4-year surveillance 2016 - Ovarian cancer (2011) NICE guideline CG122

Appendix B: stakeholder consultation comments table

Consultation dates: 01/12/15–14/12/15

Type	Stakeholder	Do you agree with the proposal not to update the guideline?	Comments Insert each new comment on a new row	Comments on equality issues or areas excluded from the original scope Insert each new comment on a new row	Response
SH	British Gynaecological Cancer Society	Disagree	"For any woman who has normal serum CA125 (less than 35 IU/ml), or CA125 of 35 IU/ml or greater but a normal ultrasound: assess her carefully for other clinical causes of her symptoms and investigate if appropriate if no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent". In the recently published paper from the UKTOCS (Risk Algorithm Using Serial Biomarker Measurements Doubles the Number of Screen-Detected Cancers Compared With a Single-Threshold Rule in the United Kingdom Collaborative Trial of Ovarian Cancer Screening. Menon U, etal. J Clin Oncol. 2015 Jun 20;33(18):2062-71. Epub 2015 May 11), it was found that screening by using ROCA doubled the number of screen-detected iEOCs compared with a fixed cutoff of 35. This means that we should consider that even with normal CA125 and normal US, patients who have symptoms, and where no other cause can be found, should return to their GP for serial CA125 and repeat US		Thank you for your comment. This has now been added to the decision matrix for the 4-year surveillance for the clinical question 'For women with suspected ovarian cancer, what serum tumour marker tests should be routinely carried out to aid in diagnosis?'. The surveillance review decision has been amended to reflect that this section of the guideline should be updated.
SH	British Gynaecological Cancer Society	Disagree	*1.3.1.2 Do not include systematic retroperitoneal lymphadenectomy (block dissection of lymph nodes from the pelvic side walls to the level of the renal veins) as part of standard surgical treatment in women with suspected*		Thank you for your comment. The trial you refer to by Maggioni 2006 was not part of the surveillance

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			ovarian cancer whose disease appears to be confined to the ovaries (that is, who appear to have stage I disease). This is not in accordance with international recommendations This against the ESMO guidelines (Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ledermann JA, Raja FA, Fotopoulou C, Gonzalez-Martin A, Colombo N, Sessa C; ESMO Guidelines Working Group. Ann Oncol. 2013 Oct;24 Suppl 6:vi24-32. doi: 10.1093/annonc/mdt333). Also according to the single prospective randomized trial regarding this topic (sampling versus systematic/en bloc LND in early stage disease; Br J Cancer. 2006 Sep 18;95(6):699-704. Epub 2006 Aug 29. Randomised study of systematic lymphadenectomy in patients with epithelial ovarian cancer macroscopically confined to the pelvis. Maggioni A, Benedetti Panici P, Dell'Anna T, Landoni F, Lissoni A, Pellegrino A, Rossi RS, Chiari S, Campagnutta E, Greggi S, Angioli R, Manci N, Calcagno M, Scambia G, Fossati R, Floriani I, Torri V, Grassi R, Mangioni C.) showed that patients who underwent systematic LND had a significantly higher rate of positive lymph nodes at histologic examination than patients in the sampling only arm (9 vs 22%, P=0.007), meaning that 13% (!) of apparently early stage patients have missed occult stage III disease that is missed, if only LN- sampling is performed. This has immense impact on type and duration of adjuvant treatment. Additionally patients who are truly stage I after optimal staging (as indicated by the CG122 document itself 2 lines below) do not need chemotherapy if all LN are negative. If however we do not perform systematic/en bloc LND then staging is not optimal and so we have to treat patients with		review as it was published in 2006 and therefore was not in the search dates for the surveillance review, which searched for evidence published between 9 July 2012 to 1 June 2015. The trial was included in CG122. For more information please see 'section 4.1 The role of systematic retroperitoneal lymphadenectomy' in the full guideline. The ESMO guideline was not included in the surveillance review as surveillance reviews do not consider other guidelines only published primary studies and systematic reviews,

