



Epithelial ovarian cancer

A national clinical guideline

1	Introduction	1
2	Screening and the role of prophylactic oophorectomy	3
3	Diagnosis	6
4	Surgical management	8
5	Chemotherapy	13
6	Follow up	18
7	Clinical trials	19
8	Management of malignant bowel obstruction in relapsed disease	20
9	Specialist palliative care	22
10	Information for patients	23
11	Implementation	25
12	Development of the guideline	26
	Annexes	29
	References	33

October 2003

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1 ⁺⁺	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1 ⁺	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2 ⁺⁺	High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; <i>or</i> A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; <i>or</i> Extrapolated evidence from studies rated as 2 ⁺

GOOD PRACTICE POINTS

<input checked="" type="checkbox"/>	Recommended best practice based on the clinical experience of the guideline development group
-------------------------------------	---

© Scottish Intercollegiate Guidelines Network
ISBN 1 899893 93 8
First published 2003

SIGN consents to the photocopying of this guideline for the purpose of implementation in NHSScotland

Scottish Intercollegiate Guidelines Network
Royal College of Physicians
9 Queen Street
Edinburgh EH2 1JQ

www.sign.ac.uk

1 Introduction

1.1 THE NEED FOR A GUIDELINE

Ovarian cancer is the fourth most frequently diagnosed cancer in women in Scotland, representing 4.6% of all newly diagnosed cancers, or around 600 new cases per year in Scotland.¹ Ovarian cancer occurs as either an epithelial or a non-epithelial tumour. Epithelial tumours account for over 90% of all ovarian cancers.

The disease is rare in girls and in women under the age of 30 years, with incidence increasing with age, reaching its maximum in the sixth decade.¹ The aetiology of the disease is unknown. It is more common in nulliparous women, and epidemiological studies have shown a significant reduction in ovarian cancer risk in women who have used the oral contraceptive pill.² Most cases of epithelial ovarian cancer are sporadic, occurring in individuals with no family history of the disease. Among women in Scotland with no family history the lifetime risk of developing ovarian cancer is estimated to be 1 in 59.³ In 5 to 10% of women with the disease, an inherited predisposition may be a major contributory cause.⁴

For the majority of women with epithelial ovarian cancer standard therapy consists of surgery followed by chemotherapy. Survival is dependent on the stage of cancer at initial presentation (see *Annex 1*). Whilst stage I disease has a five year survival rate of 85%, stage IV disease has a five year survival rate of only approximately 10%.⁵

Epithelial ovarian cancer is described as a 'silent killer' as in over 60% of cases advanced disease is found at initial presentation.⁶

In Scotland the overall five year survival rate is 30%, and around 400 women die from the disease per year.¹ This rate has not changed significantly in the past 20 years and international comparison of five year survival rates shows that Scotland's rate lies in the lowest quartile amongst European countries.⁷

Treatment is not usually curative. A typical patient will develop relapsed disease requiring repeated courses of chemotherapy. Relapsed disease is invariably fatal and its diagnosis has a huge impact on patients and their carers. The absence of a recognisable preventable cause and of any effective screening programme means that prospects for improving survival lie with optimal management after initial presentation. The goal for health professionals must be to ensure that where cure is not possible a woman can have a good quality of life with judicious use of surgery and chemotherapy.

1.2 REMIT OF THE GUIDELINE

This guideline is concerned with epithelial ovarian cancer only. The management of borderline tumours is not included within this guideline. Management requires a multidisciplinary approach that may include primary care staff, medical and clinical oncologists, gynaecologists, specialist nurses, community nurses, allied health professionals, geneticists, pathologists, specialists in laboratory medicine, pharmacists, radiologists and palliative care specialists. The guideline also highlights areas of controversy as well as recommending good practice where evidence exists.

1.3 DEFINITIONS

The International Federation of Gynaecology and Obstetrics (FIGO) staging system used throughout this guideline is given in Annex 1.⁸ The histological classification of ovarian cancer is given in Annex 2.

1.4 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of medical care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor, following discussion of the options with the patient, in light of the diagnostic and treatment choices available. It is advised however that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

1.5 REVIEW AND UPDATING

This guideline was issued in 2003 and will be considered for review when new evidence becomes available. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk

2 Screening and the role of prophylactic oophorectomy

2.1 INTRODUCTION

At present the value of general population screening remains uncertain and cannot be recommended. Results from the current UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) are not expected until 2011. Screening in the high risk population is discussed in section 2.3.

2.2 IDENTIFYING WOMEN AT HIGH RISK OF DEVELOPING OVARIAN CANCER

2.2.1 DEFINING HIGH RISK GROUPS USING FAMILY HISTORY

Family history can be used to define women who are at increased risk of ovarian cancer.⁹ Individuals at high risk are those with a first degree relative (mother, father, sister, brother, daughter or son) affected by cancer within a family that meets one of the following criteria:

- two or more individuals with ovarian cancer, who are first degree relatives of each other
- one individual with ovarian cancer at any age, and one with breast cancer diagnosed under age 50 years, who are first degree relatives of each other*
- one relative with ovarian cancer at any age, and two with breast cancer diagnosed under 60 years, who are connected by first degree relationships*
- known carrier of relevant cancer gene mutations (eg BRCA 1 or 2)
- untested first degree relative of a predisposing gene carrier
- three or more family members with colon cancer, or two with colon cancer and one with stomach, ovarian, endometrial, urinary tract or small bowel cancer in two generations. One of these cancers must be diagnosed under age 50 years
- an individual with both breast and ovarian cancer.

* *In these categories a second degree relative may be counted if the transmission is via the paternal line (eg a sister and a paternal aunt or a sister and two paternal aunts).*

- Women with a family history that appears to place them at high risk of developing ovarian cancer should be offered referral to a Clinical Genetics Service for assessment and confirmation of their family history. They may then be eligible for referral for screening via a research trial.

2.2.2 DEFINING HIGH RISK GROUPS USING GENETIC TESTING

In most cases risk estimates are based on a family history. The lifetime risk estimate for individuals who have one first degree relative with ovarian cancer is two to five times the population risk.^{4,10} Evidence regarding the lifetime risk when an individual has more than one affected relative is sparse but this is estimated at 3 to 23%.^{4,11}

Two types of ovarian cancer susceptibility genes have been identified: the breast and ovarian cancer tumour suppressor genes (BRCA1 and BRCA2) and the mismatch repair genes associated with Hereditary Nonpolyposis Colorectal Cancer (HNPCC) families.¹² Mutations in the BRCA1 gene are estimated to confer a 30% lifetime risk of ovarian cancer up to age 60 years and mutations in BRCA2 gene are estimated to confer an ovarian cancer risk of 27% up to age 70 years.^{4,13} The mismatch repair genes confer an increased lifetime risk of ovarian cancer of approximately 9 to 12% in addition to an increased risk of endometrial cancer.¹⁴ Relatively few Scottish patients are classed as high risk from BRCA1 or BRCA2 mutations already detected in other members of the family. Such highly penetrant cancer predisposing genes are estimated to account for only a small proportion, perhaps 5 to 10% of all ovarian cancers.⁴

2⁺⁺

3

2.2.3 REFERRAL TO CANCER GENETICS

Referral rates to most UK cancer genetics centres are approximately 200 per year per million of the population.²⁴ This is 30-fold lower than that suggested by a survey of breast cancer family history.¹⁵ General practitioners (GPs) and practice nurses are unhappy about taking responsibility for controlling access to these specialist services.¹⁶⁻²² Although GPs are highly selective in the cases they refer to cancer genetics clinics, over 25% of patients seen at these clinics are judged to be at low (close to population) risk.¹⁵

4

One randomised controlled trial (RCT) demonstrated that the provision of an education pack helped GPs to reach the correct decisions in relation to familial cancer risk. The addition of face-to-face teaching sessions added no further value.²³ GPs benefit from expert support from a specialist genetics service.²² Highest demand and utilisation of familial cancer services relates to breast and/or ovarian cancer.²⁴

1+, 4

- Close collaboration between primary care and specialist cancer genetics services should be developed and encouraged so that genetic cancer risk assessment can be carried out efficiently.
- Primary care clinicians should formally enquire about the woman's family history.

2.3 SCREENING IN HIGH RISK GROUPS

One systematic review²⁵ and three small cohort studies²⁶⁻²⁸ suggest that presymptomatic screening by grey scale ultrasound (with or without Doppler), CA125 (see section 3.1.2), pelvic examination, or combinations of these, are not effective in detecting tumours at an early stage (see Annex 1). No clear evidence was identified as to whether screening in high risk groups has an impact on mortality from ovarian cancer.

1+, 3

- D Screening for ovarian cancer in high risk groups should only be offered in the context of a research study designed to gather data on:**
 - sensitivity and specificity of the screening tool
 - FIGO stages of cancers detected through screening
 - residual risk of primary peritoneal cancer following prophylactic oophorectomy.

2.4 PSYCHOLOGICAL CONSEQUENCES OF SCREENING

Five case series studies²⁹⁻³³ and one qualitative study³⁴ demonstrate that women with a family history of ovarian cancer who seek advice and screening may have higher levels of anxiety and depression than are found in the general population.

3

Two studies regarding the long term psychological consequences of screening in women who require surgical intervention for false positive results highlight the need for screening tools with higher specificity and the importance of incorporating support services in screening programmes.^{30,34}

- D Screening programmes for women at increased risk of ovarian cancer should include mechanisms for providing emotional and psychological support.**

2.5 PROPHYLACTIC OOPHORECTOMY

Women identified as being at high risk of ovarian cancer can be offered prophylactic oophorectomy. The decision whether or not to proceed to prophylactic oophorectomy is influenced by the fact that most women at increased risk of ovarian cancer are also at increased risk of breast cancer and there is evidence that oophorectomy reduces breast cancer risk in these cases.³⁵

2++

Two large cohort studies confirm the benefits of prophylactic oophorectomy for carriers of BRCA1 or BRCA2 mutations, reducing the risk of primary peritoneal carcinoma to between 0.1%³⁶ and 0.5% per year.³⁵ This is considerably less than the lifetime risk of ovarian cancer for those who retain their ovaries.

Studies have shown that 2.3% of patients undergoing prophylactic oophorectomy had previously unsuspected early stage ovarian cancer.^{28,35} These studies also confirm the substantial reduction in breast cancer risk for mutation carriers who undergo prophylactic oophorectomy. This does not appear to be abrogated by giving hormone replacement therapy (HRT) to women whose ovaries are removed before the natural menopause.

2⁺⁺, 3

Women who are carriers of the BRCA1 or BRCA2 mutations should be advised that a proportion of intraperitoneal epithelial cancers arise in the Fallopian tubes so that these should be removed along with the ovaries.

C Women with genetic mutations of BRCA1 or BRCA2 genes should be counselled regarding prophylactic oophorectomy and removal of Fallopian tubes at a relevant time of their life.

High risk women in whom mutations have not been identified should be counselled at around the age of 40 years regarding prophylactic oophorectomy.

2.5.1 QUALITY OF LIFE ISSUES

One qualitative study,³⁷ one retrospective case control study³⁸ and one cohort study³⁹ were identified. Two of the studies report that women with BRCA1 or BRCA2 mutations regard prophylactic oophorectomy as an acceptable option for ovarian cancer risk reduction.^{37,39} The cohort study found that these patients do not expect prophylactic oophorectomy to impair their quality of life.³⁹ The qualitative study found that women with BRCA1 or BRCA2 mutations have strong opinions regarding the costs and benefits of prophylactic oophorectomy and that they would like more information about the physical and emotional after-effects of prophylactic oophorectomy both before, and after, surgery.³⁷

3, 4

The retrospective case control study investigated women who had chosen prophylactic oophorectomy instead of prolonged screening and suggested that these women may have more physical and emotional symptoms than women who remain on an ovarian cancer screening programme but that they report equivalent levels of cancer worry.³⁸

3

The studies identified highlight the importance of counselling, support and information for women making a decision about prophylactic oophorectomy. There is insufficient evidence to make a recommendation.

Women who decide to have prophylactic oophorectomy should be offered counselling, support and information before and after surgery.

3 Diagnosis

3.1 PRIMARY CARE

3.1.1 SIGNS AND SYMPTOMS

Retrospective studies show that women with ovarian cancer present with non-specific symptoms including abdominal pain and bloating; changes in bowel habit, urinary and/or pelvic symptoms.⁴⁰⁻⁴² Cachexia is uncommon and women with advanced disease often look surprisingly well. Most women with ovarian cancer present with advanced disease. On average, a GP will see only one new case every five years.⁴³ No high quality evidence was identified on symptoms or signs suggestive of early ovarian cancer. Patients who present with non-specific gastrointestinal symptoms may be misdiagnosed as suffering from irritable bowel syndrome.

2+
2-
3

One descriptive study examined the impact of delayed referral from primary care on survival.⁴⁴ Delay in referral was not found to be a frequent occurrence and did not impact on survival.⁴⁴

3

- GPs should include ovarian cancer in the differential diagnosis when women present with recent onset persistent non-specific abdominal symptoms (including women whose abdominal and pelvic clinical examinations appear normal).

3.1.2 BLOOD TESTS - THE ROLE OF CA125

Measurement of serum CA125 is the blood test most widely used to detect ovarian cancer. CA125 is a glycoprotein antigen. Elevated concentrations of CA125 are associated with malignant tumours of the pancreas, breast, lung, colon and ovary.⁴⁵ Menstruation and benign conditions such as endometriosis, pelvic inflammatory disease and liver disease can also be associated with elevated concentrations of CA125.⁴⁶ CA125 may also be elevated in women with ascites, pleural or pericardial effusions and in women who have had a recent laparotomy.⁴⁷

3, 4

Approximately 80% of patients with advanced ovarian cancer have elevated concentrations of CA125. A maximum of only 50% of patients with clinically detectable stage I disease have elevated CA125 levels.⁴⁸ Despite its poor sensitivity and specificity, CA125 is most useful for detecting and monitoring non-mucinous epithelial tumours of the ovary.⁴⁹

No studies were identified that assessed the usefulness of the measurement of serum CA125 in women with vague abdominal symptoms hence the guideline development group cannot recommend the routine measurement of CA125.

- D** Women with a pelvic mass should be referred to gynaecology irrespective of the CA125 test result.

3.2 SECONDARY CARE

Women referred to gynaecology with suspected ovarian cancer need ultrasound assessment. This will identify a pelvic mass and the presence of metastatic disease. Where no obvious disease is identified the dilemma for the gynaecologist is deciding whether the pelvic mass is likely to be malignant and who should operate on the patient. Prognosis in ovarian cancer correlates strongly with the ability to achieve optimal cytoreduction, which is more feasible in surgical centres with the greatest surgical experience (see section 4.4). The risk of malignancy index (RMI) scoring system can be used to predict whether the mass is malignant.

3.2.1 THE RISK OF MALIGNANCY SCORING SYSTEM

There are two scoring systems, RMI 1 and RMI 2, each of which calculates scores using ultrasound features, menopausal status and preoperative CA125 level according to the equation:

RMI score = ultrasound score x menopausal score x CA125 level in U/ml.

The original RMI 1 scoring system and the revised RMI 2 system are both outlined in Table 1.^{50,51} The RMI 2 score gives greater weight to the ultrasound findings and menopausal status than the RMI 1 score.

Table 1: The risk of malignancy index (RMI) scoring system^{50,51}

Feature	RMI 1 Score	RMI 2 Score
Ultrasound features: <ul style="list-style-type: none"> ■ multilocular cyst ■ solid areas ■ bilateral lesions ■ scites ■ intra-abdominal metastases 	0 = none 1 = one abnormality 3 = two or more abnormalities	0 = none 1 = one abnormality 4 = two or more abnormalities
Premenopausal Postmenopausal	1 3	1 4
CA125	U/ml	U/ml
RMI score = ultrasound score x menopausal score x CA125 level in U/ml.		

