

Ovarian cancer: recognition and initial management

Clinical guideline

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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.

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 assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline partially replaces CG61.

This guideline is partially replaced by NG12.

This guideline is the basis of QS18.

Introduction

Ovarian cancer is the leading cause of death from gynaecological cancer in the UK, and its incidence is rising. It is the fifth most common cancer in women, with a lifetime risk of about 2% in England and Wales.

The outcome for women with ovarian cancer is generally poor, with an overall 5-year survival rate of less than 35%. This is because most women who have ovarian cancer present with advanced disease. The stage of the disease is the most important factor affecting outcome. The woman's general health at the time of presentation is also important because it affects what treatments can be used. Most women have had symptoms for months before presentation, and there are often delays between presentation and specialist referral. There is a need for greater awareness of the disease and also for initial investigations in primary and secondary care that enable earlier referral and optimum treatment.

Despite the relatively poor overall survival rates for ovarian cancer, there has been a two-fold increase in survival over the last 30 years. This has coincided with the advent of effective chemotherapy, and the introduction of platinum-based agents in particular, as well as changes in surgical practice. More recently, there has been a significant shift towards greater specialisation in the delivery of care, resulting from the implementation of the cancer service guidance 'Improving outcomes in gynaecological cancers'^[1]. It is likely that some or all of these changes have contributed to the improved survival rates, emphasising the need to ensure that women with diagnosed ovarian cancer are treated in specialist centres that can provide comprehensive cancer care.

This guideline does not cover the entire care pathway for ovarian cancer. It focuses on areas where there is uncertainty or wide variation in clinical practice with regard to the detection, diagnosis and initial management of ovarian cancer. The guideline recommendations are applicable to women with epithelial ovarian cancer (the most common type of ovarian cancer), as well as women with fallopian tube carcinoma, primary peritoneal carcinoma or borderline ovarian cancer (see section 2 for further details).

The guideline assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

^[1] Improving outcomes in gynaecological cancers. Cancer service guidance (1999). Department of Health, National Cancer Guidance Steering Group

Patient-centred care

This guideline offers best practice advice on the care of women with suspected or diagnosed ovarian cancer.

Treatment and care should take into account patients' needs and preferences. Women with ovarian cancer should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If women do not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) and the [code of practice that accompanies the Mental Capacity Act](#). In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the woman agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Awareness of symptoms and signs

- Carry out tests in primary care (see section 1.1.2) 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^[2]:
 - 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.
- Carry out appropriate tests for ovarian cancer (see section 1.1.2) in any woman of 50 or over who has experienced symptoms within the last 12 months that suggest irritable bowel syndrome (IBS)^[3], because IBS rarely presents for the first time in women of this age.

Asking the right question – first tests

- Measure serum CA125 in primary care in women with symptoms that suggest ovarian cancer (see section 1.1.1).
- If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis.
- 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.

Malignancy indices

- Calculate a risk of malignancy index I (RMI I) score^[4] (after performing an ultrasound; see recommendation 1.2.3.1) and refer all women with an RMI I score of 250 or greater to a specialist multidisciplinary team.

Tissue diagnosis

- 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.

The role of systematic retroperitoneal lymphadenectomy

- 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 I disease).

Adjuvant systemic chemotherapy for stage I disease

- Do not offer adjuvant chemotherapy to women who have had optimal surgical staging^[5] and have low-risk stage I disease (grade 1 or 2, stage Ia or 1b).

Support needs of women with newly diagnosed ovarian cancer

- 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.

^[2] See also the NICE guideline on [suspected cancer: recognition and referral](#).

^[3] See [Irritable bowel syndrome in adults](#) (NICE clinical guideline 61).

^[4] See the [appendix](#) for details of how to calculate an RMI I score.

^[5] 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 BA, Kitchener HC, Dickinson HO (2009) Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. Cochrane Database of Systematic Reviews issue 3: CD004706].