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			chemo where we could have omitted it.		
SH	British Gynaecological Cancer Society	Disagree	*1.3.2.2 Offer women with high-risk stage I disease (grade 3 or stage Ic) adjuvant chemotherapy consisting of six cycles of carboplatin.* There are no RCTs that suggest that single agent carbo is safe for stage 1 compared to carbo+paclitaxel. In the absence of such data treatment should the same as for advanced disease. It is a basic principle of oncology that for curative treatment, maximal therapy should be used until such time as trials show that less is as good a more. The paradigm here is testicular cancer. *Carbo+paclitaxel as first line. The guidance should be updated to include a statement saying that patients must be informed that over the last 20 years, all international RCTs including those performed in the UK by MRC and other national trials groups, have had carbo+paclitaxel as the control arm for fit patients.*		Thank you for your comment. No new evidence was identified in this area which impacted on current recommendations. For information about how the recommendation was reached in CG122 please see please see 'section 4.2 Adjuvant systemic chemotherapy for stage I disease' in the full guideline.
SH	British Gynaecological Cancer Society	Disagree	***1.4.1.1 Management of early (stage II-IV) ovarian cancer.*** This sentence does not make sense as stage III and IV are not early but advanced ovarian cancers		Thank you for your comment. This has now been amended to 'Management of advanced (stage II–IV) ovarian cancer'.
SH	British Gynaecological Cancer Society	Disagree	***1.5.1.1-2*** Bevacizumab is approved by the CDF (at a dose below the labelled dose as given in ICON7). Currently NICE cannot review the data that show a survival benefit for women with a poorer prognosis. Guidelines are weakened by the absence		Thank you for your comment. For NICE guidance on bevacizumab please refer to TA284. Bevacizumab in

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			of important information such as this. Point 4.4. that recommends a prospective study to happen in evaluating the LND in ovarian cancer This study has actually happened and is the LION trial, which randomized 650 patients in systematic versus NO LND. Results are anticipated 2018, so we will have the answer we need		combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer (2013) NICE technology appraisal guidance 285. TA285 does not recommend Bevacizumab for given with gemcitabine and carboplatin for treating adults with the first recurrence of platinum-sensitive advanced ovarian cancer (including fallopian tube or primary peritoneal cancer) that has not been previously treated with bevacizumab or other vascular endothelial growth factor inhibitors The NICE technology appraisal programme also terminated the following appraisal, due to no evidence submission: Bevacizumab for treating relapsed, platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal

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					cancer (terminated appraisal) (2015) NICE technology appraisal guidance 353 We have taken note of the ongoing LION trial for future surveillance reviews.
SH	International Ovarian Tumor Analysis trial	Disagree	Dear members of the National Institute for Health and Care Excellence, The International Ovarian Tumour Analysis group has serious concerns regarding the provisional decision to not update the **NICE guideline on CG122 Ovarian cancer: recognition and initial management** (in particular section 3.2: malignancy indices) as it does not include recent evidence from systematic reviews or validation studies. The guideline refers to the systematic review and meta-analysis by Geomini et al., where RMI I was outperforming other models in terms of sensitivity and specifity.[1] To endorse this, a rapid communication by Raza et al. is mentioned, reporting on a monocentric observational study with only 104 patients. With a questionable cut-off value of 450, RMI was found to have a sensitivity of 96.2% and a specificity of 98.7%.[2] We remark that in the analysis of this study, sensitivity and specificity were calculated for the detection of invasive epithelial ovarian cancer. In total eight borderline and non-epithelial tumours had RMI values below 450. However, since then more algorithms and validation studies were published. Recent evidence clearly shows that IOTA algorithms have better performance than the RMI. It is		Thank you for your comment. The search dates for the 4 year surveillance review were 9 July 2012 to 1 June 2015. A number of the studies provided in the comment are outside of the search dates for this surveillance review. For further information of NICE guidance and products that cover search dates prior to 9 July 2012, please see • Ovarian Cancer: NICE Evidence Update (January 2013). • the full guideline of CG122. Nunes 2014 was included in the decision matrix of the 4-year surveillance review of

