1.1.2.1 Measure serum CA125 in primary care in women with symptoms that suggest ovarian cancer (see the <u>section on awareness of symptoms and signs</u>).
- 1.1.2.2 If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis.
- 1.1.2.3 If the ultrasound suggests ovarian cancer, refer the woman for further investigation using a <u>suspected cancer pathway referral</u>.
- 1.1.2.4 For any woman who has normal serum CA125 (less than 35 IU/ml), or CA125 of 35 IU/ml or greater but a normal ultrasound:
  - assess her carefully for other clinical causes of her symptoms and investigate if appropriate
  - if no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent.

### 1.2 Establishing the diagnosis in secondary care

#### 1.2.1 Tumour markers: which to use?

- 1.2.1.1 Measure serum CA125 in secondary care in all women with suspected ovarian cancer, if this has not already been done in primary care.
- 1.2.1.2 In women under 40 with suspected ovarian cancer, measure levels of alpha fetoprotein (AFP) and beta human chorionic gonadotrophin (beta-hCG) as well as serum CA125, to identify women who may not have epithelial ovarian cancer.

#### 1.2.2 Malignancy indices

1.2.2.1 Calculate a risk of malignancy index I (RMI I) score (after performing an ultrasound; see recommendation 1.2.3.1 in the section on imaging in the diagnostic pathway: which procedures?) and refer all women with an RMI I score of 250 or greater to a specialist multidisciplinary team.

See the appendix for details of how to calculate an RMI I score.

#### 1.2.3 Imaging in the diagnostic pathway: which procedures?

- 1.2.3.1 Perform an ultrasound of the abdomen and pelvis as the first imaging test in secondary care for women with suspected ovarian cancer, if this has not already been done in primary care.
- 1.2.3.2 If the ultrasound, serum CA125 and clinical status suggest ovarian cancer, perform a CT scan of the pelvis and abdomen to establish the extent of disease. Include the thorax if clinically indicated.
- 1.2.3.3 Do not use MRI routinely for assessing women with suspected ovarian cancer.

#### 1.2.4 Tissue diagnosis

#### Requirement for tissue diagnosis

- 1.2.4.1 If offering cytotoxic chemotherapy to women with suspected advanced ovarian cancer, first obtain a confirmed tissue diagnosis by histology (or by cytology if histology is not appropriate) in all but exceptional cases.
- 1.2.4.2 Offer cytotoxic chemotherapy for suspected advanced ovarian cancer without a tissue diagnosis (histology or cytology) only:
  - in exceptional cases, after discussion at the multidisciplinary team and
  - after discussing with the woman the possible benefits and risks of starting chemotherapy without a tissue diagnosis.

#### Methods of tissue diagnosis other than laparotomy

- 1.2.4.3 If surgery has not been performed, use histology rather than cytology to obtain a tissue diagnosis. To obtain tissue for histology:
  - use percutaneous image-guided biopsy if this is feasible
  - consider laparoscopic biopsy if percutaneous image-guided biopsy is not feasible or has not produced an adequate sample.

Use cytology if histology is not appropriate.

# 1.3 Information and support for women with newly diagnosed ovarian cancer

- 1.3.1.1 Offer all women with newly diagnosed ovarian cancer information about their disease, including psychosocial and psychosexual issues, that:
  - is available at the time they want it
  - includes the amount of detail that they want and are able to deal with

• is in a suitable format, including written information.

#### 1.3.1.2 Ensure that information is available about:

- the stage of the disease, treatment options and prognosis
- how to manage the side effects of both the disease and its treatments in order to maximise wellbeing
- sexuality and sexual activity
- fertility and hormone treatment
- symptoms and signs of disease recurrence
- genetics, including the chances of family members developing ovarian cancer (see <u>NICE's guideline on ovarian cancer: identifying and managing familial</u> and genetic risk)
- self-help strategies to optimise independence and coping
- where to go for support, including support groups
- how to deal with emotions such as sadness, depression, anxiety and a feeling
  of a lack of control over the outcome of the disease and treatment.

# 1.4 Management of suspected early (stage 1) ovarian cancer

#### 1.4.1 The role of systematic retroperitoneal lymphadenectomy

1.4.1.1 Perform retroperitoneal lymph node assessment as part of optimal surgical staging in women with suspected ovarian cancer whose disease appears to be confined to the ovaries (that is, who appear to have stage 1 disease).