Four cohort studies exploring the role of RMI scores were identified.⁵⁰⁻⁵³ Three of these studies compared the two RMI scores using cut-off values above 200 to indicate malignancy.⁵¹⁻⁵³ The RMI 2 score was more sensitive than the RMI 1 system with results of 74 to 80% at a specificity of 89 to 92% and positive predictive values around 80%.⁵¹⁻⁵³

Other scoring methods have been used to estimate the risk of malignancy in a pelvic mass.^{54,55} A complex logistical regression model performed less well than the RMI scoring system.⁵⁴ Colour flow and pulsed wave Doppler techniques show limited clinical application in isolation.⁵⁵

- C**
- **The RMI scoring system is the method of choice for predicting whether or not an ovarian mass is likely to be malignant.**
 - **Women with an RMI score >200 should be referred to a centre with experience in ovarian cancer surgery.**

2+

3.2.2 VALUE OF COMPUTERISED TOMOGRAPHY (CT) AFTER ULTRASOUND

The use of RMI scoring is not appropriate when obvious metastatic disease has been identified by ultrasound. In this situation the gynaecologist may wish to obtain a CT scan to obtain more information on the extent of metastatic disease. It is the view of the guideline development group that CT is better than US for retroperitoneal assessment, and the detection of omental and peritoneal disease. If the gynaecologist wishes to assess the extent of involvement of the peritoneum, omentum and retroperitoneum prior to surgery a CT scan should be used.

4 Surgical management

4.1 PREPARATION FOR SURGERY

4.1.1 BOWEL PREPARATION

Only a minority of ovarian cancer patients require bowel resection at the time of either primary surgery or surgery for recurrent disease. One retrospective review showed incidences of colonic surgery in ovarian cancer patients of 14% and 34% for primary and secondary surgery respectively.⁵⁶ A second retrospective cohort study confirmed the significantly lower incidence of infectious complications in those patients receiving preoperative bowel preparation.⁵⁷ Preoperative bowel preparation for patients undergoing colorectal surgery is described in the SIGN Guideline for Colorectal Cancer.⁵⁸

2⁺

C Preoperative bowel preparation in ovarian cancer patients should be undertaken where clinical findings and imaging reveal that advanced disease with bowel involvement is present.

4.1.2 STOMA COUNSELLING AND MARKING

A poorly sited stoma due to missing or inadequate preoperative marking can lead to an awkwardly fitting appliance, with subsequent leakage, painful excoriated skin and failure of the appliance to remain secure. This contributes to poor physical and psychological rehabilitation in the postoperative period. Preoperative patient counselling and potential stoma site marking by a trained stoma nurse reduce the incidence of postoperative stoma complications.⁵⁸⁻⁶⁰

2⁺⁺

B Patients for whom preoperative bowel preparation is indicated should see a trained stoma nurse for counselling and potential stoma site marking.

4.1.3 VENOUS THROMBOEMBOLIC PROPHYLAXIS (VTE)

Ovarian cancer patients are at significant risk of developing VTE.⁶¹ Perioperative VTE prophylaxis reduces this risk.⁶¹ Unfractionated heparin (UFH)⁶² or low molecular weight heparins (LMWH)⁶³ can be used. VTE prophylaxis is described in a previous SIGN Guideline.⁶¹

1⁺⁺ 4

4.1.4 CA125 ESTIMATION

Preoperative serum CA125 levels can be used to predict disease bulk, and may be of benefit in identifying patients in whom optimal cytoreductive surgery is feasible.^{64,65} CA125 levels are higher in serous rather than mucinous tumours, as well as in postmenopausal compared to premenopausal patients.⁶⁶ The sensitivity and specificity of CA125 in predicting the possibility of cytoreductive surgery range from 62 to 78% and 73 to 83% respectively.^{64,65} It is not possible to determine if a particular preoperative CA125 level can be used to predict whether optimal cytoreduction is possible. CA125 may be elevated in women who have had a recent laparotomy (see section 3.1.2).

3,1⁻

D Serum CA125 levels are useful in predicting disease bulk and should be assayed preoperatively in women with pelvic masses.

4.1.5 OTHER TUMOUR MARKERS

Carcinoembryonic antigen (CEA) is a tumour marker found in the blood of patients suffering from colorectal cancer. There is no correlation between the CEA level and the FIGO stage of ovarian carcinoma.⁶⁷

3

Measurement of α fetoprotein (AFP) and human chorionic gonadotropin (hCG) in younger women can help exclude non-epithelial ovarian tumours.⁴⁷

4

D Routine preoperative CEA estimation should not be performed in patients with ovarian cancer.

4.1.6 ANTIBIOTIC PROPHYLAXIS

The SIGN Guideline on Antibiotic Prophylaxis in Surgery describes the benefits, principles and administration procedures of antibiotic prophylaxis in surgery.⁶⁸

4.2 PATHOLOGY

Pathological examination of ovarian and other tissues defines the nature of the tumour and its stage. Staging is performed by examining histological sections of tissue samples and cytological assessment of fluid samples. It is important to adequately sample the ovary using a minimum of a block of tissue for each centimetre of the maximum diameter of the tumour.

4.2.1 INTRAOPERATIVE TECHNIQUES

Epithelial ovarian tumours display a spectrum of pathological changes. Tumours can be benign, borderline (low malignant potential or atypical proliferating lesions), or malignant (see Annex 2). Intraoperative frozen section can be used to confirm the presence of malignant disease but cannot precisely confirm borderline disease.⁶⁹⁻⁷¹ It is important that surgeons are aware of the limitations of this technique. There is no evidence that intraoperative frozen section can define the grade of the cancer.

2+

The clinical situations where the intraoperative, pathological assessment of an ovarian lesion is helpful are:

- to confirm malignancy where clinical assessment reveals a complex ovarian cyst with no apparent metastatic disease
- to exclude the presence of metastatic disease where suspicious looking extra ovarian lesions are present if fertility conserving surgery is planned for patients with malignant disease confined to an ovary.

D

To minimise the need for a second operative staging procedure, intraoperative frozen section assessment can be used to diagnose malignancy and to exclude metastatic disease.

4.3 MANAGEMENT OF EARLY DISEASE

Early disease refers to disease confined to the ovaries (see Annex 1). There are two clinical scenarios where early disease could be encountered:

- the first is where the gynaecologist is alerted to the possibility of malignancy being present prior to the laparotomy
- the second is where the gynaecologist had no suspicion of cancer being present prior to surgery.

To minimise the risk of the gynaecologist encountering the second scenario, use should be made of the RMI scoring system if an isolated pelvic mass is discovered on preoperative imaging (see section 3.2.1). In young women the possibility of a non-epithelial ovarian tumour being present should also be considered (see section 4.1.5).

The surgical dilemma in early disease is how comprehensively to stage a case and in particular whether to assess retroperitoneal nodes and take random peritoneal biopsies. The presence of positive retroperitoneal nodes or peritoneal implants upstages the case to stage III (see Annex 1).

Proponents of comprehensive staging argue that it is important to give accurate prognostic information to a patient and that choice of chemotherapy regimen might be influenced by knowledge of the stage of disease (see section 5). Descriptive studies have reported that at least 15% of patients thought to have disease confined to the ovaries are found to have positive lymph nodes.⁷²⁻⁷⁴ The opponents of comprehensive staging argue that it cannot be recommended as routine practice due to the lack of RCT data demonstrating any survival benefit conferred to those who undergo full staging including retroperitoneal nodal assessment.

3, 4

The publication of the ICON 1 and ACTION chemotherapy trials (see section 5) means that it is unlikely that future studies will be designed to answer the role of comprehensive staging in early disease.^{75,76}

In the ACTION chemotherapy trial (see section 5) one third of patients were optimally staged. Adjuvant chemotherapy in this group of patients was not associated with a statistically significant improvement in overall and disease-free survival. The validity of a subgroup analysis in this study is questionable given the small number of patients involved. When the data from the ACTION trial were combined with that from the ICON 1 trial (in which the majority of patients were not optimally staged) platinum-based adjuvant chemotherapy resulted in an 8% improvement in overall survival and an 11% improvement in disease-free survival.⁷⁷

1+

The guideline development group suggest the following to ensure that cases of suspected stage I disease are thoroughly assessed:

- staging should be through a mid-line incision to allow palpation of all peritoneal surfaces
- assessment of peritoneal cytology, hysterectomy, removal of ovaries and Fallopian tubes and infracolic omentectomy should be performed
- capsular rupture during surgery should be avoided.
- Aim to exclude disease involving the liver, spleen, peritoneum, retroperitoneal nodes, appendix and diaphragm by close clinical inspection and palpation.
- Cases where only the ovarian cyst was removed should be discussed within the multidisciplinary team. If there is concern that there is a likelihood of metastatic disease restaging is recommended.

4.3.1 FERTILITY CONSERVING SURGERY

In women who wish to conserve their fertility, adequate staging (excluding disease involving the liver, spleen, peritoneum, retroperitoneal nodes, appendix and diaphragm) is required and the risk of recurrent disease developing must be discussed.

No data from RCTs were found. One cohort study reported a 9% risk of recurrence (involvement of contralateral ovary or extraovarian disease) in women treated with fertility sparing surgery.⁷⁸ In this study 56 women aged under 40 years with histologically confirmed ovarian cancer (Grades 1, 2 and 3, see Annex 2) underwent fertility sparing surgery which involved adequate staging (unilateral salpingo-oophorectomy, omentectomy, appendectomy, biopsies from peritoneal cavity and retroperitoneal lymph node sampling).⁷⁸ The mean age of the women was 29 years and 32 had FIGO 1A disease, two had FIGO 1B disease and 22 FIGO 1C disease (see Annex 1). Five women developed recurrence (9%) and in two of these women recurrence involved the residual ovary (3.6%). Metastatic endometrial cancer was found at a second look operation in one woman.

2+

In another publication the risk of endometrial cancer being present (metastatic involvement or synchronous tumour) has been reported to be as high as 14%, particularly when the ovarian tumour is of endometrioid or clear cell subtypes.⁷⁹

4

- In women who wish to conserve their fertility a unilateral salpingo-oophorectomy may be performed if the contralateral ovary appears normal.

4.4 OPTIMAL SURGERY FOR ADVANCED DISEASE

Advanced disease refers to cases where the disease has spread beyond the ovaries (FIGO stage Ic and above, see Annex 1). Treatment for these cases involves surgery and chemotherapy. This section addresses the issue of surgery before the initiation of chemotherapy. Imaging with ultrasound prior to surgery can identify advanced disease. It is unclear whether additional imaging with computerised tomography is necessary with every case of advanced disease (see section 3.2.2).

There are two surgical scenarios:

- aggressive surgical cytoreduction with the aim of leaving no residual disease
- optimal cytoreduction where residual tumour deposits are no more than 2 cm in diameter.

As complete resection of all tumour deposits (aggressive cytoreduction) is usually impossible in advanced disease, surgical treatment for the majority of these patients involves performing optimal cytoreductive surgery.

Three meta-analyses demonstrated a strong correlation between optimal cytoreduction and survival.⁸⁰⁻⁸² None of the meta-analyses determined whether the improved survival and the feasibility of aggressive cytoreduction were related to intrinsic tumour biology.

One meta-analysis looked at the independent contribution of both cytoreductive surgery and platinum based chemotherapy on overall survival.⁸⁰ Each 10% increase in maximal cytoreductive surgery was associated with a 4.1% increase in median survival time. Platinum-based chemotherapy produced an estimated 53% rise in median survival time. In this analysis patients were treated with non-platinum based therapy as well as platinum-based therapy hence the magnitude of benefit induced by chemotherapy is likely to be exaggerated. A subsequent meta-analysis has confirmed this.⁸³

The question of specialty of surgeon has been addressed in a retrospective population-based review of 1,866 women treated in Scotland over five non-consecutive years.⁶ The review reports on 1,032 patients operated on by general gynaecologists, 351 by specialist gynaecologists and 216 by general surgeons. The demographics of the three patient groups were different: those cared for by the general gynaecologists had an expected better prognosis after surgery than those operated on by the specialist gynaecologists and the group cared for by the general surgeons were the poorest prognostic group. An attempt was made to correct these differences by adjusting for patient age, histology, tumour differentiation, presence of ascites and socioeconomic status. The results were analysed for each FIGO stage and the endpoint for analysis was death by three years. Of those with stage III disease, those operated on by specialist gynaecologists had a 25% reduction in death compared to those operated on by general gynaecologists ($P = 0.005$). Those operated on by general surgeons had the lowest survival rates. Similar trends were found in the other FIGO stages, but were not significant. These data are supported by a similar retrospective review of 12,316 patients in which patient survival was significantly better in the group operated on by specialist 'gynaecological oncologists' compared to 'obstetrician gynaecologists' and general surgeons.⁸⁴

Patients with stage IV disease are increasingly being treated with chemotherapy prior to surgery when there is no doubt that the primary tumour is ovarian (see section 5.4). A multidisciplinary team should manage these cases.

C If aggressive cytoreduction is not possible then optimal cytoreduction is the recommended surgical procedure if performance status allows this to take place.

D Patients with stage III disease should be operated on by a gynaecological oncologist rather than a general gynaecologist or general surgeon.

Bowel surgery should only be performed where obstruction is imminent or where it enables optimal cytoreduction or aggressive cytoreduction to be achieved.

1-

2+

4.5 INTERVAL DEBULKING SURGERY

Interval debulking surgery (IDS) refers to surgery performed in women whose tumour mass has decreased following three courses of chemotherapy and who have previously been suboptimally cytoreduced.

The potential role for IDS has been examined in three RCTs,⁸⁵⁻⁸⁷ with two of these studies demonstrating different results. The first did not demonstrate a statistically significant improvement in survival in the group of women who underwent IDS,⁸⁵ whilst the second reported an increase of six months median survival for those who had IDS.⁸⁶ In the second study 127 women who had IDS were followed up. Following three courses of chemotherapy 83 of the women had tumours greater than 1cm. Of these 83, only 37 had tumours measuring less than 1cm left behind after IDS. It is not possible to identify the characteristics of the small group who responded to chemotherapy and who were left with a decreased tumour load after IDS.⁸⁶ Preliminary results from the third RCT suggest that when the first operation is done by a gynaecological oncologist IDS is not recommended even if optimal cytoreduction was not achieved.⁸⁷

1+

C Interval debulking surgery is recommended, if performance status allows, where there is evidence of response to chemotherapy as determined by CA125 and imaging.

4.6 RELAPSED DISEASE

There are insufficient data to make recommendations on the surgical management of relapsed disease. Quality of life issues were not considered in the literature identified.⁸⁸

A multidisciplinary team should decide whether there is a role for surgery in the management of relapsed disease where there has been a significant period of disease remission.

4.7 SPECIALIST NURSING

One RCT has suggested that the involvement of a nurse specialist has a beneficial effect on patient care (statistical significance was not achieved).⁸⁹ Two studies in breast cancer patients also support the role of specialist nurses.^{90,91} NHS Quality Improvement Scotland standards state that patients should have access to a specialist nurse in gynaecological cancer.⁹²

1,2,4

Patients should be given their diagnosis of ovarian cancer after surgery in the presence of a nurse who is a fully integrated member of the clinical team. If a nurse specialist is not available this should be a dedicated named nurse or link nurse.

Patients with ovarian cancer should have access to an appropriately trained nurse, who is an integral member of the gynaecological cancer team, throughout their journey of care.

5 Chemotherapy

5.1 INTRODUCTION

Ovarian cancer is a chemosensitive disease, and the use of immediate first line platinum-based chemotherapy improves the prognosis for patients with advanced disease. Although most women with ovarian cancer will have some response to chemotherapy, the likelihood of relapse is high.⁹³ Twenty five years of clinical research have defined the role of existing chemotherapeutic agents in the first line management of advanced ovarian cancer.

5.2 TIMING OF CHEMOTHERAPY

One observational study indicates that the interval from primary surgery to chemotherapy is not an independent prognostic factor for progression-free survival.⁹⁴ Consensus of the epithelial ovarian cancer guideline development group is that chemotherapy should be started no later than eight weeks after surgery.

3

- Chemotherapy should be started no later than eight weeks after surgery.