1 Guidance

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

1.1 Detection in primary care

Recommendations in this section have been incorporated into [suspected cancer](#) (NICE guideline NG12).

1.1.1 Awareness of symptoms and signs

- 1.1.1.1 Refer the woman urgently^[6] if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously uterine fibroids)^[7].
- 1.1.1.2 Carry out tests in primary care (see section 1.1.2) 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^[7]:
- 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.
- 1.1.1.3 Consider carrying out tests in primary care (see section 1.1.2) 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 section 1.1.2) in any woman of 50 or over who has experienced symptoms within the last 12 months that suggest irritable bowel syndrome (IBS)^[8], because IBS rarely presents for the first time in women of this age.

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 section 1.1.1).
- 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 urgently^[6] for further investigation^[7].
- 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^[8] (after performing an ultrasound; see recommendation 1.2.3.1) and refer all women with an RMI I score of 250 or greater to a specialist multidisciplinary team.

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 Management of suspected early (stage I) ovarian cancer

1.3.1 The role of systematic retroperitoneal lymphadenectomy

- 1.3.1.1 Perform retroperitoneal lymph node assessment^[10] as part of optimal surgical staging^[5] in women with suspected ovarian cancer whose disease appears to be confined to the ovaries (that is, who appear to have stage I disease).
- 1.3.1.2 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 I disease).

1.3.2 Adjuvant systemic chemotherapy for stage I disease

- 1.3.2.1 Do not offer adjuvant chemotherapy to women who have had optimal surgical staging^[11] and have low-risk stage I disease (grade 1 or 2, stage Ia or Ib).
- 1.3.2.2 Offer women with high-risk stage I disease (grade 3 or stage Ic) adjuvant chemotherapy consisting of six cycles of carboplatin.
- 1.3.2.3 Discuss the possible benefits and side effects of adjuvant chemotherapy with women who have had suboptimal surgical staging^[11] and appear to have stage I disease.

1.4 Management of advanced (stage II–IV) ovarian cancer

Note that recommendations 1.1 and 1.2 in NICE technology appraisal guidance 55 ([Guidance on the use of paclitaxel in the treatment of ovarian cancer](#)) are on first-line chemotherapy in the treatment of ovarian cancer.

1.4.1 Primary surgery

- 1.4.1.1 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.

1.4.2 Intraperitoneal chemotherapy

1.4.2.1 Do not offer intraperitoneal chemotherapy to women with ovarian cancer, except as part of a clinical trial.

1.5 Support needs of women with newly diagnosed ovarian cancer

1.5.1.1 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.

1.5.1.2 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
- 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.

More information

You can also see this guideline in the NICE Pathway on [ovarian cancer](#).

To find out what NICE has said on topics related to this guideline, see our web page on [ovarian cancer](#).

For full details of the evidence and the committee's discussions, see the [evidence reviews](#). You can also find information about [how the guideline was developed](#), including details of the committee.

^[6] An urgent referral means that the woman is referred to a gynaecological cancer service within the national target in England and Wales for referral for suspected cancer, which is currently 2 weeks.

^[7] See also the NICE guideline on [suspected cancer: recognition and referral](#).

^[8] See [Irritable bowel syndrome in adults](#) (NICE clinical guideline 61).

^[9] See the appendix for details of how to calculate an RMI I score.

^[10] 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.

^[11] 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 BA, Kitchener HC, Dickinson HO (2009) Adjuvant (post-surgery) chemotherapy for early stage epithelial ovarian cancer. Cochrane Database of Systematic Reviews issue 3: CD004706].

2 Research recommendations

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

2.1 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.

2.2 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.

2.3 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 three 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).

$$\text{RMI} = \text{U} \times \text{M} \times \text{CA125}$$

- 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 2–5).
- 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.

Update information

June 2015: Recommendations in section 1.1 have been incorporated into section 1.5 of the NICE guideline on [suspected cancer](#).

Minor changes since publication

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

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Accreditation