Lymph node assessment involves sampling of retroperitoneal lymphatic tissue from the para-aortic area and pelvic side walls if there is a palpable abnormality,

or random sampling if there is no palpable abnormality.

Optimal surgical staging constitutes: midline laparotomy to allow thorough assessment of the abdomen and pelvis; a total abdominal hysterectomy, bilateral salpingo-oophorectomy and infracolic omentectomy; biopsies of any peritoneal deposits; random biopsies of the pelvic and abdominal peritoneum; and retroperitoneal lymph node assessment (Winter-Roach et al. 2009).

1.4.1.2 Do not include systematic retroperitoneal lymphadenectomy (block dissection of lymph nodes from the pelvic side walls to the level of the renal veins) as part of standard surgical treatment in women with suspected ovarian cancer whose disease appears to be confined to the ovaries (that is, who appear to have stage 1 disease).

#### 1.4.2 Adjuvant systemic chemotherapy for stage 1 disease

- 1.4.2.1 Do not offer adjuvant chemotherapy to women who have had optimal surgical staging and have low-risk stage 1 disease (grade 1 or 2, stage 1a or 1b).
- 1.4.2.2 Offer women with high-risk stage 1 disease (grade 3 or stage 1c) adjuvant chemotherapy consisting of 6 cycles of carboplatin.
- 1.4.2.3 Discuss the possible benefits and side effects of adjuvant chemotherapy with women who have had suboptimal surgical staging and appear to have stage 1 disease.

Optimal surgical staging constitutes: midline laparotomy to allow thorough assessment of the abdomen and pelvis; a total abdominal hysterectomy, bilateral salpingo-oophorectomy and infracolic omentectomy; biopsies of any peritoneal deposits; random biopsies of the pelvic and abdominal peritoneum; and retroperitoneal lymph node assessment (Winter-Roach et al. 2009).

# 1.5 Management of advanced (stage 2 to 4) ovarian cancer

#### 1.5.1 Primary surgery

1.5.1.1 If performing surgery for women with ovarian cancer, whether before chemotherapy or after neoadjuvant chemotherapy, the objective should be complete resection of all macroscopic disease.

#### 1.5.2 Intraperitoneal chemotherapy

1.5.2.1 Do not offer intraperitoneal chemotherapy to women with ovarian cancer, except as part of a clinical trial. See also NICE's interventional procedures guidance on cytoreduction surgery with hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis, which recommends that this procedure should only be used with special arrangements for clinical governance, consent, and audit or research.

#### 1.5.3 First-line systemic anti-cancer therapy

- 1.5.3.1 Paclitaxel in combination with a platinum-based compound or platinum-based therapy alone (cisplatin or carboplatin) are recommended as options in NICE technology appraisal guidance for first-line chemotherapy for treating ovarian cancer. For full details, see the guidance on paclitaxel (TA55, 2005).
- 1.5.3.2 Bevacizumab with paclitaxel and carboplatin is not recommended in NICE technology appraisal guidance for first-line treatment of advanced ovarian cancer. For full details, see the guidance on bevacizumab (TA284, 2013). However, NHS England recommends bevacizumab with paclitaxel and carboplatin as an option for first-line induction treatment for advanced (stage 3 and 4) ovarian cancer at a dose of 7.5 mg/kg or 15 mg/kg. For more information, see the NHS England Cancer Drugs Fund list.

In April 2025, a dose of 7.5 mg/kg was an off-label use of bevacizumab. See

NICE's information on prescribing medicines.

#### 1.5.4 Systemic anti-cancer therapy for maintenance treatment

- 1.5.4.1 Rucaparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance for BRCA mutation-negative and homologous recombination deficiency positive advanced (stage 3 and 4) high-grade epithelial ovarian cancer after complete or partial response to first-line platinum-based chemotherapy. For full details, see the guidance on rucaparib (TA1055, 2025).
- 1.5.4.2 Rucaparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance for BRCA mutation-negative advanced (stage 3 and 4) high-grade epithelial ovarian cancer where homologous recombination deficiency status is negative or unknown and bevacizumab is not a treatment option, after complete or partial response to first-line platinum-based chemotherapy. For full details, see the guidance on rucaparib (TA1055, 2025).
- 1.5.4.3 Olaparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance for BRCA mutation-positive advanced (stage 3 and 4) high-grade epithelial ovarian cancer after response to first-line platinum-based chemotherapy. For full details, see the guidance on olaparib (TA962, 2024).
- 1.5.4.4 Olaparib with bevacizumab for maintenance treatment is recommended as an option in NICE technology appraisal guidance for homologous recombination deficiency positive, advanced (stage 3 and 4), high-grade epithelial ovarian cancer after complete or partial response to first-line platinum-based chemotherapy with bevacizumab. For full details, see the guidance on olaparib with bevacizumab (TA946, 2024).
- 1.5.4.5 Niraparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance within the Cancer Drugs Fund for advanced (stage 3 and 4) high-grade epithelial ovarian cancer after response to first-line platinum-based chemotherapy only if the conditions in the managed access agreement are followed. For full details, see the guidance on niraparib (TA673, 2021).