5.3 EARLY STAGE DISEASE

Adjuvant systemic treatment of early stage (FIGO stage I) ovarian cancer remains a controversial area. The National Institutes of Health (NIH) guideline recommends carboplatin chemotherapy for patients with early stage disease and additional risk factors, to reduce the risk of disease recurrence and ensuing risk of death.⁹⁵ Additional risk is conferred by the presence of moderate or poorly differentiated tumours, stage Ic disease including surgical rupture, and clear cell histological subtype.⁹⁶

4,2+

Two RCTs demonstrate the role of adjuvant chemotherapy for early stage epithelial cancer patients.^{75,76} The ICON 1 trial found a significant reduction (9%) in odds of death and an improvement in recurrence-free survival (11%) for early stage epithelial cancer patients following the use of adjuvant chemotherapy compared with observation following surgery.⁷⁶ The ACTION trial found no difference in overall survival but disease-free survival was significantly improved in women who had undergone non-optimal surgical staging (8%).⁷⁵ In the ACTION study one third of patients were optimally staged whereas in the ICON study the majority of patients were not optimally staged. Analysis of combined data from these studies demonstrated that platinum-based adjuvant chemotherapy improved overall survival by 8% and recurrence-free survival by 11% at five years.⁷⁷

1+

- B Carboplatin can be offered to all early stage epithelial ovarian cancer patients.**

- Chemotherapy for patients with disease confined to the ovaries where the tumour is well differentiated (FIGO stage 1a grade 1 and FIGO stage 1b grade 1, *see Annexes 1 and 2*), may be deferred if optimal surgery has been performed.

5.4 NEOADJUVANT CHEMOTHERAPY

There is debate about the precise sequence in which surgery and chemotherapy should be used in a woman with advanced disease. The usual approach is to operate first. No evidence from RCTs could be identified on the role of neoadjuvant chemotherapy. Descriptive studies demonstrate that in advanced disease chemotherapy can be offered as a first treatment option where there is no doubt about the diagnosis.^{97,98} In advanced disease neoadjuvant chemotherapy and delayed primary surgery or primary surgery followed by chemotherapy are currently being compared in a European Organisation for Research and Treatment of Cancer (EORTC) RCT.

3

5.5 ADVANCED DISEASE

5.5.1 ROLE OF PLATINUM AGENTS

Meta-analyses show significant benefit for use of platinum.^{99,100} | 1++

A First line chemotherapy treatment of epithelial ovarian cancer should include a platinum agent either in combination or as a single agent, unless specifically contraindicated.

5.5.2 CHOICE OF PLATINUM AGENTS

The platinum-based drugs cisplatin and carboplatin are equally efficacious in the treatment of epithelial ovarian cancer.⁹⁹ Carboplatin has a more favourable toxicity profile and, as it can be delivered as an outpatient regimen, is simpler to administer than cisplatin. The combination of carboplatin and paclitaxel is as efficacious as cisplatin and paclitaxel combination therapy.¹⁰¹ | 1++

A Carboplatin is the platinum drug of choice in both single and combination therapy.

5.5.3 TAXANES

Two high quality RCTs support the use of paclitaxel and cisplatin as an efficacious combination for advanced ovarian cancer.^{102,103} As these trials were limited to surgically managed patients who were fit enough to meet the entrance criteria for clinical trials, the general applicability of taxanes remains in question. The use of taxane combination therapy is widespread throughout Scotland and has been recommended by NICE and NHS Quality Improvement Scotland.¹⁰⁴ A further study has suggested that carboplatin can be substituted for cisplatin.¹⁰¹ | 1++

Although one RCT has shown that single agent cisplatin yielded both equivalent response rates and equivalent overall survival to cisplatin and paclitaxel, this trial is difficult to interpret due to treatment crossover issues.¹⁰² The study recommends the taxane combination on the grounds of reduced toxicity compared to single agent cisplatin. The ICON 3 trial demonstrates equal effectiveness for carboplatin or CAP (the combination regimen containing cyclophosphamide, doxorubicin and cisplatin) compared with paclitaxel and carboplatin in ovarian cancer.¹⁰⁵ ICON 3 does not imply that paclitaxel has no role in the treatment of ovarian cancer, but it does suggest that the dramatic difference seen in the earlier studies was principally due to the inferiority of the cyclophosphamide and cisplatin control arm. An interpretation of a meta-analysis of all these studies does suggest a slight benefit for the taxane and platinum combination.¹⁰⁵ | 1+
1++

A Paclitaxel is recommended in combination therapy with platinum in the first line post-surgery treatment of epithelial ovarian cancer where the potential benefits justify the toxicity of the therapy.

A Patients who choose less toxic therapy or who are unfit for taxanes should be offered single agent carboplatin.

Where carboplatin is used as a single agent in first line therapy attention should be paid to platinum dose optimisation.

5.5.4 CYCLOPHOSPHAMIDE

The combination of platinum and cyclophosphamide has been shown to be inferior to platinum and taxane in two RCTs.^{103,106} The use of cyclophosphamide offers no clinical benefit over other currently used cytotoxic agents in the treatment of ovarian cancer. | 1++

A Cyclophosphamide is not recommended in the first line chemotherapy treatment of epithelial ovarian cancer.

5.5.5 THE ROLE OF ANTHRACYCLINES

The addition of doxorubicin to cisplatin and cyclophosphamide provides a small but significant survival advantage.¹⁰⁷ The ICON 2 study showed that single agent carboplatin was as effective as the combination regimen containing cyclophosphamide, doxorubicin and cisplatin (CAP).¹⁰⁰ Meta-analysis has shown the CAP regimen to be marginally superior to cisplatin and cyclophosphamide.¹⁰⁰

1+

The role of anthracyclines in first line treatment is unclear. They may be of benefit if incorporated into first line treatment, but further research is required.

A The use of anthracyclines in first line chemotherapy treatment of epithelial ovarian cancer is not recommended outside RCTs.

5.6 RELAPSED DISEASE

5.6.1 SYSTEMIC THERAPY IN RECURRENT OVARIAN CANCER

The impact of chemotherapy on survival is marginal for patients with relapsed disease, particularly those with platinum-resistant relapse. As the palliative effect of chemotherapy for recurrent disease has not been tested in an RCT against best supportive care, the magnitude of effect attributable to chemotherapy in this setting is unknown.

A prospective study has demonstrated that patients whose ovarian cancer recurs more than six months after the last cycle of chemotherapy (platinum sensitive) have a good chance of responding to further palliative platinum therapy.¹⁰⁸ Patients whose ovarian cancer recurs within six months after the last cycle of chemotherapy (platinum resistant) have a low chance of response to further platinum chemotherapy. Such patients achieve a 10 to 40% overall response rate to active non-platinum agents.¹⁰⁸

2+

One RCT has shown that patients whose ovarian cancer recurs 12 months or more after first-line platinum-based chemotherapy who are rechallenged with a platinum-based regimen achieve significant improvement (seven to nine months advantage) in median progression-free and overall survival compared with paclitaxel.¹⁰⁹

1+

The ICON 4 trial assigned platinum sensitive women with relapsed ovarian cancer to one of two arms: paclitaxel plus a platinum-based drug or a platinum-based drug alone. There was a 7% improvement in survival at two years for those who received the combination of paclitaxel and platinum. Median survival increased by five months.¹¹⁰

1+

An RCT of paclitaxel versus topotecan (a topoisomerase inhibitor) in patients with platinum treated recurrent ovarian cancer demonstrated equivalence in overall response rate and median duration of response. Topotecan demonstrated more myelotoxicity.¹¹¹

1+

An RCT that compared topotecan with pegylated liposomal doxorubicin (PLD) in similar cohorts of patients found equivalent response rates, progression-free survival and overall survival.¹¹² There was a significant progression-free survival and overall survival advantage for PLD in platinum-sensitive patients that did not occur for platinum-resistant patients. NICE and NHS Quality Improvement Scotland have noted the possible cost and logistical advantages of PLD over topotecan.^{113,114} Meta-analyses of observational studies suggest that tamoxifen may produce a response in a low proportion of women with recurrent ovarian cancer.¹¹⁵ No randomised studies were identified. Symptomatic platinum-resistant recurrence (treatment free interval less than six months) is less sensitive to chemotherapy, and the optimal agents have yet to be defined.

1+

2+

B Chemotherapy for recurrent ovarian cancer should be regarded as palliative in intent and should be reserved for symptomatic recurrence of disease.

B Symptomatic platinum-sensitive cancer recurrence can be treated with further platinum and paclitaxel.

C Tamoxifen should be considered in patients for whom chemotherapy is not appropriate.

- Patient care should be discussed within the multidisciplinary team and where possible patients should be entered into appropriate clinical trials.
- The optimal agents in platinum-resistant disease have yet to be defined and treatment should be based on specialist judgement.
- Cautious clinical judgement should be used when considering the use of platinum and paclitaxel in patients with symptomatic platinum-sensitive cancer recurrence after a treatment-free interval of 6-12 months.

5.6.2 ROLE OF ERYTHROPOETIN

Anaemia is common in ovarian cancer, occurring in 50-60% of patients who are receiving chemotherapy.¹¹⁶ Anaemia can be effectively treated by blood transfusion or by the use of erythropoetin. Erythropoetin can be recommended as a safe and effective alternative for patients with anaemia who cannot be transfused. There is no evidence suggesting that erythropoetin is more effective than blood transfusion.^{117,118} The quality of life benefits offered by erythropoetin are inconsistent.¹¹⁷

1++

B If erythropoetin is used to treat anaemia it should only be when the haemoglobin concentration is ≤ 10 g/dL and the dose should not exceed 450 units/kg/week.

5.7 INTRAPERITONEAL CHEMOTHERAPY

Two RCTs investigating the benefits of intraperitoneal chemotherapy in maximally cytoreduced cases of ovarian cancer have been reported.^{119,120} Both studies reported significantly better survival in the women receiving intraperitoneal therapy but design flaws in both trials mean that intraperitoneal therapy cannot yet be recommended for routine use in optimally cytoreduced cases.^{119,120} The results of a Gynecologic Oncology Group (GOG) study evaluating intraperitoneal chemotherapy are awaited.¹²¹

1-

- Intraperitoneal therapy should not be routinely offered outwith clinical trials.

5.8 ADMINISTRATION OF CHEMOTHERAPY

It is the responsibility of the gynaecological cancer team to ensure that chemotherapy is given according to published guidelines and national standards.¹²²⁻¹²⁴

4

D Staff should be experienced, trained in the safe administration of chemotherapy and be involved in on going continuing professional development (CPD) and reappraisal.

D Hospital based administration of chemotherapy should take place during the working day in designated areas equipped to deal with any medical emergencies.

- Chemotherapy should be administered in environments that meet the standards set out in national guidance.

5.9 IMPACT OF CHEMOTHERAPY ON QUALITY OF LIFE IN RELAPSED DISEASE

The management of ovarian cancer is usually characterised by multiple chemotherapeutic regimens. Response rates, especially in platinum-resistant patients, may be low and the toxicity associated with treatment impacts on patients' quality of life.¹²⁵ The large number of varying, often complex tools applied to assess quality of life means that meta-analysis of the research is not feasible.¹²⁶ One small prospective study of palliative chemotherapy and quality of life indicates that women with advanced ovarian cancer, and those receiving prolonged cycles of chemotherapy, report deterioration in their quality of life.¹²⁷ Four cohort studies report similar findings.^{125, 128-130} Women with advanced cancer are willing to tolerate reduced quality of life for minimal therapeutic benefit.^{125,127-130}

3, 2+

- D** Women should be given accurate information on their likely response to chemotherapy, including adverse effects, so that they can make an informed decision about whether or not to proceed with treatment.
- D** The impact of chemotherapy toxicities on patients' quality of life must be balanced against their anticipated response to treatment.

6 Follow up

Absence of symptoms does not indicate absence of disease. Approximately 40% of women with no clinical or ultrasound evidence of disease are found to have disease at second look laparotomy.⁸⁸

The primary aims of regular routine follow up are to provide reassurance and to identify disease recurrence before symptoms occur and performance status deteriorates. The process of attending clinics and awaiting results of investigations generates anxiety.

Four studies assessed different follow up modalities including clinical examination, ultrasound, CA125, and MRI scanning. A confirmed rise in CA125 to more than twice the upper limit of normal accurately predicts relapse with a sensitivity of 86% and a positive predictive value of 95%.^{131,132} Lead times between two to four months prior to clinical progression were observed. MRI scanning has a 90% sensitivity in detecting recurrence as defined by second look laparotomy.¹³³ In a study looking at follow up of stage I borderline ovarian tumours in a series of 24 recurrences, it was found that ultrasound had a 100% sensitivity in detecting the pathology, CA125 had a 53% sensitivity and physical examination a 26% sensitivity.¹³⁴

3

CA125 measurement and MRI have a role in detecting presymptomatic disease. Standard therapy for relapsed disease is primarily for symptom control. It is unclear whether early treatment for relapse in those who are asymptomatic offers any benefit over waiting until the symptomatic stage. A Medical Research Council and European Organisation for Research and Treatment of Cancer randomised control trial (OVO5) is addressing this issue.

There are no RCTs specific to ovarian cancer that assess whether follow up at a multidisciplinary clinic reduces the risk of death. A descriptive study demonstrates that an independent prognostic factor for improved survival is follow up at a multidisciplinary clinic.¹³⁵

3

- Patients who are not in clinical trials should be followed up within local multidisciplinary specialist clinics.
- The primary care team should be made aware of the follow up protocol for those patients not in trials.

7 Clinical trials

Randomised clinical trials provide the strongest evidence on the efficacy of surgical and chemotherapy treatments for ovarian cancer. Despite their value, recruitment to trials is often limited with only a small proportion of ovarian cancer patients receiving treatment as part of a clinical trial.

A systematic review and an observational study exploring barriers to participation in clinical trials in the UK were identified.^{136,137} The systematic review found that patients who are more knowledgeable about the randomisation process are less likely to participate in trials.¹³⁷ This suggests that participation in trials might be improved by increasing awareness about the other benefits of being involved in a trial in addition to the possibility of receiving the experimental treatment.

1⁺⁺,
3

The observational study explored recruitment to an individual trial in the UK and found that most people considered for trial inclusion did not meet inclusion criteria.¹³⁶ Participation by people eligible for the study was high as long as their physician decided that they should be considered for the study. This study indicated that patient selection may result in different outcomes between participants and non-participants, specifically, older and more severely ill patients were less likely to be entered into trials, possibly causing better outcomes to be observed for trial patients.

3

A systematic review of 14 studies was identified that looked at whether participation in RCTs is beneficial or harmful for patients.¹³⁸ The review included cancer treatment studies but was not exclusively limited to them. The study considered different possible sources of effect and bias. Eight of the studies included in the review showed a statistically significant positive effect from trial participation, and six did not. No studies showed a negative outcome. The review concluded that a positive effect was more likely when a trial compared a known effective treatment with a new treatment. The review also concluded that it is not possible to separate protocol effect from possible bias due to clinician selection.¹³⁸

2⁺⁺

C Clinical trials should have appropriate inclusion criteria and should incorporate recognised standard treatment.

8 Management of malignant bowel obstruction in relapsed disease

The true incidence of malignant intestinal obstruction due to progressive disease (not at primary diagnosis) is not known. Two autopsy studies of patients with ovarian cancer described cancer involvement in the bowel.^{139,140} In one study 70% of patients had involvement of the small bowel and 78% involvement of the large bowel with an overall 51% incidence of intestinal obstruction.¹³⁹ In the other study there was small bowel involvement in 42% of cases and large bowel involvement in 49%.¹⁴⁰ Several pathophysiological mechanisms may be involved in intestinal obstruction due to progressive disease:¹⁴¹

- intraluminal obstruction
- intramural obstruction
- extramural obstruction
- motility disorders
- constipation.