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			disappointing that the guideline does not take into account the largest studies characterising ovarian masses in the literature. In a meta-analysis of Kaijser et al., comparing the ability of 19 methods to discriminate between benign and malignant adnexal masses before surgery, the IOTA Simple Rules and logistic regression model LR2 were superior to all other methods. The Simple Rules had a sensitivity of 93% and a specificity of 81% when classifying inconclusive tumours as malignant, LR2 had a sensitivity of 92% and a specificity of 83%, and RMI had a sensitivity of 72% and a specificity of 92%. In postmenopausal patients only, this meta-analysis found a sensitivity of 93% and a specificity of 76% for Simple Rules, a sensitivity of 94% and a specificity of 70% for LR2, and a sensitivity of 79% and a specificity of 90% for RMI.[3] On prospective validation both by the IOTA group (two studies including 1938 and 2403 patients, respectively)[4,5] and by other research teams (nine studies including a total of 2072 tumours)[6-14], the Simple Rules were applicable in 79% of tumours (range between studies, 77 to 94%). Sensitivity for pooled data was 94% (range, 79 to 97%), and specificity was 77% (range, 70 to 88%). The malignancy rate was 3.5% (range, 1% to 9%) in cases classified as benign, 87.5% (range, 69% to 94%) in cases classified as malignant, and 41.7% (range, 13% to 53%) in inconclusive cases. Head-to-head comparison studies of RMI and LR2 or Simple Rules consistently show superior performance of the IOTA methods. On external validation data from IOTA phase 2, LR2 had an AUC of 0.928 and RMI of 0.915 in postmenopausal patients (n=997)[15,16]. On IOTA phase 3 data, AUCs for postmenopausal patients were 0.897 for LR2 and 0.850 for RMI (n=1049)[5]. When an LR2-based triage		CG122. Some of the studies you refer to that are published within the search dates were not included for the following reasons: • not in English • the study type was not included in the protocol for the original guideline clinical question • there was no useable data in the abstract (eg. no analysis of results) • inappropriate comparisons or outcomes The studies you refer to which fit within the inclusion criteria and search dates have now been included in the decision matrix for the 4 year surveillance of CG122. The surveillance review decision has been amended to reflect that this section of the guideline should be

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			protocol was compared to the RMI-based triage protocol from the RCOG guideline on IOTA phase 2 data from postmenopausal patients, it was observed that the RCOG protocol classified 37% of benign tumours as low risk and 80% of invasive tumours as high risk (n=742)[17]. For the LR2-based protocol the corresponding figures were 42% and 93%, respectively. Timmerman et al. found a sensitivity of 93% and a specificity of 92% for Simple Rules in postmenopausal patients from IOTA phase 2 where Simple Rules gave a conclusive result. For RMI, 84% sensitivity and 91% specificity was obtained for the same patients.[4] In IOTA phase 3 data (pre- and postmenopausal patients, n=2403), RMI had a sensitivity of 67% and a specificity of 91%. When inconclusive patients were considered to be benign, Simple Rules on these data had a sensitivity of 69% and a specificity of 94%. These results suggest that evidence-based approaches to the preoperative characterisation of adnexal masses should incorporate the use of Simple Rules or the LR2 model. In addition several external validation studies have now shown that the Simple Rules keep their performance even in the hands of less experienced ultrasound examiners.[7,8,9,11-14] In a further independent meta-analysis on the simple rules the pooled sensitivity when rules were applicable was 93% and specificity 95%, based on a total of 3568 patients.[18] We hope that given this evidence, the NICE guideline on establishing the diagnosis of ovarian cancer in secondary care (the section on malignancy indices in particular) can undergo the appropriate updating. **References:**		updated.

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			1. Geomini P, Kruitwagen R, Bremer GL, Cnossen J, Mol BWJ. The accuracy of risk scores in predicting ovarian malignancy – a systematic review. *Obstet Gynecol* 2009; **113**: 384–394. 2. Raza A, Mould T, Wilson M, Burnell M, Bernhardt L. Increasing the effectiveness of referral of ovarian masses from cancer unit to cancer center by using a higher referral value of the risk of malignancy index. Int J Gynecol Cancer 20(4):552-4, 2010 3. Kaijser J, Sayasneh A, Van hoorde K, et al: Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: A systematic review and meta-analysis. Hum Reprod Update 20(3):449-462, 2014 4. Timmerman D, Ameye L, Fischerova D, et al: Simple ultrasound rules to distinguish between benign and malignant adnexal masses before surgery: prospective validation by IOTA group. BMJ 341:c6839, 2010 5. Testa AC, Kaijser J, Wynants L, et al: Strategies to diagnose ovarian cancer: new evidence from phase 3 of the multicentre international IOTA study. Br J Cancer 111(4):680-688, 2014 6. Fathallah K, Huchon C, Bats AS, et al: Validation externe des critères de Timmerman sur une série de 122 tumeurs ovariennes. Gynecol Obstet Fertil 39(9):477-481, 2011 7. Hartman CA, Juliato CRT, Sarian LO, et al: Ultrasound criteria and CA 125 as predictive variables of ovarian cancer in women with adnexal tumors. Ultrasound Obstet Gynecol 40(3):360-366, 2012		