1.5.4.6 Bevacizumab for maintenance treatment is recommended as an option by NHS England for advanced (stage 3 and 4) ovarian cancer previously treated with a 7.5 mg/kg dose of bevacizumab in combination with carboplatin and paclitaxel. See the NHS England Cancer Drugs Fund list.

In April 2025, this was an off-label use of bevacizumab. See <u>NICE's information</u> on prescribing medicines.

# 1.6 Systemic anti-cancer therapy for recurrent or relapsed ovarian cancer

#### 1.6.1 Systemic anti-cancer therapy options

- 1.6.1.1 For medicines recommended as options in NICE technology appraisal guidance for treating recurrent ovarian cancer, see the guidance on:
  - paclitaxel in combination with platinum or as monotherapy (TA389, 2016)
  - pegylated liposomal doxorubicin hydrochloride (PLDH) as monotherapy (TA389, 2016)
  - PLDH in combination with platinum (TA389, 2016).
- 1.6.1.2 For medicines not recommended in NICE technology appraisal guidance for treating the first recurrence of platinum-sensitive ovarian cancer, see the guidance on:
  - gemcitabine in combination with carboplatin (TA389, 2016)
  - trabectedin in combination with PLDH (TA389, 2016)
  - topotecan (TA389, 2016)
  - bevacizumab in combination with gemcitabine and carboplatin (TA285, 2013).
- 1.6.1.3 Topotecan is not recommended in NICE technology appraisal guidance for treating recurrent platinum-resistant or platinum-refractory ovarian cancer. For

full details, see the guidance on topotecan (TA389, 2016).

1.6.1.4 Trametinib is recommended as an option by NHS England for treating serous low-grade ovarian or peritoneal cancer that has recurred or progressed following at least 1 platinum-based chemotherapy. See the <a href="NHS England Cancer Drugs Fund">NHS England Cancer Drugs Fund</a> list.

In April 2025, this was an off-label use of trametinib. See <u>NICE's information on</u> prescribing medicines.

#### 1.6.2 Systemic anti-cancer therapy for maintenance treatment

- 1.6.2.1 Rucaparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance for relapsed platinum-sensitive high-grade epithelial ovarian cancer that has completely or partially responded to platinum-based chemotherapy. For full details, see the guidance on rucaparib (TA1007, 2024).
- 1.6.2.2 Olaparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance for BRCA mutation-positive relapsed, platinum-sensitive, high-grade epithelial ovarian cancer, after 2 or more courses of platinum-based chemotherapy. For full details, see the guidance on olaparib (TA908, 2023).
- 1.6.2.3 Niraparib for maintenance treatment is recommended as an option in NICE technology appraisal guidance for treating relapsed, platinum-sensitive high-grade serous epithelial ovarian cancer in adults that has responded to the most recent course of platinum-based chemotherapy if:
  - they have a BRCA mutation and have had 2 courses of platinum-based chemotherapy, or
  - they do not have a BRCA mutation and have had 2 or more courses of platinum-based chemotherapy.

For full details, see the guidance on niraparib (TA784, 2022).

### 1.6.3 Neurotrophic tyrosine receptor kinase (NTRK) fusionpositive solid tumours

The point at which to use genomic biomarker-based therapy in solid tumour treatment pathways is uncertain. See the <u>NICE topic page on genomic biomarker-based cancer</u> treatments.

### Terms used in this guideline

#### Suspected cancer pathway referral

Person to receive a diagnosis or ruling out of cancer within 28 days of being referred urgently by their GP for suspected cancer. For further details, see <a href="NHS England's webpage">NHS England's webpage</a> on faster diagnosis of cancer.

### Recommendations for research

The committee has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

# 1 Relationship between duration of symptoms of ovarian cancer and stage at diagnosis

Further research should be undertaken on the relationship between the duration and frequency of symptoms in women with ovarian cancer before diagnosis, the stage of disease at diagnosis and subsequent survival.

