



**PROPOSED REVIEW OF SIGN GUIDELINE
CONSULTATION FORM**

Title of guideline	SIGN 75: Epithelial Ovarian Cancer
Date of publication	October 2003
SIGN scoping search – sources	<p>MeSH headings for the condition specified and any common variations as free text, plus terms for the interventions and care processes discussed in the guideline</p> <p>Sources: Guidelines: NICE; National Library for Health guidelines finder; National Guidelines Clearinghouse; GIN Web site. Technology appraisals: NICE; UK HTA database (Southampton); INAHTA database. Cochrane reviews: Cochrane Library. Other good quality systematic reviews: UK HTA database (Southampton); DARE.</p>
SIGN scoping search - summary	<p>Guidelines – 9 (3 on screening, 1 on genetic risk assessment) HTAs – 2 Cochrane reviews – 1 Other good quality systematic reviews – 13</p>
Other guidelines/HTAs	<p>First-line chemotherapy for postoperative patients with stage II, III or IV epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer. Gynecology Disease Site Group. Covens A, Carey M, Bryson P, Verma S, Fung Kee Fung M. First-line chemotherapy for postoperative patients with stage II, III or IV epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Jun [online update]. 38 p. (Practice guideline report; no. 4-1-2). [67 references]</p> <p>Screening for ovarian cancer: recommendation statement. Screening for ovarian cancer: recommendation statement. Ann Fam Med 2004 May-Jun;2(3):260-2.</p> <p>Screening for ovarian cancer: recommendation statement. U.S. Preventive Services Task Force. Am Fam Physician 2005 Feb 15;71(4):759-62. Ovarian cancer screening. Bohm-Velez M, Fleischer AC, Andreotti RF, Fishman EK, Horrow MM, Hricak H, Thurmond A, Zelop C, Expert Panel on Women's Imaging. Ovarian cancer screening. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 7 p. [18 references]</p> <p>Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: recommendation statement. Ann Intern Med 2005 Sep 6;143(5):355-61</p> <p>Staging and follow-up of ovarian cancer. Javitt MC, Fleischer AC, Andreotti RF, Bohm-Velez M, Horrow MM, Hricak H, Thurmond A, Zelop C, Expert Panel on Women's Imaging. Staging and follow-up of ovarian cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 4 p. [31 references].</p> <p>Adjuvant care for stage 1 ovarian cancer. Gynecology Cancer Disease Site Group. Elit L, Fyles A, Chambers A, Fung Kee Fung M, Covens A, Carey M. Adjuvant care for stage I ovarian cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 May 3. 33 p. (Practice guideline report; no. 4-13). [62 references]</p> <p>Prophylactic oophorectomy. American College of Obstetricians and Gynecologists (ACOG). Prophylactic oophorectomy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 1999 Sep. 7 p. (ACOG practice bulletin; no. 7). [33 references]</p>

	<p>Clinical practice guidelines for the management of women with epithelial ovarian cancer (CP 98) Publication Date: 1 March 2004 Published By: NHMRC (AU) - National Health and Medical Research Council</p> <p>Review of the clinical effectiveness and cost effectiveness of paclitaxel for ovarian cancer Guidance type: Technology appraisal Date issued: January 2003 NICE</p> <p>Topotecan, pegylated liposomal doxorubicin hydrochloride and paclitaxel for the treatment of advanced ovarian cancer (review of existing guidance numbers 28, 45 and 55 (for relapsed disease only)) Guidance type: Technology appraisal Date issued: May 2005 NICE</p>
Main conclusions from new evidence	<ul style="list-style-type: none"> ▪ A Cochrane review compared the effectiveness of intravenous chemotherapy to chemotherapy administered directly into the peritoneal cavity. The evidence suggests an improvement in survival if some of the chemotherapy is administered via the intraperitoneal route. There is an increase in adverse effects principally relating to the presence of a peritoneal catheter, including pain, catheter blockage, gastrointestinal effects and infection. <i>The guideline reports on RCTs with methodological flaws and has a holding statement about awaiting the outcome of the GOG study. There is a good practice point which recommends against intraperitoneal chemotherapy.</i> ▪ A systematic review suggested that carboplatin plus paclitaxel should be the standard treatment for stage II to IV ovarian cancer. Carboplatin may be administered in doses ranging from 4 to 6 AUC. Paclitaxel may be administered in doses ranging from 135 to 175 mg/m² over a 3-hour period. Single-agent carboplatin may be used in women who wish to minimise toxicity. <i>The guideline recommends that first line chemotherapy should include a platinum agent either in combination or as a single agent (A) and says that carboplatin is the platinum drug of choice in both single and combination therapy (A). Paclitaxel is recommended in combination with platinum in the first line post-surgery treatment (A).</i> ▪ A systematic review of adjuvant therapy for early stage (epithelial) ovarian cancer stated that women who have been adequately staged with well-differentiated ovarian cancer confined to one or both ovaries with an intact ovarian capsule (FIGO Stages IA/IB) can be managed by observation. Other women should be offered adjunctive treatment with platinum-based chemotherapy. <i>The guideline acknowledges that this is a controversial area and makes some good practice points to aid accurate staging in patients at stage I. The guideline recommends that carboplatin can be offered to all early stage epithelial ovarian cancer patients (B).</i> ▪ A meta-analysis concludes that consistent referral of patients with advanced ovarian carcinoma to expert centres for initial surgery may be the best means currently available for improving the overall survival rate. <i>The guideline does not address when to refer to expert centres. There is a recommendation that women with an RMI score > 200 should be referred to a centre with experience in ovarian cancer surgery (C).</i>
New areas that could be added to the guideline	<ul style="list-style-type: none"> ▪ Referral to specialist centres
Summary of the recommendations that could be updated	<ul style="list-style-type: none"> ▪ Recommendations on intraperitoneal chemotherapy. ▪ Recommendations the standard treatment for stage II to IV ovarian cancer. ▪ Recommendations on adjuvant therapy for early stage (epithelial) ovarian cancer.