8.1 SURGICAL MANAGEMENT

There is no clear evidence nor consensus on the surgical management of patients with advanced cancer. Surgery can only benefit selected patients with mechanical obstruction and should not be routine practice.¹⁴¹

1⁺⁺

Prognostic criteria to help select patients who are likely to benefit from surgical intervention have been identified. They are given for guidance and may not cover the complexities of an individual situation.¹⁴²⁻¹⁴⁶ Each contraindication stands alone.

2⁺

C Surgery for malignant bowel obstruction in patients with advanced ovarian cancer must be justified on the basis of achieving a significant benefit.

Table 2: Contraindications to surgery for malignant bowel obstruction in patients with advanced ovarian cancer

Absolute Contraindications
Patient refusal
Previous abdominal surgery which showed diffuse metastatic cancer
Involvement of proximal stomach
Intra-abdominal carcinomatosis demonstrated radiologically with a contrast study revealing a severe motility problem
Diffuse palpable intra-abdominal masses (having excluded faecal masses)
Massive ascites which rapidly recurs after drainage
Relative Contraindications
Non-symptomatic extensive extra-abdominal malignant disease (eg widespread metastases and pleural effusion)
Poor general performance status
Poor nutritional status (eg marked weight loss/cachexia, marked hypoalbuminaemia and low lymphocyte count)
Severe cachexia
Small bowel obstruction
Previous radiotherapy of the abdomen or pelvis

8.2 NON-SURGICAL MANAGEMENT

Symptoms of bowel obstruction (general abdominal pain, colic, nausea, vomiting, anorexia, dehydration) in women in whom surgery is not considered to be an option can be managed by pharmacological means.¹⁴⁷ Usually the onset of bowel obstruction is gradual over many weeks with symptoms becoming more continuous and severe. 2+

8.2.1 PAIN, NAUSEA AND VOMITING

The clinical aim is to control nausea, reduce the frequency and severity of vomiting to an acceptable level and to avoid a nasogastric tube (NGT), by using corticosteroids, antiemetic or antisecretory drugs. The route of drug delivery should be parenteral, normally by subcutaneous infusion.

A Cochrane review concluded that there was weak evidence that corticosteroids (dexamethasone 6-16 mg intravenously) may help the resolution of inoperable obstruction in some patients and the side effects of treatment were few.¹⁴⁸ 1+

Antiemetics are effective in controlling nausea.¹⁴⁹ Cyclizine is the first line antiemetic often used with a single bedtime dose of haloperidol. Levomepromazine in a single, low dose at bedtime is helpful when nausea persists. There does not appear to be a routine role for 5HT3 antagonists (eg ondansetron) in managing nausea subsequent to obstruction. 4

Two trials have examined the antisecretory effects of octreotide and hyoscine butylbromide in patients with inoperable bowel obstruction. In one study all patients in the trial had an NGT¹⁵⁰ and in the other trial no patient had an NGT.¹⁵¹ Octreotide was more effective and faster than hyoscine butylbromide in reducing the amount of gastrointestinal secretions in patients with NGTs.¹⁵⁰ Octreotide was also more effective than hyoscine butylbromide in reducing the intensity of nausea and the number of vomiting episodes in patients without an NGT.¹⁵¹ 1-

NGTs are an ineffective means of controlling nausea and vomiting in malignant bowel obstruction.^{152,153} NGTs are occasionally used in faeculent vomiting (the vomiting of small bowel contents infected by colonic bacteria), gastric outflow obstruction, or persistent vomiting whilst waiting for the delayed action of pharmacological agents. 3

Regular mouth care is the treatment of choice for dry mouth.¹⁵⁴ Parenteral hydration is sometimes indicated in patients who have nausea. 3

When laxatives are used in partial obstruction, the dose should be adjusted to maintain a comfortable stool without colic. Lactulose may add to the bowel volume. A combination of senna and docusate, or docusate alone should be used if colic is a problem.¹⁴⁹ In complete, inoperable obstruction, all laxatives should be stopped. 4

Pain (visceral and colic) can often be controlled using analgesic drugs most often given by syringe driver. Colic is a common problem. It is not relieved by strong opioids, but responds rapidly to parenteral hyoscine butylbromide. In complete, inoperable obstruction this can be given as a continuous subcutaneous infusion.¹⁴⁹ Involvement of the coeliac plexus can cause a severe visceral neuropathic pain that may partly respond to opioids or need an anti-neuropathic pain agent such as gabapentin.¹⁵⁵ For a more detailed discussion of pain assessment and management see SIGN guideline number 44 on the control of pain in patients with cancer.¹⁵⁶ 3, 4

C Symptoms of bowel obstruction can be relieved by using the following drug categories either alone or in combination:

- antiemetic
- antisecretory
- analgesic
- corticosteroids.

9 Specialist palliative care

Patients who develop ovarian cancer may need rehabilitative, functional, social and/or financial support services. These can be provided by agencies both within and outwith the health service, most of which are available in specialist palliative care settings. The evaluation of the effectiveness of specialist palliative care involves assessment of the different dimensions of care provided, such as pain and other symptom control, psychological care, care of the family and carers, rehabilitation and terminal care.

The General Medical Council has stated that every member of the medical profession requires generic palliative care skills. NHS Quality Improvement Scotland has set standards for the provision of both basic and specialist palliative care.^{157,158} Specialist palliative care is an integral component of the care of patients with advanced malignancy, required at varying times during their illness.

A systematic review of the effectiveness of specialist palliative care teams identified 18 studies, including five RCTs.¹⁵⁹ Involvement of specialist palliative care teams was associated with patients spending more time at home, greater satisfaction amongst patients and carers, better symptom control, a reduction in the number of inpatient hospital days, a reduction in overall cost and an increase in the number of patients dying where they wished.

1+

Three RCTs were identified that included patients with a variety of cancers, which, in the context of palliative care, are reasonable to relate to patients with ovarian cancer.¹⁶⁰⁻¹⁶² Two studies looked at the effect of coordinating services within the NHS, local authorities and the voluntary sector via nurse coordinators. A total of 203 cancer patients expected to live for less than one year were randomly assigned to either the intervention or the routine services group. Patients assigned to the intervention group spent fewer days in hospital, required fewer home visits and their family were less likely to feel angry about their relative's death.^{160,161} The third RCT used place of death as the outcome measure in a study of 434 patients with incurable malignant disease.¹⁶² The intervention group had inpatient and outpatient hospital services provided by the palliative medicine unit. This unit served as a link to community services, produced guidelines, maintained communication between different services and invited community staff to participate in an educational programme. In the intervention group, more patients died at home and spent less time in nursing homes in their last months of life.

1+

B Patients with advanced ovarian cancer require a coordinated, multiprofessional approach with access to a specialist palliative care team.

D Patients with persistent poorly controlled symptoms should be referred to specialist palliative care.

10 Information for patients

10.1 SUPPORT NEEDS OF PATIENTS, FAMILIES AND CARERS

A diagnosis of cancer throws patients and their families into an unfamiliar world where they have to cope with unusual medical, financial and legal issues. Healthcare professionals can support patients and carers, enabling them to cope with the diagnosis of cancer and its associated emotional and psychological distress. Information and support are key parts of the National Cancer Strategy.¹⁶³

A systematic review of studies involving women with gynaecological cancer shows that providing them with information is beneficial, can improve ability to cope and facilitate their participation in treatment decisions.¹⁶⁴ 1+

Patients diagnosed with cancer for the first time often want information addressing their immediate concerns regarding their disease, treatment options, what they might expect during return appointments and who to go to for information. Four studies indicate that cancer patients want information on their treatment and prognosis.¹⁶⁵⁻¹⁶⁸ Patients prefer to receive written information to assist them to make an informed choice.¹⁶⁶ 2+

A cohort study carried out in the West of Scotland highlighted that cancer patients want to know the medical name of their illness, their treatment choices, how treatments work, the likely side effects and chances of cure.¹⁶⁸ 2+

Eight RCTs¹⁶⁹⁻¹⁷⁶ and one systematic review¹⁷⁷ were identified in relation to the information and support needs of cancer patients. None of the studies were specific to ovarian cancer but were generalisable to the ovarian cancer population. The number of participants in the trials varied from 36 to 525 and the groups were heterogeneous. The interventions studied included structured emotional support, relaxation techniques, the use of audiocassette recordings of consultations, orientation programmes and general psychological and/or emotional support. The interventions reduced anxiety levels and improved quality of life. 1+

C Patients should be offered verbal and written information throughout their journey of care and should be made aware of the support mechanisms that are in place and how to access them.

C Structured emotional support should be available to all patients and carers.

Voluntary sector agencies can be used to expand the levels of support available to patients and carers.

10.2 FURTHER INFORMATION FOR PATIENTS, FAMILIES AND CARERS

CancerBACUP Scotland

Suite 2, 3rd Floor, Cranston House, 104-114 Argyle Street, Glasgow G2 8BH
 Tel: 0141 223 7676, Fax: 0141 248 8422. Freephone help line available 9am to 7pm,
 Monday to Friday: 0808 800 1234
www.cancerbacup.org.uk

Offers a free cancer information service staffed by qualified and experienced cancer nurses. There are a growing number of CancerBACUP centres in hospitals and a freephone information service on all types of cancer, staffed by specialist cancer nurses. Produces over 50 booklets and 'CancerBACUP News' three times a year.

Cancer Research UK

PO Box 123, 61 Lincoln's Inn Fields, London WC2A 3PX
 Tel: 020 7242 0200, Fax: 020 7269 3100
www.cancerresearchuk.org

Macmillan Cancer Relief Scotland

Osbourne House, 1-5 Osbourne Terrace, Edinburgh EH12 5HG
 Tel: 0131 346 5346, Fax: 0131 346 5347
 Helpline: 0808 808 2020, Monday to Friday 9am to 6pm
www.macmillan.org.uk

A UK charity supporting people with cancer and their families with specialist information, treatment and care.

Maggie's Centres Scotland

The Stables, Western General Hospital, Edinburgh, EH4 2XU
 Tel: 0131 537 3131, Fax: 0131 537 3130
 The Gatehouse, Western Infirmary, 10 Dumbarton Road, Glasgow, G11 6PA
 Tel: 0141 330 3311, Fax: 0141 330 3363

Email: maggies.centre@ed.ac.uk
www.maggies.ed.ac.uk

The goal of Maggie's is to keep people who have cancer as healthy in mind and body as is possible, by enabling them to participate actively in the treatment of their disease.

Tak Tent Cancer Support Scotland

Flat 5, 30 Shelley Court, Gartnavel Complex, Glasgow, G12 0YN
 Tel: 0141 211 0122, Fax: 0141 211 3988
 Email: tak.tent@care4free.net
www.taktent.org.uk

Promotes the care of cancer patients, their families, friends and the staff involved professionally in cancer care by providing practical and emotional support, information, counselling and therapies as required. Network of local support groups throughout Scotland. The Youth Group, conTak, provides support for 16 to 25 year olds affected by cancer.

Ovacome

Elizabeth Garrett Anderson Hospital, Huntley Street, London, WC1E 6DH
 Tel: 020 7380 9589. Office is staffed Monday to Friday 9am to 4pm
 Email: ovacome@ovacome.org.uk
www.ovacome.org.uk/

A UK wide charity providing information and support for all those affected by ovarian cancer including patients, relatives, carers and health professionals. Newsletter produced four times a year and fact sheets on many aspects of ovarian cancer are available on request.

11 Implementation

The recommendations with resource implications are discussed in Annex 3.

11.1 MANAGED CLINICAL NETWORKS

Managed Clinical Networks (MCNs) are defined as: *'linked groups of health professionals and organisations from primary, secondary and tertiary care, working in a coordinated manner, unconstrained by existing professional and Health Board boundaries, to ensure equitable provision of high quality clinically effective services throughout Scotland.'*¹⁷⁸

MCNs require an administrative infrastructure so they have financial implications. In the case of ovarian cancer, the core members of the MCN would be allied health professionals, gynaecological oncologists, general practitioners, laboratory medicine specialists, gynaecologists, medical and clinical oncologists, nurses, pathologists, radiologists and palliative care specialists.

- The health professionals involved in the care of women with ovarian cancer should be represented in a managed clinical network.

11.2 RECOMMENDATIONS FOR RESEARCH

Surgical and chemotherapy research questions need to be answered by large randomised controlled trials. Patients should be entered into appropriate clinical trials wherever possible (eg MRC, EORTC, GOG and the Scottish Gynaecological Cancer Trials Group). Seven other areas where evidence is lacking have been identified in the course of developing this guideline:

1. Does measurement of CA125 in primary care for patients with recent onset non-specific abdominal symptoms increase the likelihood of detecting ovarian cancer?
2. Do delayed referrals from primary care impact upon survival?
3. Does input and support from a Clinical Nurse Specialist impact on the quality of life of patients with ovarian cancer?
4. What is the impact on quality of life for women undergoing prophylactic surgery because of a strong family history of ovarian cancer?
5. What are the relative effects of best supportive care versus chemotherapy in patients with relapsed disease?
6. What is the best follow up regimen for women with ovarian cancer?
7. Does input from a palliative medicine specialist impact upon quality of life in the management of malignant bowel obstruction?

12 Development of the guideline

12.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations, funded by NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in *SIGN 50: A guideline developer's handbook*, available at www.sign.ac.uk

12.2 THE GUIDELINE DEVELOPMENT GROUP

Dr Nadeem Siddiqui <i>Chairman</i>	<i>Consultant Gynaecologist and Oncologist, Stobhill Hospital, Glasgow</i>
Dr Chris Hardwick <i>Secretary</i>	<i>Specialist Registrar in Obstetrics and Gynaecology, North Glasgow Hospitals NHS Trust</i>
Dr Ian Aitken	<i>General Practitioner, Glasgow</i>
Mr Andrew Anderson	<i>National Coordinator, Maggie's Centres, Western General Hospital, Edinburgh</i>
Mr Roger Black	<i>Head, Scottish Cancer Intelligence Unit, Information and Statistics Division (ISD), Common Services Agency, Edinburgh</i>
Ms Sandra Bredin	<i>Clinical Nurse Specialist, Stobhill Hospital, Glasgow</i>
Mrs Anne Coote	<i>Patient Helpline Coordinator, Argyll and Clyde Health Council, Paisley</i>
Mrs Inez Crow	<i>District Nurse, Falkirk</i>
Ms Linda Davidson	<i>Staff Nurse, Crosshouse Hospital, Kilmarnock</i>
Dr Heather Deans	<i>Consultant Radiologist, Aberdeen Royal Infirmary</i>
Dr Sonia Devereux	<i>General Practitioner, Forfar</i>
Mr Craig Eriksen	<i>Consultant Colorectal Surgeon, Perth Royal Infirmary</i>
Dr Marie Fallon	<i>Senior Lecturer in Palliative Medicine, Western General Hospital, Edinburgh</i>
Dr Hani Gabra	<i>Consultant in Medical Oncology, Western General Hospital, Edinburgh</i>
Professor David Hole	<i>Professor of Epidemiology and Biostatistics, West of Scotland Cancer Surveillance Unit, Department of Public Health, University of Glasgow</i>
Dr Brian Magowan	<i>Consultant Gynaecologist, Borders General Hospital, Melrose</i>
Mrs Jean McAllister	<i>Principal Biochemist, North Glasgow University Hospitals NHS Trust</i>
Dr David W M Millan	<i>Consultant in Pathology, Western Infirmary, Glasgow</i>
Miss Kath Nattress	<i>Macmillan Clinical Nurse Specialist, Western General Hospital, Edinburgh</i>
Dr David Parkin	<i>Consultant Gynaecological Oncologist, Aberdeen Royal Infirmary</i>
Mr Mark Parsons	<i>Principal Clinical Pharmacist, Ninewells Hospital, Dundee</i>
Dr Denny Phillips	<i>Consultant Gynaecologist, Perth Royal Infirmary</i>
Dr Nicholas Reed	<i>Clinical Director, Beatson Oncology Centre, Glasgow</i>
Mr Duncan Service	<i>Information Services Officer, SIGN</i>
Dr Sally Stearns	<i>Health Economist, Health Economics Research Unit, University of Aberdeen</i>
Professor Michael Steele	<i>Professor in Medical Science, University of St Andrews</i>
Mrs Diane Stirling	<i>Macmillan Clinical Nurse Specialist, Western General Hospital, Edinburgh</i>
Ms Joanne Topalian	<i>Programme Manager, SIGN</i>
Dr Sara Twaddle	<i>Health Economist, North Glasgow Hospitals NHS Trust</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. Declarations of interests were made by all members of the guideline development group. Further details are available from the SIGN Executive.