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			8. Alcázar JL, Pascual MÁ, Olartecoechea B, et al: IOTA simple rules for discriminating between benign and malignant adnexal masses: Prospective external validation. Ultrasound Obstet Gynecol 42(4):467-471, 2013 9. Sayasneh A, Wynants L, Preisler J, et al: Multicentre external validation of IOTA prediction models and RMI by operators with varied training. Br J Cancer 108(12):2448-2454, 2013 10. Tantipalakorn C, Wanapirak C, Khunamornpong S, et al: IOTA Simple Rules in Differentiating between Benign and Malignant Ovarian Tumors. Asian Pacific J Cancer Prev 15:5123-5126, 2014 11. Nunes N, Ambler G, Foo X, et al: Use of IOTA simple rules for diagnosis of ovarian cancer: meta-analysis. Ultrasound Obstet Gynecol 44(5):503-514, 2014 12. Tinnangwattana D, Vichak-ururote L, Tontivuthikul P, et al: IOTA Simple Rules in Differentiating between Benign and Malignant Adnexal Masses by Non-expert Examiners. Asian Pacific J Cancer Prev 16:3835-3838, 2015 13. Ruiz de Gauna B, Rodriguez D, Olartecoechea B, et al: Diagnostic performance of IOTA simple rules for adnexal masses classification: a comparison between two centers with different ovarian cancer prevalence. Eur J Obstet Gynecol Reprod Biol 191:10-14, 2015 14. Knafel A, Banas T, Nocun A et al: The Prospective External Validation of International Ovarian Tumor Analysis (IOTA) Simple Rules in the Hands of Level I and II Examiners. Ultraschall Med 10.1055/s-0034-		

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			1398773 15. Van Holsbeke C, Van Calster B, Bourne T, Ajossa S, Testa AC, Guerriero S, Fruscio R, Lissoni AA, Czekierdowski A, Savelli L, Van Huffel S, Valentin L, Timmerman D. External validation of diagnostic models to estimate the risk of malignancy in adnexal masses. Clin Cancer Res 18(3):815-825, 2012 16. Timmerman D, Van Calster B, Testa AC, Guerriero S, Fischerova D, Lissoni AA, Van Holsbeke C, Fruscio R, Czekierdowski A, Jurkovic D, Savelli L, Vergote I, Bourne T, Van Huffel S, Valentin L. Ovarian cancer prediction in adnexal masses using ultrasound-based logistic regression models: a temporal and external validation study by the IOTA group. Ultrasound Obstet Gynecol 36:226–234, 2010 17. Van Calster B, Timmerman D, Valentin L, McIndoe A, Ghaem- Maghami S, Testa AC, Vergote I, Bourne T. Triaging women with ovarian masses for surgery: observational diagnostic study to compare RCOG guidelines with an International Ovarian Tumour Analysis (IOTA) group protocol. BJOG 119:662–671, 2012 18. Nunes N, Ambler G, Foo X, et al. Use of IOTA Simple Rules for diagnosis of ovarian cancer: meta-analysis. Ultrasound Obstet Gynecol 44: 503-14, 2014		
SH	Target Ovarian Cancer	Agree			Thank you for your comment.
SH	Ovarian Cancer	Disagree	Ovarian Cancer Action believe that the decision not to revise		Thank you for your

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	Action		the NICE guideline on CG122 Ovarian cancer: recognition and initial management is misguided. This guideline has not been reviewed for four years which, is not only inappropriate, but also demonstrates that ovarian cancer is not being given the attention it deserves. Particularly in light of Dame Sally Davies' recent call for a national audit of ovarian cancer surgery, we believe that more focus must be given to ovarian cancer to improve best practice in treating the disease. The following are specific examples Ovarian Cancer Action has identified as to why the guidelines needs updating:		comment. A 4 year surveillance review was carried out on this guideline, which informed the consultation on the proposed decision to not update this guideline. This consultation is on the 4 year surveillance review of the guideline. An NICE Evidence Update was also published in 2013. Please see Ovarian Cancer: NICE Evidence Update (January 2013). NICE is committed to keeping guidelines current. A formal check of the need to update a guideline is usually undertaken by NICE every 2 years, and is always undertaken at least every 4 years from the date of guideline publication. For more information please refer to 'Developing NICE guideline: the manual. Chapter 13 Ensuring that published guidelines are current and accurate.' Following stakeholder consultation the surveillance

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					review decision has been amended to reflect that the section on serum tumour marker tests of the guideline should be updated.
			1. Section 1.1.2 – Asking the right question – There is a significant importance of family history in Ovarian Cancer. We recommend an addition to the guidelines that questions regarding family history of breast and ovarian cancer are asked by the treating physician.		Thank you for your comment. The scope of CG122 excludes 'Surveillance of high-risk groups, including women with a family history of ovarian cancer'. At the 4 year surveillance point NICE asked topic experts if they felt the exclusion in the scope were still justified and the majority of topic experts that responded felt that they were. NICE also asked if there was any uncertainty in areas outside of the scope. The majority of topic experts that responded said there were none. The area you refer to was not raised in the responses. The surveillance review did not identify any new evidence in this area. Following stakeholder feedback the surveillance review decision has been