#### Why this is important

Most women presenting with ovarian cancer have advanced disease and have had symptoms for months. Greater awareness among both women and healthcare professionals might result in women presenting earlier with less advanced disease, leading to better outcomes. There is insufficient understanding of the factors that influence earlier diagnosis in women with ovarian cancer, especially the relationship between duration of symptoms and stage at diagnosis. Data demonstrating benefits from earlier presentation will justify investment in raising awareness among women and healthcare professionals. This is likely to be a population-based study that records both the duration and frequency of symptoms.

# 2 Imaging in the diagnostic pathway for women with ovarian cancer

Large multicentre case–control studies should be conducted to compare the accuracy of CT versus MRI for staging and for predicting optimal cytoreduction in women with ovarian cancer.

#### Why this is important

Currently most women with ovarian cancer will undergo a CT scan before surgery to

assess the extent and resectability of disease. CT and MRI are complementary in their abilities to detect disease, but no adequate studies have been performed that compare their effectiveness in women with suspected ovarian cancer. No comparative studies have been undertaken evaluating surgical outcome. A prospective study in women undergoing primary surgery would be feasible.

# 3 The value of primary surgery for women with advanced ovarian cancer

Research should be undertaken to determine the effectiveness of primary surgery for women with advanced ovarian cancer whose tumour cannot be fully excised.

#### Why this is important

Most women with advanced ovarian cancer undergo surgery at some point. Previous studies have shown that surgery after the completion of chemotherapy has no therapeutic value. Studies are being performed to investigate whether the timing of surgery during primary chemotherapy influences outcome. No studies have evaluated whether primary surgery itself has any therapeutic value when compared with chemotherapy alone. The potential advantages of surgery have to be offset against the morbidity, occasional mortality and undoubted costs associated with it. This would be a prospective randomised clinical trial recruiting women who have biopsy-proven advanced ovarian cancer and who are fit enough to receive surgery and chemotherapy. Women would be randomised to either chemotherapy and surgery (conventional arm) or chemotherapy alone (experimental arm). Primary outcome measures would be survival at 1 and 5 years.

# Appendix: Risk of malignancy index (RMI I)

RMI I combines 3 pre-surgical features: serum CA125 (CA125), menopausal status (M) and ultrasound score (U). The RMI is a product of the ultrasound scan score, the menopausal status and the serum CA125 level (IU/ml).

#### $RMI = U \times M \times CA125$

- The ultrasound result is scored 1 point for each of the following characteristics: multilocular cysts, solid areas, metastases, ascites and bilateral lesions. U = 0 (for an ultrasound score of 0), U = 1 (for an ultrasound score of 1), U = 3 (for an ultrasound score of 2 to 5).
- The menopausal status is scored as 1 = pre-menopausal and 3 = post-menopausal.
- The classification of 'post-menopausal' is a woman who has had no period for more than 1 year or a woman over 50 who has had a hysterectomy.
- Serum CA125 is measured in IU/ml and can vary between 0 and hundreds or even thousands of units.

# Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the <u>NICE</u> topic page on ovarian cancer.

For full details of the evidence and the guideline committee's discussions, see the <u>full</u> <u>guideline and evidence reviews</u>. You can also find information about <u>how the guideline was developed</u>, including <u>details of the committee</u>.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

### **Update information**

October 2023: We updated recommendations 1.1.1.1 and 1.1.2.3 in line with NHS England's standard on faster diagnosis of cancer.

June 2015: Recommendations in section 1.1 have been incorporated into section 1.5 of the <u>NICE guideline on suspected cancer</u>. Recommendation 1.1.2.1 in this guideline partially replaces recommendation 1.1.1.3 in the <u>NICE guideline on irritable bowel syndrome in adults</u> (February 2008). This guideline was previously called ovarian cancer: the recognition and initial management of ovarian cancer.

#### Minor changes since publication

April 2025: We added links to relevant technology appraisal guidance in the <u>section on management of advanced (stage 2 to 4) ovarian cancer</u> and a <u>new section on systemic anti-cancer therapy for recurrent or relapsed ovarian cancer.</u>

**January 2025:** We added a link to NICE's interventional procedures guidance on cytoreduction surgery with hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis (IPG688) to the section on intraperitoneal chemotherapy.

**December 2017:** Two out of date recommendations for research have been removed.

ISBN: 978-1-4731-5442-1