12.3 SYSTEMATIC LITERATURE REVIEW

Literature searches were initially conducted in Medline, Embase, Cinahl, Cancerlit, and the Cochrane Library using the year range 1993-2001. The literature search was updated with new material during the course of the guideline development process. Key websites on the Internet were also used, such as the National Guidelines Clearinghouse. These searches were supplemented by the reference lists of relevant papers and group members' own files. The Medline version of the main search strategies can be found on the SIGN website.

12.4 CONSULTATION AND PEER REVIEW

12.4.1 NATIONAL OPEN MEETING

The national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents their draft recommendations for the first time. The national open meeting for this guideline was held in June 2002 and was attended by representatives of all key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

12.4.2 SPECIALIST REVIEW

SIGN is grateful to the following people for commenting on the peer review draft:

Dr James Beattie	<i>Director of Guideline Development, Royal College of General Practitioners (Scotland)</i>
Ms Helen Berrie	<i>District Nurse, Wallace Medical Centre, Falkirk</i>
Dr Kirsty Boyd	<i>Consultant in Palliative Care Medicine, The Royal Infirmary of Edinburgh</i>
Dr Bernard L Croall	<i>Clinical Senior Lecturer, Department of Clinical Biochemistry, Grampian University Hospitals Trust, Aberdeen</i>
Dr Jo Davis	<i>Consultant Gynaecologist and Oncologist, Stobhill Hospital, Glasgow</i>
Dr Ian Duncan	<i>Reader in Obstetrics and Gynaecology, Ninewells Hospital, Dundee</i>
Professor Ian Jacobs	<i>Professor of Gynaecological Oncology, Director of Cancer Institute, Barts and the London Hospital, London</i>
Professor Stan Kaye	<i>Consultant Oncologist, Royal Marsden Hospital, London</i>
Professor Sean Kehoe	<i>Professor of Gynaecological Cancer, Nuffield Department of Obstetrics and Gynaecology, Oxford</i>
Dr Harpreet Kohli	<i>Medical Director, Health Technology Assessment, NHS Quality Improvement Scotland</i>
Ms Ruth Payne	<i>Administrator, Ovacome, London</i>
Dr Claud Regnard	<i>Consultant in Palliative Medicine, St Oswald's Hospice, Newcastle upon Tyne</i>
Dr Terry Rollason	<i>Consultant Histopathologist, Birmingham Women's Hospital</i>
Professor John Smyth	<i>Consultant Medical Oncologist, Western General Hospital, Edinburgh</i>
Dr Allan Stevenson	<i>Consultant Radiologist, Western General Hospital, Edinburgh</i>
Dr Paul Symonds	<i>Reader in Clinical Oncology, Leicester Royal Infirmary</i>

Four general practitioners were also invited to review the draft guideline but did not submit any comments.

12.5 EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an Editorial Group comprising the relevant specialty representatives on SIGN Council to ensure that the peer reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The Editorial Group for this guideline was as follows:

Mr Douglas Harper	<i>Royal College of Surgeons</i>
Dr Grahame Howard	<i>Royal College of Radiologists, Faculty of Oncology</i>
Professor Gordon Lowe	<i>Chairman of SIGN, Co-editor</i>
Ms Fiona McMillan	<i>Lead Pharmacist, North Glasgow NHS Trust</i>
Dr Gillian Penney	<i>Royal College of Obstetrics and Gynaecology</i>
Dr Safia Qureshi	<i>Programme Director, SIGN, Co-editor</i>
Dr Bernice West	<i>School of Nursing and Midwifery, Faculty of Health and Social Care, The Robert Gordon University, Aberdeen</i>

Annex 1

Staging carcinoma of the ovary

INTERNATIONAL FEDERATION OF GYNAECOLOGY AND OBSTETRICS (FIGO) NOMENCLATURE^B

Stage I - Growth limited to the ovaries

- Ia** Growth limited to one ovary; no ascites containing malignant cells present. No tumour on the external surface; capsule intact
- Ib** Growth limited to both ovaries; no ascites containing malignant cells present. No tumour on the external surfaces; capsules intact
- Ic** *Tumour either Stage Ia or Ib, but with tumour on surface of one or both ovaries, or with capsule ruptured, or with ascites present containing malignant cells, or with positive peritoneal washings.

Stage II - Growth involving one or both ovaries with pelvic extension

- IIa** Extension and/or metastases to the uterus and/or Fallopian tubes
- IIb** Extension to other pelvic tissues
- IIc** *Tumour either Stage IIa or IIb, but with tumour on surface of one or both ovaries; or with capsule(s) ruptured; or with ascites present containing malignant cells or with positive peritoneal washings.

Stage III - Tumour involving one or both ovaries with histologically confirmed peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes. Superficial liver metastases equals stage III. Tumour is limited to the true pelvis, but with histologically proven malignant extension to small bowel or omentum.

- IIIa** Tumour grossly limited to the true pelvis, with negative nodes, but with histologically confirmed microscopic seeding of abdominal peritoneal surfaces, or histologically proven extension to small bowel or mesentery
- IIIb** Tumour of one or both ovaries with histologically confirmed implants, peritoneal metastasis of abdominal peritoneal surfaces, none exceeding 2 cm in diameter; nodes are negative
- IIIc** Peritoneal metastasis beyond the pelvis > 2 cm in diameter and/or positive retroperitoneal or inguinal nodes.

Stage IV

Growth involving one or both ovaries with distant metastases. If pleural effusion is present, there must be positive cytology to allot a case to Stage IV. Parenchymal liver metastasis equals Stage IV.

* In order to evaluate the impact on prognosis of the different criteria for allotting cases to Stage Ic or IIc, it would be of value to know if rupture of the capsule was spontaneous, or caused by the surgeon; and if the source of malignant cells detected was peritoneal washings, or ascites.

Annex 2

Classification of ovarian cancer

Ovarian neoplasms are a heterogeneous group of tumours classified according to morphological and clinical features. The main subgroups are:

- epithelial tumours
- sex cord – stromal tumours
- germ cell tumours
- miscellaneous and metastatic tumours.

The majority of ovarian tumours (59% of all ovarian tumours and up to 90% of all primary ovarian malignancies) are epithelial. Epithelial tumours can be further classified as follows:

- serous
- mucinous
- endometrioid
- mixed mesodermal / carcinosarcoma
- clear cell
- transitional cell
- mixed epithelial
- undifferentiated carcinomas.

The most common tumours are serous and mucinous lesions.

Mixed mesodermal tumours are now considered to be carcinomas with areas of sarcomatous differentiation.

- A **benign** tumour has no abnormal cytological or proliferative features and no evidence of stromal invasion. There is no significant malignant potential.
- A **borderline** (low malignant potential or atypically proliferating) tumour is a lesion which has abnormal cytological and proliferative features within its epithelium but which has no evidence of invasion into the stromal supporting tissues. Extraovarian disease can occur and these tumour deposits are referred to as implants. Non-invasive implants are associated with a good prognosis. Invasive implants are associated with a prognosis that is intermediate between those of benign and malignant tumours. Most borderline tumours present as stage I lesions and are cured by surgery. Stage by stage the overall survival of women with borderline tumours is superior to women with epithelial ovarian cancer.
- A **malignant** tumour is present when there is evidence of invasion into the stromal tissues of the ovary. This is usually associated with cytological atypia and increased proliferative activity. Invasion is best defined as the presence of irregular spiculated or ragged epithelial islands with individual cells extending into the stromal tissues. These stromal tissues can display reactive changes such as necrosis or an immature fibroblastic response. These cytological and proliferative changes can occur focally within the ovarian mass. An ovarian tumour must be adequately sampled for histological examination.
- **Primary peritoneal cancer** is a tumour which shows similar morphological characteristics to ovarian cancer but which has no or minimal ovarian involvement.

GRADING OF OVARIAN CANCER

There is no single universally accepted system for grading ovarian cancers. Many studies have used different systems proposed either by FIGO or WHO or the American Gynecologic Oncology Group (GOG). A newly proposed grading system, based on the Nottingham system of breast cancer grading, assesses the architectural pattern of the ovarian tumour, cytological atypia and the mitotic activity within the tumour.¹⁷⁹⁻¹⁸¹ The FIGO staging system described in Annex 1 is a surgical staging system which does not incorporate the grade of the tumour.

PSEUDOMYXOMA PERITONEI

Pseudomyxoma peritonei is a clinical condition characterised by the presence of mucinous material within the peritoneal cavity. This condition may originate from either the ovary or gastrointestinal tract. In gynaecological pathology it is more often seen in association with borderline mucinous ovarian tumours. In view of the debate about the primary site of origin of these tumours the appendix should be examined. Pathological examination of the mucinous material and associated tissues should specify whether epithelial cells are present or not. The cytological characteristics of the cells should also be described.

BRAC1 AND BRAC2

BRCA1, a gene on chromosome 17 and BRCA2, a gene on chromosome 13, increase susceptibility to breast and ovarian cancer.

Annex 3

Resource implications of recommendations

A literature review was undertaken to identify relevant economic evaluations. Where these did not exist or where they were of poor quality, the recommendations were assessed by guideline development group members.

Guideline section		Recommendation	Likely resource implication
4.3.1	D	To minimise the need for a second operative staging procedure, intraoperative frozen-section assessment can be used to diagnose malignancy and to exclude metastatic disease.	Although this service is available in some centres, there is a national shortage of pathologists. Addressing the shortage of pathologists is a national issue. Undertaking such work is labour intensive for technicians and histopathologists which has an opportunity cost in terms of other work which may be delayed.
4.5	D	Patients with stage III disease should be operated on by a gynaecological oncologist rather than a general gynaecologist or general surgeon.	<p>There are major resource implications due to the UK shortage of gynaecological oncologists. Addressing this shortage requires a UK-wide initiative to increase the number of trainees to ensure the shortfall is met.</p> <p>There would be associated costs of additional gynaecological oncologists including additional theatre sessions, dedicated beds, specialist nursing staff and other support staff.</p> <p>Guidance on Commissioning Cancer Services suggests that there should be one gynaecological oncologist per 500,000 population.¹⁸² For Scotland, this implies a minimum of 11 gynaecological oncologists.</p>
7	C	Clinical trials should have appropriate inclusion criteria and should incorporate recognised standard treatment.	<p>Clinical trials may have implications for the NHS in terms of:</p> <ul style="list-style-type: none"> ■ new efficacious agents being identified, which require to be continued in patients participating in the trial ■ additional workload or opportunity costs of time foregone to treat other patients while undertaking the trial. This is covered to some degree by the NHS R&D support fund <p>These may be balanced by the provision of new therapies that would not otherwise be available to patients.</p>
10.1	C	<ul style="list-style-type: none"> ■ Patients should be offered verbal and written information throughout their journey of care and should be made aware of the support mechanisms that are in place and how to access them. ■ Structured emotional support should be available to all patients and carers. 	More nurses with appropriate skills to provide information throughout the journey of care are required. There are implications for nurse training and for services offering emotional support to patients and their families.