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					amended to reflect a new review question on risk factors should be added.
			2. Section 1.4.2 - Intraperitoneal chemotherapy - There should be an emphasis that IP trials have been associated with significantly longer overall survival and progression free survival, however issues and discrepancies in dosage and scheduling as well as higher toxicity have prevented IP chemo to be established in advanced disease. Further studies with comparable dosage to intravenous regimes and intravenous targeted treatments are warranted to establish value.		Thank you for your comment. The surveillance review makes reference to identified evidence and guideline impacts for intraperitoneal chemotherapy under the clinical question 'For women with ovarian cancer, is intra-peritoneal chemotherapy effective in primary management?'. However the identified evidence did not impact on the current guideline recommendations. For further information on the recommendations in CG122 please see 'section 5.2 Intraperitoneal chemotherapy' in the full guideline.
			3. The guidelines conflict with European Society for Medical Oncology (ESMO) guidelines. The statement "Do not include systematic retroperitoneal lymphadenectomy (block dissection of lymph nodes from the pelvic side walls to the level of the renal veins) as part of standard surgical treatment in women with suspected ovarian cancer whose disease appears to be confined to the ovaries (that is, who		Thank you for your comment. New evidence was not identified in this area in the 4 year surveillance review for CG122. For further information on the recommendations in CG122

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			appear to have stage I disease)" is against the ESMO guidelines (Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up).		please see 'section 4.1 The role of systematic retroperitoneal lymphadenectomy' in the full guideline.
			4. The guidelines are out of date. Point 4.4 recommends a prospective study to happen in evaluating the lymph node dissection (LND) in ovarian cancer. This study has actually happened and is the Lymphadenectomy in Ovarian Neoplasms (LION) trial, which randomized 650 patients in systematic versus NO LND. Additionally the statement "No studies have evaluated whether primary surgery itself has any therapeutic value when compared with chemotherapy alone" is incorrect. The collaborative European Organisation for Research and Treatment of Cancer (EORTC) and Gynecologic Oncology Group (GOG) effort initiated already in the 1990s a randomized phase 3 study to establish the effect on survival of debulking surgery. 140 patients were assigned to undergo debulking surgery and 138 were assigned not to undergo surgery. Debulking surgery significantly lengthened progression-free and overall survival. The risk of death was reduced by one third, after adjustment for a variety of prognostic factors.		Thank you for your comment. The statement you refer to is from CG122 and not from the 4-year surveillance review of CG122. This consultation is on the 4 year surveillance review of the guideline. The studies you refer to are from the 1990's. Therefore this is outside of the remit of the 4 year surveillance review of CG122, which searched for evidence published between 9 July 2012 to 1 June 2015. The LION trial is an ongoing trial and we have taken note of this for future surveillance reviews.
			In summary, we believe that if the guidelines are not revised, NICE will miss an opportunity to target hereditary cancers and clarify discrepancies around Intraperitoneal chemotherapy. We also believe that the guidelines are now outdated, and conflict with ESMO guidelines. We recommend that the NICE guideline on CG122 Ovarian cancer: recognition and initial management is reviewed, not		Thank you for your comment. The scope of CG122 excludes 'Surveillance of high-risk groups, including women with a family history of ovarian cancer'. At the 4

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			just to address these specific concerns, but to show a commitment to best practice in treatment for this disease. If the guidelines are not revised now, we would ask when they will be? If it is another year hence, another 4,300 women in the UK will have been diagnosed with ovarian cancer who could benefit from improved guidelines.		year surveillance point we asked topic experts if they felt the exclusion in the scope were still justified and the majority of topic experts that responded felt that they were. We also asked if there was any uncertainty in areas outside of the scope. The majority of topic experts that responded said there were none. The area you refer to was not raised in the responses. Following stakeholder feedback the surveillance review decision has been amended to reflect a new review question on risk markers should be added. A 4 year surveillance review was carried out on this guideline, which informed the consultation on the proposed decision to not update this guideline. NICE is committed to keeping guidelines current. A formal check of the need to update a guideline is usually undertaken by NICE every 2 years, and is always