Please answer the following questions as fully as possible:

Name, designation, organisation:	Other: 4 Academics: 1 Consultant Radiologist: 1 Oncology: 6 Consultant in palliative medicine: 1
1(a) Is there still a requirement for an evidence-based guideline on this topic?	
<ul style="list-style-type: none"> ▪ Yes = 10 No = 0 	

1(b) If no, should the guideline be withdrawn?	
2(a) Do you agree with the assessment of the impact of the new evidence and its likely effect on recommendations?	
<ul style="list-style-type: none"> ▪ Yes = 10 ▪ Yes. Main change is IP chemotherapy but this is still the remit of trials 	
2(b) Based on the information given above, and your own clinical judgement, does the guideline require revision in the light of new evidence? <i>Please give details.</i>	
<ul style="list-style-type: none"> ▪ Some updates required in light of new evidence that screening is <u>ineffective</u> in detecting early stage cancer among those of high risk ▪ Minimal tweaking ▪ I am not a clinician, but as policy maker I agree that in light of new emerging evidence this guideline should be reviewed ▪ I have studied my copy of this (guideline), and also the brief review sent report. In my view, there is no need to update the guideline, which remains accurate in all respects. There are no new data which justify any change. <i>(see additional comments below)</i> ▪ No – these are minor changes only and I suspect there may be bigger changes in the next 3 years that warrant waiting until these are produced ▪ the areas that could be updated are key aspects of the patient pathway and therefore an update would be helpful ▪ No revision required at present. ▪ Yes, as a general rule, I think that guidelines need to be updated on a regular base in order to ensure a broad use and acceptance. This is especially true in oncology, where new data can dramatically change the way of treating our patients. Even without new data, an 'old' guideline is at risk for being neglected because it will be considered outdated. ▪ Not based on the referral situation alone. ▪ Need to take heed most of medical oncology opinions. ▪ My expertise is in oncology imaging and there has been no significant change in the way that is practiced since the guidelines were last modified. I therefore have nothing to add to the above document. 	
3 Please list any additions to the remit of the guideline that you think would be beneficial	
<ul style="list-style-type: none"> ▪ Update evidence-base for prophylactic oophorectomy vs screening for women with BRCA 1/2 mutations ▪ Expansion on the screening and diagnosis aspects – practice and knowledge still varies widely e.g. appropriate use of tumour markers for diagnosis ▪ Some advice on use of opioids in renal impairment particularly stage 4-5 chronic kidney disease is needed even if this is just a link to the revised sections in SIGN 44 ▪ I think that it would be timely to also review the histopathology ▪ Might be worth considering how useful RMI really is in day to day practice. 	
4 Please tick your preferred option for reviewing this guideline	
a. there is no new evidence that will affect existing recommendations and the guideline should not be reviewed at this time	1
b. some recommendations will change in the light of the new evidence and selected elements of the guideline should be reviewed	11
c. the entire guideline should be reviewed	
d. the guideline should be withdrawn	

Thank you very much for taking part in this consultation.

Please return to: Safia Qureshi, SIGN Executive, 28 Thistle Street, Edinburgh EH2 1EN, safia.gureshi@nhs.net

Additional Comments:

see Stirling et al. JCO 2005;23:5588-96
Hermesen et al Br J Cancer 2007;96:1335-42
Olivier et al 2006 Gynecol Oncol 100:20-26

All report failure to detect OC at early stage by regular CA125/TV U/S screening women with strong family history and / or proven BRCA 1/2 mutations.

FOCSS study (UK) is based on an algorithm suggesting risk in CA125 level over 4 months may provide better prediction but the algorithm is based on data from post-menopausal women and may not apply to pre-menopausal (those at risk if BRCA mutation carriers) because CA125 level fluctuates through the cycle

1. There is one additional publication to which you could refer; this is the outcome of a consensus conference organised by the Gynaec Cancer Inter Group in 2004. The reference is:
du Bois A, Quinn M, Thigpen T et al. 2004 consensus statements on the management of ovarian cancer. Final document of the 3rd GCIG consensus conference. Ann. Oncol. 16 viii 7-12 2005 suppl 8.
2. In addition, the NCI (USA) put out a statement in January 2006 on intraperitoneal chemotherapy which has been controversial. While it has led to some change in practice in the USA, this is not the case in Europe. The issue is whether the GOG trial referred to in the October 2003 guideline (Armstrong et al, 2007) should change our view. Many people think that the role of ip treatment is still unclear, and this should still be confined to clinical trials (Gore et al, 2007).
3. In considering your report, you made four main conclusions where an update of the 2003 guideline may be necessary. I have dealt with the first. As regards the other three, there are no new data covered in recent systematic reviews or meta-analyses which change any of the recommendations made in the excellent October 2003 publication.

Refs: i) National Cancer Institute: clinical announcement: intraperitoneal chemotherapy for ovarian cancer: Jan 5 2006 http://ctep.cancer.gov/highlights/clin_annc_01506pdf.

ii) Gore M, de Bois A, and Vergote I. Intraperitoneal chemotherapy in ovarian cancer remains experimental. *J clin Onc.* 24 2006 4528-30.

iii) Armstrong D, Bundy B, Wenzel L et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *New Eng J Med* 354 34-43 32006.

Comments from Scottish Intercollegiate Guidelines Network Council meeting held 7th November 2007

Defer the review and seek advice from the new cancer SSG on what to do about selective reviews in cancer guidelines. Any review done would be extremely selective and focus on chemotherapy