References

- 1 Scottish Cancer Intelligence Unit. Trends in cancer survival in Scotland 1971-1995. Edinburgh: Information and Statistics Division; 2000. [cited 2 Sep 2003]. Available from url: http://www.isdscotland.org/isd/files/trends_1971-95.pdf
- 2 Franceschi S, Parazzini F, Negri E, Booth M, La Vecchia C, Beral V, et al. Pooled analysis of 3 European case-control studies of epithelial ovarian cancer: III. Oral contraceptive use. *Int J Cancer* 1991;49(1):61-5.
- 3 Information and Statistics Division. Cancer of the ovary (ICD-10 C56). Lifetime risk of developing cancer (up to the age of 90), Scotland 1994 - 1998. Edinburgh: The Division; 2002. [cited 2 Sep 2003]. Available from url http://www.isdscotland.org/isd/files/cancer_ovary_risk.xls
- 4 Thompson D, Easton DF. Cancer Incidence in BRCA1 mutation carriers. *J Natl Cancer Inst* 2002;94(18):1358-65.
- 5 Kristensen GB, Trope C. Epithelial ovarian carcinoma. *Lancet* 1997;349(9045):113-7.
- 6 Junor EJ, Hole DJ, McNulty L, Mason M, Young J. Specialist gynaecologists and survival outcome in ovarian cancer: a Scottish national study of 1866 patients. *Br J Obstet Gynaecol* 1999;106(11):1130-6.
- 7 Gatta G, Lasota MB, Verdecchia A. Survival of European women with gynaecological tumours, during the period 1978-1989. *Eur J Cancer* 1998;34(14):2218-25.
- 8 Pecorelli S, Odicino F, Maisonneuve P, Creasman W, Shepherd J, Sideri M, et al. FIGO staging of gynecologic cancer Carcinoma of the ovary. London; The International Federation of Gynecology and Obstetrics:1998. [cited 2 Sep 2003]. Available from url: <http://www.figo.org/default.asp?id=/00000039.htm>
- 9 Haites NE, Black R, Campbell H, Clark C, Davidson R, Davis J, et al. Guidelines for regional genetic centres on the implementation of genetic services for breast, ovarian and colorectal cancer families in Scotland. *CME Journal of Gynaecologic Oncology* 2000;5(3):291-307.
- 10 Bell R, Petticrew M, Luengo S, Sheldon TA. Screening for ovarian cancer: a systematic review. *Health Technol Assess* 1998;2(2):1-84. [cited 2 Sep 2003]. Available from url: <http://www.hta.nhsweb.nhs.uk/fullmono/mon202.pdf>
- 11 Stratton JF, Pharoah P, Smith SK, Easton D, Ponder BA. A systematic review and meta-analysis of family history and risk of ovarian cancer. *Br J Obstet Gynaecol* 1998;105(5):493-9.
- 12 Morrison PJ, Hodgson SV, Haites NE, editors. Familial breast and ovarian cancer: genetics, screening and management. Cambridge: Cambridge University Press; 2002.
- 13 Cancer risks in BRCA2 mutation carriers. The Breast Cancer Linkage Consortium. *J Natl Cancer Inst* 1999;91(15):1310-6.
- 14 Aamio M, Sankila R, Pukkala E, Salovaara R, Aaltonen LA, de la Chapelle A, et al. Cancer risk in mutation carriers of DNA-mismatch-repair genes. *Int J Cancer* 1999;81(2):214-8.
- 15 Hyland F, Kinmonth AL, Marteau TM, Griffin S, Murrell P, Spiegelhalter D, et al. Raising concerns about family history of breast cancer in primary care consultations: prospective, population based study. *Women's Concerns Study Group. BMJ* 2001;322(7277):27-8.
- 16 Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomised controlled trial. *Lancet* 1999;353(9160):1207-10.
- 17 Fry A, Campbell H, Gudmundsdottir H, Rush R, Porteous M, Gorman D, et al. GPs' views on their role in cancer genetics services and current practice. *Fam Pract* 1999;16(5):468-74.
- 18 Escher M, Sappino AP. Primary care physicians' knowledge and attitudes towards genetic testing for breast-ovarian cancer predisposition. *Ann Oncol* 2000;11(9):1131-5.
- 19 Rose PW, Watson E, Yudkin P, Emery J, Murphy M, Fuller A, et al. Referral of patients with a family history of breast/ovarian cancer-GPs' knowledge and expectations. *Fam Pract* 2001;18(5):487-90.
- 20 Bankhead C, Emery J, Qureshi N, Campbell H, Austoker J, Watson E. New developments in genetics-knowledge, attitudes and information needs of practice nurses. *Fam Pract* 2001;18(5):475-86.
- 21 Walter FM, Kinmonth AL, Hyland F, Murrell P, Marteau TM, Todd C. Experiences and expectations of the new genetics in relation to familial risk of breast cancer: a comparison of the views of GPs and practice nurses. *Fam Pract* 2001;18(5):491-4.
- 22 Elwyn G, Iredale R, Gray J. Reactions of GPs to a triage-controlled referral system for cancer genetics. *Fam Pract* 2002;19(1):65-71.
- 23 Watson E, Clements A, Yudkin P, Rose P, Bukach C, Mackay J, et al. Evaluation of the impact of two educational interventions on GP management of familial breast/ovarian cancer cases: a cluster randomised controlled trial. *Br J Gen Pract* 2001;51(471):817-21.
- 24 Wonderling D, Hopwood P, Cull A, Douglas F, Watson M, Burn J, et al. A descriptive study of UK cancer genetics services: an emerging clinical response to the new genetics. *Br J Cancer* 2001;85(2):166-70.
- 25 NHS Executive. Guidance on commissioning cancer services: improving outcomes in gynaecological cancer: the research evidence. London: The Executive; 1999.
- 26 Taylor L, Schwarz H. Identification of a soluble OX40 isoform: development of a specific and quantitative immunoassay. *J Immunol Methods* 2001;255(1-2):67-72.
- 27 Karlan BY, Baldwin RL, Lopez-Luevanos E, Raffel LJ, Barbuto D, Narod S, et al. Peritoneal serous papillary carcinoma, a phenotypic variant of familial ovarian cancer: implications for ovarian cancer screening. *Am J Obstet Gynecol* 1999;180(4):917-28.
- 28 Moller P, Borg A, Heimdal K, Apold J, Vallon-Christerson J, Hovig E, et al. The BRCA1 syndrome and other inherited breast or breast-ovarian cancers in a Norwegian prospective series. *Eur J Cancer* 2001;37(8):1027-32.
- 29 Erlick Robinson G, Rosen BP, Bradley LN, Rockert WG, Carr ML, Cole DE, et al. Psychological impact of screening for familial ovarian cancer: reactions to initial assessment. *Gynecol Oncol* 1997;65(2):197-205.
- 30 Wardle J, Pernet A, Collins W, Bourne T. False positive results in ovarian cancer: one year followup of psychological status. *Psychol Health* 1994;10(1):33-40.
- 31 Wardle FJ, Collins W, Pernet AL, Whitehead MI, Bourne TH, Campbell S. Psychological impact of screening for familial ovarian cancer. *J Natl Cancer Inst* 1993;85(8):653-7.
- 32 Audrain J, Schwartz MD, Lerman C, Hughes C, Peshkin BN, Biesecker B. Psychological distress in women seeking genetic counseling for breast-ovarian cancer risk: the contributions of personality and appraisal. *Ann Behav Med* 1998;19(4):370-7.
- 33 Cull A, Fry A, Rush R, Steel CM. Cancer risk perceptions and distress among women attending a familial ovarian cancer clinic. *Br J Cancer* 2001;84(5):594-9.
- 34 Pernet AL, Wardle J, Bourne TH, Whitehead MI, Campbell S, Collins WP. A qualitative evaluation of the experience of surgery after false positive results in screening for familial ovarian cancer. *Psycho-oncology* 1992;1:217-33.
- 35 Kauff ND, Satagopan JM, Robson ME, Scheuer L, Hensley M, Hudis CA et al. Risk-reducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. *N Engl J Med* 2002;346(21):1609-15.
- 36 Rebbeck TR, Lynch HT, Neuhausen SL, Narod SA, Van't Veer L, Garber JE, et al. Prophylactic oophorectomy in carriers of BRCA1 or BRCA2 mutations. *N Engl J Med* 2002;346(21):1616-22.
- 37 Hollowell N. A qualitative study of the information needs of high-risk women undergoing prophylactic oophorectomy. *Psycho-Oncology* 2000;9(6):486-95.
- 38 Fry A, Busby-Earle C, Rush R, Cull A. Prophylactic oophorectomy versus screening: psychosocial outcomes in women at increased risk of ovarian cancer. *Psycho-Oncology* 2001;10(3):231-41.
- 39 Wagner TM, Moslinger R, Langbauer G, Ahner R, Fleischmann E, Auterith A, et al. Attitude towards prophylactic surgery and effects of genetic counselling in families with BRCA mutations. *Austrian Hereditary Breast and Ovarian Cancer Group. Br J Cancer* 2000;82(7):1249-53.
- 40 Olson SH, Mignone L, Nakraseive C, Caputo TA, Barakat RR, Harlap S. Symptoms of ovarian cancer. *Obstet Gynecol* 2001;98(2):212-7.
- 41 Flam F, Einhorn N, Sjovall K. Symptomatology of ovarian cancer. *Eur J Obstet Gynecol Reprod Biol* 1988;27(1):53-7.
- 42 Goff BA, Mandel L, Muntz HG, Melancon CH. Ovarian carcinoma diagnosis. *Cancer* 2000;89(10):2068-75.
- 43 Scottish Cancer Information Unit. Cancer registration statistics Scotland 1986-1995. Edinburgh: Information and Statistics Division; 1998.
- 44 Kirwan JM, Tincello DG, Herod JJ, Frost O, Kingston RE. Effect of delays in primary care referral on survival of women with epithelial ovarian cancer: retrospective audit. *BMJ* 2002;324(7330):148-51.
- 45 Bast RC Jr, Klug TL, St John E, Jenison E, Niloff JM, Lazarus H, et al. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. *N Engl J Med* 1983;309(45):883-7.
- 46 Daoud E, Bodor G. CA-125 concentrations in malignant and nonmalignant disease. *Clin Chem* 1991;37(11):1968-74.
- 47 Sturgeon C. Practice guidelines for tumor markers use in the clinic. *Clin Chem* 2002;48(8):1151-9.
- 48 Jacobs I, Bast RC Jr. The CA 125 tumour-associated antigen: a review of the literature. *Hum Reprod* 1989;4(1):1-12.
- 49 Kabawat SE, Bast RC, Welch WR, Knapp RC, Colvin RB. Immunopathologic characterization of a monoclonal antibody that recognizes common surface antigens of human ovarian tumors of serous, endometrioid, and clear cell types. *Am J Clin Pathol* 1983;79(1):98-104.
- 50 Jacobs I, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. *Br J Obstet Gynaecol* 1990;97(10):922-9.
- 51 Tingulstad S, Hagen B, Skjeldestad FE, Onsrud M, Kiserud T, Halvorsen T, et al. Evaluation of a risk of malignancy index based on serum CA125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. *Br J Obstet Gynaecol* 1996;103(8):826-31.
- 52 Morgante G, la Marca A, Ditto A, De Leo V. Comparison of two malignancy risk indices based on serum CA125, ultrasound score and menopausal status in the diagnosis of ovarian masses. *Br J Obstet Gynaecol* 1999;106(6):524-7.
- 53 Aslam N, Tailor A, Lawton F, Carr J, Savvas M, Jurkovic D. Prospective evaluation of three different models for the pre-operative diagnosis of ovarian cancer. *BJOG* 2000;107(11):1347-53.

- 54 Taylor A, Jurkovic D, Bourne TH, Collins WP, Campbell S. Sonographic prediction of malignancy in adnexal masses using multivariate logistic regression analysis. *Ultrasound Obstet Gynecol* 1997;10(1):41-7.
- 55 Antonic J, Rakar S. Colour and pulsed Doppler US and tumour marker CA 125 in differentiation between benign and malignant ovarian masses. *Anticancer Res* 1995;15(4):1527-32.
- 56 Tamussino KF, Lim PC, Webb MJ, Lee RA, Lesnick TG. Gastrointestinal surgery in patients with ovarian cancer. *Gynecol Oncol* 2001;80(1):79-84.
- 57 Donato D, Angelides A, Irani H, Penalver M, Averette H. Infectious complications after gastrointestinal surgery in patients with ovarian carcinoma and malignant ascites. *Gynecol Oncol* 1992;44(1):40-7.
- 58 Scottish Intercollegiate Guidelines Network (SIGN). Management of colorectal cancer. Edinburgh: SIGN; 2003. (SIGN publication no. 67). [cited 3 Sep 2003]. Available from url: <http://www.sign.ac.uk/pdf/sign67.pdf>
- 59 Bass EM, Del Pino A, Tan A, Pearl RK, Orsay CP, Abcarian H. Does preoperative stoma marking and education by the enterostomal therapist affect outcome? *Dis Colon Rectum* 1997;40(4):440-2.
- 60 Park JJ, Del Pino A, Orsay CP, Nelson RL, Pearl RK, Cintron JR, et al. Stoma complications: the Cook County Hospital experience. *Dis Colon Rectum* 1999;42(12):1575-80.
- 61 Scottish Intercollegiate Guidelines Network (SIGN). Prophylaxis of venous thromboembolism. Edinburgh: SIGN; 2002. (SIGN publication no. 62). [cited 3 Sep 2003]. Available from url: <http://www.sign.ac.uk/guidelines/fulltext/62/index.html>
- 62 Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. *N Engl J Med* 1988;318(18):1162-73.
- 63 Koch A, Bouges S, Ziegler S, Dinkel H, Daures JP, Victor N. Low molecular weight heparin and unfractionated heparin in thrombosis prophylaxis after major surgical intervention: update of previous meta-analyses. *Br J Surg* 1997;84(6):750-9.
- 64 Chi DS, Venkatraman ES, Masson V, Hoskins WJ. The ability of preoperative serum CA-125 to predict optimal primary tumor cytoreduction in stage III epithelial ovarian carcinoma. *Gynecol Oncol* 2000;77(2):227-31.
- 65 Gemer O, Segal S, Kopmar A. Preoperative CA-125 level as a predictor of non optimal cytoreduction of advanced epithelial ovarian cancer. *Acta Obstet Gynecol Scand* 2001;80(6):583-5.
- 66 Maggino T, Gadducci A. Serum markers as prognostic factors in epithelial ovarian cancer: an overview. *Eur J Gynaecol Oncol* 2000;21(1):64-9.
- 67 Kudoh K, Kikuchi Y, Kita T, Tode T, Takano M, Hirata J, et al. Preoperative determination of several serum tumor markers in patients with primary epithelial ovarian carcinoma. *Gynecol Obstet Invest* 1999;47(1):52-7.
- 68 Scottish Intercollegiate Guidelines Network (SIGN). Antibiotic prophylaxis in surgery. Edinburgh: SIGN; 2000. (SIGN publication no. 45). [cited 3 Sep 2003]. Available from url: <http://www.sign.ac.uk/guidelines/fulltext/45/index.html>
- 69 Yeo EL, Yu KM, Poddar NC, Hui PK, Tang LC. The accuracy of intraoperative frozen section in the diagnosis of ovarian tumors. *J Obstet Gynaecol Res* 1998;24(3):189-95.
- 70 Houck K, Nikrui N, Duska L, Chang Y, Fuller AF, Bell D, et al. Borderline tumors of the ovary: correlation of frozen and permanent histopathologic diagnosis. *Obstet Gynecol* 2000;95:839-43.
- 71 Usubutun A, Altinok G, Kucukali T. The value of intraoperative consultation (frozen section) in the diagnosis of ovarian neoplasms. *Acta Obstet Gynecol Scand* 1998;77(10):1013-6.
- 72 Young RC, Decker DG, Wharton JT, Piver MS, Sindelar WF, Edwards BK, et al. Staging laparotomy in early ovarian cancer. *JAMA* 1983;250(22):3072-6.
- 73 Helewa ME, Krepert GV, Lotocki R. Staging laparotomy in early epithelial ovarian carcinoma. *Am J Obstet Gynecol* 1986;154(2):282-6.
- 74 Hand R, Fremgen A, Chmiel JS, Recant W, Berk R, Sylvester J, et al. Staging procedures, clinical management, and survival outcome for ovarian carcinoma. *JAMA* 1993;269(9):1119-22.
- 75 Trimbos JB, Vergote I, Bolis G, Vermorken JB, Mangioni C, Madronal C, et al. European Organisation for Research and Treatment of Cancer-Adjuvant ChemoTherapy in Ovarian Neoplasm. Impact of adjuvant chemotherapy and surgical staging in early-stage ovarian carcinoma: European Organisation for Research and Treatment of Cancer-Adjuvant ChemoTherapy in Ovarian Neoplasm trial. *J Nat Cancer Inst* 2003;95(2):113-25.
- 76 Colombo N, Guthrie D, Chiari S, Parmar M, Qian W, Swart AM, et al. International Collaborative Ovarian Neoplasm (ICON) collaborators. International Collaborative Ovarian Neoplasm trial 1: a randomized trial of adjuvant chemotherapy in women with early-stage ovarian cancer. *J Nat Cancer Inst* 2003;95(2):125-32.
- 77 Trimbos JB, Parmar M, Vergote I, Guthrie D, Bolis G, Colombo N, et al. International Collaborative Ovarian Neoplasm 1; European Organisation for Research and Treatment of Cancer Collaborators. International Collaborative Ovarian Neoplasm trial 1 and Adjuvant Chemotherapy in Ovarian Neoplasm trial: two parallel randomized phase III trials of adjuvant chemotherapy in patients with early-stage ovarian carcinoma. *J Nat Cancer Inst* 2003;95(2):105-12.
- 78 Zanetta G, Chiari S, Rota S, Bratina G, Maneo A, Torri V, et al. Conservative surgery for stage I ovarian carcinoma in women of childbearing age. *Br J Obstet Gynaecol* 1997;104(9):1030-5.
- 79 Kottmeier HL. Surgical treatment - conservative surgery. In: Gentil F, Junqueira AC, editors. *Ovarian cancer*. New York: Springer Verlag 1968. IUCC monograph series no. 11.
- 80 Hunter RW, Alexander ND, Soutter WP. Meta-analysis of surgery in advanced ovarian carcinoma: is maximum cytoreductive surgery an independent determinant of prognosis? *Am J Obstet Gynecol* 1992;166(2):504-11.
- 81 Voest EE, van Houwelingen JC, Neijt JP. A meta-analysis of prognostic factors in advanced ovarian cancer with median survival and overall survival (measured with the log (relative risk) as main objectives. *Eur J Cancer Clin Oncol* 1989;25(4):711-20.
- 82 Allen DG, Heintz AP, Touw FW. A meta-analysis of residual disease and survival in stage III and IV carcinoma of the ovary. *Eur J Gynaecol Oncol* 1995;16(5):349-56.
- 83 Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* 2002;20(5):1248-59.
- 84 Nguyen HN, Averette HE, Hoskins W, Penalver M, Sevin BU, Steren A. National survey of ovarian carcinoma. Part V. The impact of physician's specialty on patients' survival. *Cancer* 1993;72(12):3663-70.
- 85 Redman CW, Warwick J, Luesley DM, Varna R, Lawton FG, Blackledge GR. Intervention debulking surgery in advanced epithelial ovarian cancer. *Br J Obstet Gynaecol* 1994;101(2):142-6.
- 86 van der Burg ME, van Lent M, Buyse M, Kobierska A, Colombo N, Favalli G, et al. The effect of debulking surgery after induction chemotherapy on the prognosis in advanced epithelial ovarian cancer. Gynecological Cancer Cooperative Group of the European Organization for Research and Treatment of Cancer. *N Engl J Med* 1995;332(10):629-34.
- 87 Rose PG, Nerenstone S, Brady M, Clarke-Pearson D, Olt G, Rubin SC, et al. A phase III randomized study of interval secondary cytoreduction in patients with advanced stage ovarian carcinoma with suboptimal residual disease: a Gynecologic Oncology Group study [abstract]. Alexandria (VA): American Society of Clinical Oncology; 2002. [cited 3 Sep 2003]. Available from url: http://www.asco.org/ac/1,1003,12-002326-00_18-002002-00_19-00802-00_29-00A,00.asp
- 88 Bristow RE, Lagasse LD, Karlan BY. Secondary surgical cytoreduction for advanced epithelial ovarian cancer. Patient selection and review of the literature. *Cancer* 1996;78(10):2049-62.
- 89 Maughan K, Clarke C. The effect of a clinical nurse specialist in gynaecological oncology on quality of life and sexuality. *J Clin Nurs* 2001;10(2):221-9.
- 90 McArdle JM, George WD, McArdle CS, Smith DC, Moodie AR, Hughson AV, et al. Psychological support for patients undergoing breast cancer surgery: a randomised study. *BMJ* 1996;312(7034):813-6.
- 91 Ambler N, Rumsey N, Harcourt D, Khan F, Cawthorn S, Barker J. Specialist nurse counsellor interventions at the time of diagnosis of breast cancer: comparing 'advocacy' with a conventional approach. *J Adv Nurs* 1999;29(2):445-53.
- 92 Clinical Standards Board for Scotland. Clinical standards: gynaecological (ovarian) cancer. Edinburgh: The Board; 2001. [cited 3 Sep 2003]. Available from url: http://www.clinicalstandards.org/pdf/finalstand/Ovarian_Cancer.pdf
- 93 Clark TG, Stewart ME, Altman DG, Gabra H, Smyth JF. A prognostic model for ovarian cancer. *Br J Cancer* 2001;85(7):944-52.
- 94 Flynn PM, Paul J, Cruickshank DJ, Scottish Gynaecological Cancer Trials Group. Does the interval from primary surgery to chemotherapy influence progression-free survival in ovarian cancer? *Gynecol Oncol* 2002;86(3):354-7.
- 95 Ovarian cancer: screening, treatment, and followup. NIH Consensus Statement 1994;12(3):1-29. [cited 3 Sep 2003]. Available from url: http://odp.od.nih.gov/consensus/cons/096/096_intro.htm
- 96 Vergote I, De Brabanter J, Fyles A, Bertelsen K, Einhorn N, Sevelde P, et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet* 2001;357(9251):176-82.
- 97 Vergote I, De Wever I, Tjalma W, Van Gramberen M, Declodt J, van Dam P. Neoadjuvant chemotherapy or primary debulking surgery in advanced ovarian carcinoma: a retrospective analysis of 285 patients. *Gynecol Oncol* 1998;71(3):431-6.
- 98 Schwartz PE, Rutherford TJ, Chambers JT, Kohorn EI, Thiel RP. Neoadjuvant chemotherapy for advanced ovarian cancer: long-term survival. *Gynecol Oncol* 1999;72(1):93-9.
- 99 Advanced Ovarian Cancer Trialists Group. Chemotherapy for advanced ovarian cancer (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 100 ICON2: randomised trial of single-agent carboplatin against three-drug combination of CAP (cyclophosphamide, doxorubicin, and cisplatin) in women with ovarian cancer. ICON Collaborators. *International Collaborative Ovarian Neoplasm Study*. *Lancet* 1998;352(9140):1571-6.
- 101 Neijt JP, Engelholm SA, Tuxen MK, Sorensen PG, Hansen M, Sessa C, et al. Exploratory phase III study of paclitaxel and cisplatin versus paclitaxel and carboplatin in advanced ovarian cancer. *J Clin Oncol* 2000;18(17):3084-92.