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					undertaken at least every 4 years from the date of guideline publication. For more information please refer to 'Developing NICE guideline: the manual. Chapter 13 Ensuring that published guidelines are current and accurate.' Following stakeholder consultation the surveillance review decision has been amended to reflect that the section on serum marker tests of the guideline should be updated.
SH	FUJIREBIO DIAGNOSTICS	Disagree	Human Epididymis 4 gene WFDC2 (HE4) could potentially contribute for improving clinical setting in the recognition of ovarian cancer. *Enclosed in Annex, a list of published articles* An update of - Chapter 2: detection in primary care / First tests - Chapter 3: Establishing the diagnosis in secondary care / Tumour markers		Thank you for your comment. The search dates for the 4 year surveillance review were 9 July 2012 to 1 June 2015. A number of the studies you have provided are outside of the search dates for this surveillance review. For further information on NICE guidance and products that cover search dates prior to 9 July 2012, please see • Ovarian Cancer: NICE Evidence

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					Update (January 2013). • the full guideline of CG122. Some of the studies you refer to that are published within the search dates were not included for the following reasons: • not in English • the study type was not included in the protocol for the original guideline clinical question • there was no useable data in the abstract (eg. no analysis of results) • inappropriate comparisons or outcomes The studies you refer to which fit within the inclusion criteria and search dates have now been included in the decision matrix for the 4 year surveillance of CG122.

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					The surveillance review decision has been amended to reflect that this section of the guideline should be updated.

Type	Stakeholder	Do you agree with the proposal to remove the research recommendation?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
SH	British Gynaecological Cancer Society	Agree			Thank you for your comment. We have decided that at this current point in time we will not remove the research recommendation 'A prospective randomised trial should be undertaken to evaluate the therapeutic effect, associated risks and cost effectiveness of systematic retroperitoneal lymphadenectomy in women with ovarian cancer whose disease appears to be confined to the ovaries.'
SH	Target Ovarian Cancer	Agree			Thank you for your comment. We have decided that at this current point in time we will not remove the research

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					recommendation 'A prospective randomised trial should be undertaken to evaluate the therapeutic effect, associated risks and cost effectiveness of systematic retroperitoneal lymphadenectomy in women with ovarian cancer whose disease appears to be confined to the ovaries.'
SH	The Society and College of Radiographers	Agree		In section 4.3 it recommends further case control studies to examine the effectiveness of MRI and CT in women with suspected ovarian cancer. A short search of the literature indicates that there are still limited publications (2010-2015 date range) that could be considered to measure effectiveness. A systematic review (see below) which evaluates or the role of MRI and IV gadolinium in differentiating between malignant and benign adnexal masses is of note. Gynecol Oncol. 2014 Mar;132(3):661-8. doi: 10.1016/j.ygyno.2013.10.022. Epub 2013 Oct 29. • **Pelvic MRI as the "gold standard" in the subsequent evaluation of ultrasound-indeterminate adnexal lesions: a systematic review.** Anthoulakis C[1], Nikoloudis N[2].	Thank you for your comment. We will keep the research recommendation: 'Large multicentre case–control studies should be conducted to compare the accuracy of CT versus MRI for staging and for predicting optimal cytoreduction in women with ovarian cancer.' The study you refer to has not been included due to no reporting of the analysis of the results in the abstract. It is outside of the remit of the surveillance review process to add additional research recommendations.

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				Therefore The Society and College of Radiographers agrees that the NICE guidance for imaging does not require an update (section 1.2.3) and we would agree that further research as stated in section 4.3 still remains. It maybe be worthwhile adding to section 4.3 a recommendation for further research in the role of whole body MRI and DWI in the staging of ovarian cancer. This technique is being developed for other oncology presentations.	
SH	Ovarian Cancer Action	Disagree		Reasons and impacts on women with ovarian cancer/at risk of ovarian cancer as above.	Thank you for your comment. We have decided that at this current point in time we will not remove the research recommendation 'A prospective randomised trial should be undertaken to evaluate the therapeutic effect, associated risks and cost effectiveness of systematic retroperitoneal lymphadenectomy in women with ovarian cancer whose disease appears to be confined to the ovaries.'
SH	FUJIREBIO DIAGNOSTICS	Disagree		4.1 Relationship between duration of symptoms of ovarian cancer and stage at diagnosis Particularly, this item. This understanding is missing to improve the earlier diagnosis in women with ovarian cancer.	Thank you for your comment. We have decided that at this current point in time we will not remove the research recommendation 'A prospective randomised trial should be undertaken to evaluate the therapeutic effect, associated risks and cost effectiveness of systematic retroperitoneal lymphadenectomy in women with ovarian cancer whose disease appears to be confined to the ovaries.'