- 102 Muggia FM, Braly PS, Brady MF, Sutton G, Niemann TH, Lentz SL, et al. Phase III randomized study of cisplatin versus paclitaxel versus cisplatin and paclitaxel in patients with suboptimal stage III or IV ovarian cancer: a gynecologic oncology group study. *J Clin Oncol* 2000;18(1):106-15.
- 103 Piccart MJ, Bertelsen K, James K, Cassidy J, Mangioni C, Simonsen E, et al. Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin-cyclophosphamide in women with advanced epithelial ovarian cancer: three-year results. *J Natl Cancer Inst* 2000;92(9):699-708.
- 104 National Institute for Clinical Excellence. Guidance on the use of paclitaxel in the treatment of ovarian cancer. London: The Institute; 2003. Technology appraisal no. 55. [cited 3 Sep 2003]. Available from url: http://www.nice.org.uk/pdf/55_Paclitaxel_ovarianreviewfullguidance.pdf
- 105 International Collaborative Ovarian Neoplasm Group. Paclitaxel plus carboplatin versus standard chemotherapy with either single-agent carboplatin or cyclophosphamide, doxorubicin, and cisplatin in women with ovarian cancer: the ICON3 randomised trial. *Lancet* 2002;360(9332):505-15.
- 106 McGuire WP, Hoskins WJ, Brady MF, Kucera PR, Partridge EE, Look KY, et al. Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patients with stage III and stage IV ovarian cancer. *N Engl J Med* 1996;334(1):1-6.
- 107 West RJ, Zweig SF. Meta-analysis of chemotherapy regimens for ovarian carcinoma: a reassessment of cisplatin, cyclophosphamide and doxorubicin versus cisplatin and cyclophosphamide. *Eur J Gynaecol Oncol* 1997;18(5):343-8.
- 108 Blackledge G, Lawton F, Redman C, Kelly K. Response of patients in phase II studies of chemotherapy in ovarian cancer: implications for patient treatment and the design of phase II trials. *Br J Cancer* 1989;59(4):650-3.
- 109 Cantu MG, Buda A, Parma G, Rossi R, Floriani I, Bonazzi C, et al. Randomized controlled trial of single-agent paclitaxel versus cyclophosphamide, doxorubicin, and cisplatin in patients with recurrent ovarian cancer who responded to first-line platinum-based regimens. *J Clin Oncol* 2002;20(5):1232-7.
- 110 Parmar MK, Ledermann JA, Colombo N, du Bois A, Delaloye JF, Kristensen GB, et al. Paclitaxel plus platinum-based chemotherapy versus conventional platinum-based chemotherapy in women with relapsed ovarian cancer: the ICON4/AGO-OVAR2.2 trial. *Lancet* 2003;361(9375):2099-106.
- 111 ten Bokkel Huinink W, Gore M, Carmichael J, Gordon A, Malfetano J, Hudson I, et al. Topotecan versus paclitaxel for the treatment of recurrent epithelial ovarian cancer. *J Clin Oncol* 1997;15(6):2183-93.
- 112 Gordon AN, Fleagle JT, Guthrie D, Parkin DE, Gore ME, Lacave AJ. Recurrent epithelial ovarian carcinoma: a randomized phase III study of pegylated liposomal doxorubicin versus topotecan. *J Clin Oncol* 2001;19(14):3312-22.
- 113 National Institute for Clinical Excellence. Guidance on the use of pegylated liposomal doxorubicin hydrochloride (PLDH) for the treatment of advanced ovarian cancer. London: The Institute; 2002. Technology appraisal no. 45. [cited 3 Sep 2003]. Available from url: <http://www.nice.org.uk/pdf/Fullguidance-PDF-ovariancancer.pdf>
- 114 Health Technology Board for Scotland. NICE technology appraisal guidance - no. 45. Glasgow: The Board; 2002. [cited 3 Sep 2003]. Available from url: <http://www.htbs.co.uk/htbsadvice/acomment.asp?did=818>
- 115 Williams CJ, Simeria I. Tamoxifen for relapse of ovarian cancer (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 116 Ludwig H, Fritz E. Anemia in cancer patients. *Semin Oncol* 1998;25(3 Suppl 7):2-6.
- 117 Quirt I, Micucci S, Moran LA, Pater J, Browman G. Erythropoietin in the management of patients with nonhematologic cancer receiving chemotherapy. Systemic Treatment Program Committee. *Cancer Prev Control* 1997;1(3):241-8.
- 118 Seidenfeld J, Aronson N, Piper M, Flamm CR, Hasselblad V, Ziegler KM. Uses of epoetin for anemia in oncology. Rockville (MD): Agency for Healthcare Research and Quality; 2001. AHRQ publication no. 01-E009. [cited 3 Sep 2003]. Available from url: <http://hstat.nlm.nih.gov/hq/Hquest/db/3687/screen/DocTitle/odas/1/s/57118>
- 119 Alberts DS, Liu PY, Hannigan EV, O'Toole R, Williams SD, Young JA, et al. Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer. *N Engl J Med* 1996;335(26):1950-5.
- 120 Markman M, Bundy BN, Alberts DS, Fowler JM, Clark-Pearson DL, Carson LF, et al. Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the Gynecologic Oncology Group, Southwestern Oncology Group, and Eastern Cooperative Oncology Group. *J Clin Oncol* 2001;19(4):1001-7.
- 121 Armstrong DK, Bundy BN, Baergen R, Lele SB, Copeland LJ, Walker J, et al. Randomized phase III study of intravenous (IV) paclitaxel and cisplatin versus IV paclitaxel, intraperitoneal (IP) cisplatin and IP paclitaxel in optimal stage III epithelial ovarian cancer (OC): a Gynecologic Oncology Group trial (GOG 172) [abstract]. Alexandria (VA): American Society of Clinical Oncology; 2002. [cited 3 Sep 2003]. Available from url: http://www.asco.org/ac/1,1003,12-002326-00_18-002002-00_19-00803-00_29-00A,00.asp
- 122 Joint Council for Clinical Oncology. Quality control in cancer chemotherapy: managerial and procedural aspects. London: The Council; 1994.
- 123 Royal College of Radiologists' Clinical Oncology Information Network. Guidelines for cytotoxic chemotherapy in adults. A document for local expert groups in the United Kingdom preparing chemotherapy policy documents. *Clin Oncol (R Coll Radiol)* 2001;13(1):s209-48. [cited 3 Sep 2003]. Available from url: <http://www.rcr.ac.uk/upload/ChemotherapyGuideline2001.pdf>
- 124 Scottish Executive. Guidelines for the use of cytotoxic chemotherapy in the clinical environment. Edinburgh: The Executive; 2001. NHS HDL(2001)13. [cited 3 Sep 2003]. Available from url: http://www.show.scot.nhs.uk/sehd/mels/HDL2001_13.htm
- 125 Lutgendorf SK, Anderson B, Rothrock N, Buller RE, Sood AK, Sorosky JL. Quality of life and mood in women receiving extensive chemotherapy for gynecologic cancer. *Cancer* 2000;89(6):1402-11.
- 126 Montazeri A, McEwen J, Gillis CR. Quality of life in patients with ovarian cancer: current state of research. *Support Care Cancer* 1996;4(3):169-79.
- 127 Doyle C, Crump M, Pintilie M, Oza AM. Does palliative chemotherapy palliate? Evaluation of expectations, outcomes, and costs in women receiving chemotherapy for advanced ovarian cancer. *J Clin Oncol* 2001;19(5):1266-74.
- 128 Guidozi F. Living with ovarian cancer. *Gynecol Oncol* 1993;50(2):202-7.
- 129 Komblioth AB, Thaler HT, Wong G, Vlamis V, Lepore JM, Loseth DB, et al. Quality of life of women with ovarian cancer. *Gynecol Oncol* 1995;59(2):231-42.
- 130 Carter JR, Chen MD, Fowler JM, Carson LF, Twigg LB. The effect of prolonged cycles of chemotherapy on quality of life in gynaecologic cancer patients. *J Obstet Gynaecol Res* 1997;23(2):197-203.
- 131 Rustin GJ, Nelstrop AE, Tuxen MK, Lambert HE. Defining progression of ovarian carcinoma during follow-up according to CA 125: a north Thames Ovary Group Study. *Ann Oncol* 1996;7(4):361-4.
- 132 Van der Berg ME, Lammes FB, Verweij J. The role of CA 125 in the early diagnosis of progressive disease in ovarian cancer. *Ann Oncol* 1990;1(4):301-2.
- 133 Low RN, Saleh F, Song SY, Shiftan TA, Barone RM, Lacey CG, Goldfarb PM. Treated ovarian cancer: comparison of MR imaging with serum CA-125 level and physical examination - a longitudinal study. *Radiology* 1999;211(2):519-28.
- 134 Zanetta G, Rota S, Lissoni A, Meni A, Brancatelli G, Buda A. Ultrasound, physical examination, and CA 125 measurement for the detection of recurrence after conservative surgery for early borderline ovarian tumors. *Gynaecol Oncol* 2001;81(1):63-6.
- 135 Junor EJ, Hole DJ, Gillis CR. Management of ovarian cancer: referral to a multidisciplinary team matters. *Br J Cancer* 1994;70(2):363-70.
- 136 Hancock BW, Aitken M, Radstone C, Hudson GV. Why don't cancer patients get entered into clinical trials? Experience of the Sheffield Lymphoma Group's collaboration in British National Lymphoma Investigation studies. *BMJ* 1997;314(7073):36-7.
- 137 Ellis PM. Attitudes towards and participation in randomised clinical trials in oncology: a review of the literature. *Ann Oncol* 2000;11(8):939-45.
- 138 Braunholtz DA, Edwards SJL, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a "trial effect". *J Clin Epidemiol* 2001;54(3):217-24.
- 139 Dvoretzky PM, Richards KA, Angel C, Rabinowitz L, Beecham JB, Bonfiglio TA. Survival time, causes of death, and tumor/treatment-related morbidity in 100 women with ovarian cancer. *Hum Path* 1988;19(11):1273-9.
- 140 Rose PG, Piver MS, Tsukada Y, Lau TS. Metastatic patterns in histologic variants of ovarian cancer. An autopsy study. *Cancer* 1989;64(7):1508-13.
- 141 Feuer DJ, Broadley KE. Surgery for the resolution of symptoms in malignant bowel obstruction in advanced gynaecological and gastrointestinal cancer (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 142 Taylor RH. Laparotomy for obstruction with recurrent tumour. *Br J Surg* 1985;72:327.
- 143 Ketcham AS, Hoyer RC, Pilch YH, Morton DL. Delayed intestinal obstruction following treatment for cancer. *Cancer* 1970;25(2):406-10.
- 144 Rubin SC, Hoskins WJ, Benjamin I, Lewis JL Jr. Palliative surgery for intestinal obstruction in advanced ovarian cancer. *Gynecol Oncol* 1989;34(1):16-9.
- 145 van Ooijen B, van der Burg ME, Planting AS, Siersema PD, Wiggers T. Surgical treatment or gastric drainage only for intestinal obstruction in patients with carcinoma of the ovary or peritoneal carcinomatosis of other origin. *Surg Gynecol Obstet* 1993;176(5):469-74.
- 146 Lau PW, Lorentz TG. Results of surgery for malignant bowel obstruction in advanced, unresectable, recurrent colorectal cancer. *Dis Colon Rectum* 1993;36(1):61-4.
- 147 Baines M, Oliver DJ, Carter RL. Medical management of intestinal obstruction in patients with advanced malignant disease. A clinical and pathological study. *Lancet* 1985;2(8462):990-3.
- 148 Feuer DJ, Broadley KE. Corticosteroids for the resolution of malignant bowel obstruction in advanced gynaecological and gastrointestinal cancer (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 149 Twycross R, Wilcock A, Charlesworth S, Dickman A. Palliative care formulary. 2nd ed. Abingdon: Radcliffe Medical Press; 2002.