The following organisations were approached but did not respond:

- 5 Boroughs Partnership NHS Foundation Trust
- A Little Wish
- Abbott GmbH & Co KG
- AbbVie
- Action Cancer - NI
- African Health Policy Network
- Airedale NHS Trust
- Allocate Software PLC
- Almac Diagnostics
- Amgen UK
- Association for Family Therapy and Systemic Practice in the UK
- Association for Palliative Medicine of Great Britain
- Association of Anaesthetists of Great Britain and Ireland
- Association of British Healthcare Industries
- Association of British Insurers
- Association of Cancer Physicians
- Association of Chartered Physiotherapists in Oncology and Palliative Care
- Association of Clinical Pathologists
- Association of Genetic Nurses and Counsellors
- Association of the British Pharmaceutical Industry
- Astrazeneca UK Ltd

- Barnsley Hospital NHS Foundation Trust
- Baxter Healthcare
- Beckman Coulter
- Belfast Health and Social Care Trust
- Betsi Cadwaladr University Health Board
- Birmingham Women’s NHS Foundation Trust
- Birmingham Women's Health Care NHS Trust
- BME cancer.communities
- Boehringer Ingelheim
- Boehringer Ingelheim Ltd
- Boots
- Bradford District Care Trust
- Breast Cancer UK
- Brighton and Sussex University Hospital NHS Trust
- Bristol and Avon Chinese Women's Group
- British Association for Cytopathology
- British Dietetic Association
- British Medical Association
- British Medical Journal
- British National Formulary
- British Nuclear Cardiology Society
- British Nuclear Medicine Society
- British Pain Society

- British Psychological Society
- British Red Cross
- British Society for Clinical Cytology
- British Society for Human Genetics
- British Society for Immunology
- British Society of Urogynaecological Radiology
- BUPA Foundation
- Calderstones Partnerships NHS Foundation Trust
- Cambridge University Hospitals NHS Foundation Trust
- Camden Link
- Cancer Research UK
- Cancer Services Co-ordinating Group
- Cancer Voices
- Cancer52
- Capsulation PPS
- Capsulation PPS
- Care Quality Commission
- Celgene UK Ltd
- Central Manchester and Manchester Children's Hospital NHS Trust
- Chadderton Health Centre
- Chartered Society of Physiotherapy
- Cheshire and Merseyside SCN
- Children, Young People and Families NHS Network

- Clarity Informatics Ltd
- CLIC Sargent
- College of Occupational Therapists
- College of Paramedics
- Community District Nurses Association
- Cook Medical Inc.
- County Durham and Darlington NHS Foundation Trust
- Covidien Ltd.
- Croydon Clinical Commissioning Group
- Croydon Health Services NHS Trust
- Croydon University Hospital
- Daiichi Sankyo UK
- Deltex Medical
- Department for Communities and Local Government
- Department of Health
- Department of Health, Social Services and Public Safety - Northern Ireland
- Derbyshire Mental Health Services NHS Trust
- DNU Health Protection Agency
- Dudley PACT Patient Advisory Cancer Team
- DUPLICATE - SEE: Public Health Wales
- East and North Hertfordshire NHS Trust
- East Kent Hospitals University NHS Foundation Trust
- East Lancashire Hospitals NHS Trust

- East of England Strategic Clinical Network
- Economic and Social Research Council
- Eisai Ltd
- Energy Therapy World-Wide Net
- Equalities National Council
- Ethical Medicines Industry Group
- Eusapharma
- Facing Our Risk of Cancer Empowered
- Faculty of Sexual and Reproductive Healthcare
- Five Boroughs Partnership NHS Trust
- FTWW
- GE Healthcare
- Genetic Alliance UK
- George Eliot Hospital NHS Trust
- GlaxoSmithKline
- Gloucestershire Hospitals NHS Foundation Trust
- Gloucestershire LINk
- Great Western Hospitals NHS Foundation Trust
- Greater Manchester and Cheshire Cardiac and Stroke Network
- Grunenthal Ltd
- Guerbet Laboratories Ltd
- Guy's and St Thomas' NHS Foundation Trust
- Harrogate and District NHS Foundation Trust

- Health and Care Professions Council
- Health and Social Care Information Centre
- Healthcare Improvement Scotland
- Healthcare Quality Improvement Partnership
- Herts Valleys Clinical Commissioning Group
- Hindu Council UK
- Hockley Medical Practice
- Hospira UK Limited
- Human Fertilisation Embryology Authority
- Humber NHS Foundation Trust
- Hysterectomy Association
- Imaging Equipment Ltd
- Independent Cancer Patients' Voice
- Independent Healthcare Advisory Services
- Institute for Womens Health
- Institute of Biomedical Science
- Integrity Care Services Ltd.
- James Cook University Hospital
- Janssen
- Johnson & Johnson
- Joint Collegiate Council for Oncology
- KCARE
- Kidney Cancer Support Network