- 150 Ripamonti C, Mercadante S, Groff L, Zecca E, De Conno F, Casuccio A. Role of octreotide, scopolamine butylbromide, and hydration in symptom control of patients with inoperable bowel obstruction and nasogastric tubes: a prospective randomized trial. *J Pain Symptom Manage* 2000;19(1):23-34.
- 151 Mercadante S, Ripamonti C, Casuccio A, Zecca E, Groff L. Comparison of octreotide and hyoscine butylbromide in controlling gastrointestinal symptoms due to malignant inoperable bowel obstruction. *Support Care Cancer* 2000;8(3):188-91.
- 152 Bizer LS, Liebling RW, Delany HM, Gliedman ML. Small bowel obstruction: the role of nonoperative treatment in simple intestinal obstruction and predictive criteria for strangulation obstruction. *Surgery* 1981;89(4):407-13.
- 153 Koukouras D, Mastronikolis NS, Tzoracoleftherakis E, Angelopoulou E, Kalfarentzos F, Androulakis J. The role of nasogastric tube after elective abdominal surgery. *Clin Ter* 2001;152(4):241-4.
- 154 Ripamonti C, Twycross R, Baines M, Bozzetti F, Capri S, De Conno F, et al. Clinical-practice recommendations for the management of bowel obstruction in patients with end-stage cancer. *Support Care Cancer* 2001;9(4):223-33.
- 155 Pelham A, Lee MA, Regnard CB. Gabapentin for coeliac plexus pain. *Palliat Med* 2002;16(4):355-6.
- 156 Scottish Intercollegiate Guidelines Network (SIGN). Control of pain in patients with cancer. Edinburgh: SIGN; 2000. (SIGN publication no. 44). [cited 4 Sep 2003]. Available from url: <http://www.sign.ac.uk/guidelines/fulltext/44/index.html>
- 157 General Medical Council. Tomorrow's doctors. Recommendations on undergraduate medical education. London: The Council; 2002. [cited 4 Sep 2003]. Available from url: http://www.gmc-uk.org/med_ed/tomdoc.htm
- 158 Clinical Standards Board for Scotland. Clinical standards. Specialist palliative care. Revised ed. Edinburgh: The Board; 2002. [cited 4 Sep 2003]. Available from url: <http://www.clinicalstandards.org/pdf/finalstand/SPC.pdf>
- 159 Hearn J, Higginson IJ. Do specialist palliative care teams improve outcomes for cancer patients? A systematic literature review. *Palliat Med* 1998;12(5):317-32.
- 160 Addington-Hall JM, MacDonald LD, Anderson HR, Chamberlain J, Freeling P, Bland JM, et al. Randomised controlled trial of effects of coordinating care for terminally ill cancer patients. *BMJ* 1992;305(6865):1317-22.
- 161 Raftery JP, Addington-Hall JM, MacDonald LD, Anderson HR, Bland JM, Chamberlain J, et al. A randomized controlled trial of the cost-effectiveness of a district co-ordinating service for terminally ill cancer patients. *Palliat Med* 1996;10(2):151-61.
- 162 Jordhoy MS, Fayers P, Saltnes T, Ahlner-Elmqvist M, Jannert M, Kaasa S. A palliative-care intervention and death at home: a cluster randomised trial. *Lancet* 2000;356(9233):888-93.
- 163 Scottish Executive Health Department. Cancer in Scotland: action for change. Edinburgh: The Executive; 2001. [cited 4 Sep 2003]. Available from url: <http://www.scotland.gov.uk/library3/health/cscac-00.asp>
- 164 University of York. NHS Centre for Reviews and Dissemination. Management of gynaecological cancers. *Effective Health Care* 1999;5(3). [cited 4 Sep 2003]. Available from url: <http://www.york.ac.uk/inst/crd/ehc53.htm>
- 165 Harris KA. The informational needs of patients with cancer and their families. *Cancer Pract* 1998;6(1):39-46.
- 166 Mohide EA, Whelan TJ, Rath D, Gafni A, Willan AR, Czukur D, et al. A randomised trial of two information packages distributed to new cancer patients before their initial appointment at a regional cancer centre. *Br J Cancer* 1996;73(12):1588-93.
- 167 Meredith C, Symonds P, Webster L, Lamont D, Pyper E, Gillis CR, et al. Information needs of cancer patients in west Scotland: cross sectional survey of patients' views. *BMJ* 1996;313(7059):724-6.
- 168 Scott JT, Harmsen M, Pricor MJ, Entwistle VA, Sowden AJ, Watt I. Recordings or summaries of consultations for people with cancer (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.
- 169 Brown R, Butow PN, Boyer MJ, Tattersall MH. Promoting patient participation in the cancer consultation: evaluation of a prompt sheet and coaching in question-asking. *Br J Cancer* 1999;80(1-2):242-8.
- 170 Bruera E, Pituskin E, Calder K, Neumann CM, Hanson J. The addition of an audiocassette recording of a consultation to written recommendations for patients with advanced cancer: A randomized, controlled trial. *Cancer* 1999;86(11):2420-5.
- 171 Fawzy FI, Fawzy NW, Hyun CS, Elashoff R, Guthrie D, Fahey JL, et al. Malignant melanoma. Effects of an early structured psychiatric intervention, coping, and affective state on recurrence and survival 6 years later. *Arch Gen Psychiatry* 1993;50(9):681-9.
- 172 Hack TF, Pickles T, Bultz BD, Degner LF, Katz A, Davison BJ. Feasibility of an audiotape intervention for patients with cancer. A multicenter, randomized, controlled pilot study. *J Psych Onc* 1999;17(2):1-15.
- 173 Jones R, Pearson J, McGregor S, Cawsey AJ, Barrett A, Craig N, et al. Randomised trial of personalised computer based information for cancer patients. *BMJ* 1999;319(7219):1241-7.
- 174 McQuellon RP, Wells M, Hoffman S, Craven B, Russell G, Cruz J, et al. Reducing distress in cancer patients with an orientation program. *Psychooncology* 1998;7(3):207-17.
- 175 Walker LG, Walker MB, Ogston K, Heys SD, Ah-See AK, Miller ID, et al. Psychological, clinical and pathological effects of relaxation training and guided imagery during primary chemotherapy. *Br J Cancer* 1999;80(1-2):262-8.
- 176 Ong LM, Visser MR, Lammes FB, van Der Velden J, Kuenen BC, de Haes JC. Effect of providing cancer patients with the audiotaped initial consultation on satisfaction, recall, and quality of life: a randomized, double-blind study. *J Clin Oncol* 2000;18(16):3052-60.
- 177 University of York. NHS Centre for Reviews and Dissemination. Informing, communicating and sharing decisions with people who have cancer. *Effective Health Care* 2000;6(6). [cited 4 Sep 2003]. Available from url: <http://www.york.ac.uk/inst/crd/ehc66.htm>
- 178 Scottish Executive. Introduction of managed clinical networks within the NHS in Scotland. Edinburgh: The Executive; 1999. NHS MEL(1999)10. [cited 3 Sep 2003]. Available from url: http://www.show.scot.nhs.uk/sehd/mels/1999_10.htm
- 179 Silverberg SG. Histopathologic grading of ovarian carcinoma: a review and proposal. *Int J Gynecol Pathol* 2000;19(1):7-15.
- 180 Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology* 1991;19:403-10.
- 181 Pereira H, Pinder SE, Sibbering DM, Galea MH, Elston CW, Blamey RW, et al. Pathological prognostic factors in breast cancer. IV: Should you be a typer or a grader? A comparative study of two histological prognostic features in operable breast carcinoma. *Histopathology* 1995;27(3):219-26.
- 182 NHS Executive. Guidance on commissioning cancer services: improving outcomes in gynaecological cancer: the manual. London: The Executive; 1999. [cited 4 Sep 2003]. Available from url: <http://www.doh.gov.uk/cancer/pdfs/gynaemanual.pdf>

▶ FOLLOW UP

Patients who are not in clinical trials should be followed up within local multidisciplinary specialist clinics.

The primary care team should be made aware of the follow up protocol for those patients not in trials.

▶ MANAGEMENT OF MALIGNANT BOWEL OBSTRUCTION

C Surgery for malignant bowel obstruction in patients with advanced ovarian cancer must be justified on the basis of achieving a significant benefit.

C Symptoms of bowel obstruction can be relieved by using the following drug categories either alone or in combination:

- antiemetic
- antisecretory
- analgesic
- corticosteroids.

▶ SPECIALIST PALLIATIVE CARE

B Patients with advanced ovarian cancer require a coordinated, multiprofessional approach with access to a specialist palliative care team.

D Patients with persistent poorly controlled symptoms should be referred to specialist palliative care.

▶ INFORMATION FOR PATIENTS

C Patients should be offered verbal and written information throughout their journey of care and should be made aware of support mechanisms in place and how to access them.

C Structured emotional support should be available to all patients and carers.

Voluntary sector agencies can be used to expand the levels of support available to patients and carers.

▶ SOURCES OF FURTHER INFORMATION FOR PATIENTS AND CARERS

CancerBACUP Scotland

Suite 2, 3rd Floor, Cranston House, 104-114 Argyll Street, Glasgow G2 8BH
Tel: 0141 223 7676, Fax: 0141 248 8422
Freephone help line: 0800 800 1234. Available Monday to Friday, 9am to 7pm
www.cancerbacup.org.uk

Offers a free cancer information service staffed by qualified and experienced cancer nurses. There are a growing number of CancerBACUP centres in hospitals and a freephone information service on all types of cancer, staffed by specialist cancer nurses. Produces over 50 booklets and 'CancerBACUP News' three times a year.

Cancer Research UK

PO Box 123, 61 Lincoln's Inn Fields, London WC2A 3PX
Tel: 020 7242 0200, Fax: 020 7269 3100
www.cancerresearchuk.org

Macmillan Cancer Relief Scotland

Osbourne House, 1-5 Osbourne Terrace, Edinburgh EH12 5HG
Tel: 0131 346 5346, Fax: 0131 346 5347
Helpline: 0800 808 2020. Monday to Friday, 9am to 6pm
www.macmillan.org.uk

A UK charity supporting people with cancer and their families with specialist information, treatment and care.

Maggie's Centres Scotland

The Stables, Western General Hospital, Edinburgh, EH4 2XU
Tel: 0131 537 3131, Fax: 0131 537 3130

The Gatehouse, Western Infirmary, 10 Dumbarton Road, Glasgow, G11 6PA
Tel: 0141 330 3311, Fax: 0141 330 3363
Email: maggies.centre@ed.ac.uk
www.maggies.ed.ac.uk

The goal of Maggie's is to keep people who have cancer as healthy in mind and body as is possible, by enabling them to participate actively in the treatment of their disease.

Tak Tent Cancer Support Scotland

Flat 5, 30 Shelley Court, Gartnavel Complex, Glasgow, G12 0YN
Tel: 0141 211 0122, Fax: 0141 211 3988
Email: tak.tent@care4free.net
www.taktent.org.uk

Promotes the care of cancer patients, their families, friends and the staff involved professionally in cancer care by providing practical and emotional support, information, counselling and therapies as required. Network of local support groups throughout Scotland. The Youth Group, comTak, provides support for 16 to 25 year olds affected by cancer.

Ovacome

Elizabeth Garrett Anderson Hospital, Huntley Street, London, WC1E 6DH
Tel: 020 7380 9589. Office is staffed Monday to Friday, 9am to 4pm
Email: ovacome@ovacome.org.uk
www.ovacome.org.uk/

A UK wide charity providing information and support for all those affected by ovarian cancer including patients, relatives, carers and health professionals. Newsletter produced four times a year and fact sheets on many aspects of ovarian cancer are available on request.

SCREENING

- Women with a family history that appears to put them at high risk of developing ovarian cancer should be offered referral to a Clinical Genetics Service for assessment and confirmation of their family history. They may then be eligible for referral for screening via a research trial.
- Close collaboration between primary care and specialist cancer genetics services should be developed and encouraged so that genetic cancer risk assessment can be carried out efficiently.
- Primary care clinicians should formally enquire about the woman's family history.
- Screening for ovarian cancer in high risk groups should only be offered in the context of a research study designed to gather data on:
 - sensitivity and specificity of the screening tool
 - FIGO stages of cancers detected through screening
 - residual risk of primary peritoneal cancer following prophylactic oophorectomy.
- Screening programmes for women at increased risk of ovarian cancer should include mechanisms for providing emotional and psychological support.
- Women with genetic mutations of BRCA1 or BRCA2 genes should be counselled regarding prophylactic oophorectomy and removal of Fallopian tubes at a relevant time of their life.
- High risk women in whom mutations have not been identified should be counselled at around the age of 40 years regarding prophylactic oophorectomy.
- Women who decide to have prophylactic oophorectomy should be offered counselling, support and information before and after surgery.

DIAGNOSIS

- GPs should include ovarian cancer in the differential diagnosis when women present with recent onset persistent non-specific abdominal symptoms (including women whose abdominal and pelvic clinical examinations appear normal).
- Women with a pelvic mass should be referred to gynaecology irrespective of the CA125 test result.
 - The RMI scoring system is the method of choice for predicting whether or not an ovarian mass is likely to be malignant.
 - Women with an RMI score > 200 should be referred to a centre with experience in ovarian cancer surgery.

SURGERY

- Preoperative bowel preparation in ovarian cancer patients should be undertaken where clinical findings and imaging reveal that advanced disease with bowel involvement is present.

SURGERY (Contd.)

- Patients for whom preoperative bowel preparation is indicated should see a trained stoma nurse for counselling and potential stoma site marking.
- Serum CA125 levels are useful in predicting disease bulk and should be assayed preoperatively in women with pelvic masses.
- Routine preoperative CEA estimation should not be performed in patients with ovarian cancer.
- To minimise the need for a second operative staging procedure, intraoperative frozen section assessment can be used to diagnose malignancy and to exclude metastatic disease.
 - In early disease:
 - staging should be through a mid-line incision to allow palpation of all peritoneal surfaces
 - assessment of peritoneal cytology, hysterectomy, removal of ovaries and Fallopian tubes and infracolic omentectomy should be performed
 - capsular rupture during surgery should be avoided
 - aim to exclude disease involving the liver, spleen, peritoneum, retroperitoneal nodes, appendix and diaphragm by close clinical inspection and palpation
 - cases where only the ovarian cyst was removed should be discussed within the multidisciplinary team and if there is concern that there is a likelihood of metastatic disease restaging is recommended.
- In advanced disease:
 - if aggressive cytoreduction is not possible then optimal cytoreduction is the recommended surgical procedure if performance status allows this to take place.
- In advanced disease:
 - patients with stage III disease should be operated on by a gynaecological oncologist rather than a general gynaecologist or a general surgeon.
- In advanced disease:
 - bowel surgery should only be performed where obstruction is imminent or where it enables optimal cytoreduction or aggressive cytoreduction to be achieved.
- Interval debulking surgery is recommended, if performance status allows, where there is evidence of response to chemotherapy as determined by CA125 and imaging.
 - Patients should be given their diagnosis of ovarian cancer after surgery in the presence of a nurse who is a fully integrated member of the clinical team. If a nurse specialist is not available this should be a dedicated named nurse or link nurse.
- Patients with ovarian cancer should have access to an appropriately trained nurse, who is an integral member of the gynaecological cancer team, throughout their journey of care.

CHEMOTHERAPY

- Chemotherapy should be started no later than eight weeks after surgery.
- Carboplatin can be offered to all early stage epithelial ovarian cancer patients.
 - Chemotherapy for patients with disease confined to the ovaries where the tumour is well differentiated (FIGO stage 1a grade 1 and FIGO stage 1b grade 1, see Annexes 1 and 2), may be deferred if optimal surgery has been performed.
- In advanced disease:
 - first line chemotherapy treatment should include a platinum agent either in combination or as a single agent, unless specifically contraindicated
 - carboplatin is the platinum of choice in both single and combination therapy
 - paclitaxel is recommended in combination therapy with platinum in first line post-surgery treatment where the potential benefits justify the toxicity of the therapy
 - patients who choose less toxic therapy or who are unfit for taxanes should be offered single agent carboplatin
 - cyclophosphamide is not recommended in first line chemotherapy treatment
 - anthracyclines are not recommended in first line chemotherapy treatment outside RCTs.
- In relapsed disease:
 - chemotherapy for recurrent ovarian cancer should be regarded as palliative in intent and should be reserved for symptomatic recurrence of disease
 - symptomatic platinum-sensitive cancer recurrence should be treated with further platinum and paclitaxel.
- In relapsed disease:
 - Tamoxifen should be considered in patients for whom chemotherapy is not appropriate.
- In relapsed disease:
 - the optimal agents in platinum-resistant disease have yet to be defined and treatment should be based on specialist judgement
 - cautious clinical judgement should be used when considering the use of platinum and paclitaxel in patients with symptomatic platinum-sensitive cancer recurrence after a treatment free interval of 6-12 months.
- If erythropoietin is used to treat anaemia it should only be when the haemoglobin concentration is ≤ 10 g/dL and the dose should not exceed 450 units/kg/week.
- Women should be given accurate information on their likely response to chemotherapy, including adverse effects, so that they can make an informed decision on whether or not to proceed.