- King's College Hospital NHS Foundation Trust
- Lancashire Care NHS Foundation Trust
- Lancashire Teaching Hospitals NHS Trust
- Leeds Teaching Hospitals NHS Trust
- Liverpool Community Health
- London Cancer
- London cancer alliance
- Lothian University Hospitals Trust
- Luton and Dunstable Hospital NHS Trust
- Lymphoedema support network
- Macmillan Cancer Support
- Manchester Cancer
- Mastercall Healthcare
- Medicines and Healthcare Products Regulatory Agency
- Merck Sharp & Dohme UK Ltd
- Mid Yorkshire Hospitals NHS Trust
- Middlesex University
- Milton Keynes Hospital NHS Foundation Trust
- Milton Keynes NHS Foundation
- Ministry of Defence
- MRC Clinical Trials Unit
- MSD Ltd
- National Association of Primary Care

- National Cancer Action Team
- National Cancer Intelligence Network
- National Cancer Research Institute
- National Clinical Guideline Centre
- National Collaborating Centre for Cancer
- National Collaborating Centre for Mental Health
- National Collaborating Centre for Women's and Children's Health
- National Council for Palliative Care
- National Council of Women Great Britain
- National Deaf Children's Society
- National Forum of Gynaecological Oncology Nurses
- National Institute for Health Research
- National Institute for Health Research Health Technology Assessment Programme
- National Patient Safety Agency
- National Public Health Service for Wales
- National Radiotherapy Implementation Group
- NCRI - Breast CSG Working Group on Symptom Management
- Newcastle upon Tyne Hospitals NHS Foundation Trust
- NHS Barnsley Clinical Commissioning Group
- NHS Choices
- NHS Clinical Knowledge Summaries
- NHS County Durham and Darlington
- NHS England

- NHS Health at Work
- NHS Kirklees
- NHS National Programmes
- NHS North East Lincolnshire CCG
- NHS Plus
- NHS Sheffield
- NHS Somerset CCG
- NHS South Cheshire CCG
- NHS Wakefield CCG
- NHS Warwickshire North CCG
- NHSCC
- Nordion
- North and East London Commissioning Support Unit
- North of England Commissioning Support
- North Tees and Hartlepool NHS Foundation Trust
- Northern Health and Social Care Trust
- Northumbria Healthcare NHS Foundation Trust
- Nottingham City Council
- Nottingham City Hospital
- Novartis Pharmaceuticals
- Novo Nordisk Ltd
- Nursing and Midwifery Council
- Nutricia Advanced Medical Nutrition

- Ocean Process A/S
- Ovacome
- Oxford Health NHS Foundation Trust
- Oxfordshire Clinical Commissioning Group
- Parenteral and Enteral Nutrition Group
- Pelvic Pain Support Network
- PERIGON Healthcare Ltd
- Peterborough and Stamford Hospitals NHS Foundation Trust
- Pfizer
- PharmaMar
- Pharmametrics GmbH
- Pilgrims Hospices in East Kent
- Primary Care Pharmacists Association
- Primary Care Women's Health Forum
- Primrose Bank Medical Centre
- Pseudomyxoma Survivor
- Public Health England
- Queen Elizabeth Hospital King's Lynn NHS Trust
- Randox Laboratories Limited
- Rarer Cancers Foundation
- Roche Diagnostics
- Roche Products
- Roy Castle Lung Cancer Foundation

- Royal Berkshire NHS Foundation Trust
- Royal College of Anaesthetists
- Royal College of Emergency Medicine
- Royal College of General Practitioners
- Royal College of General Practitioners in Wales
- Royal College of Midwives
- Royal College of Nursing
- Royal College of Obstetricians and Gynaecologists
- Royal College of Paediatrics and Child Health
- Royal College of Pathologists
- Royal College of Physicians
- Royal College of Physicians and Surgeons of Glasgow
- Royal College of Psychiatrists
- Royal College of Psychiatrists in Scotland
- Royal College of Radiologists
- Royal College of Speech and Language Therapists
- Royal College of Surgeons of England
- Royal Cornwall Hospitals NHS Trust
- Royal Devon and Exeter NHS Foundation Trust
- Royal Pharmaceutical Society
- Royal Society of Medicine
- Royal Surrey County Hospital NHS Trust
- Sandoz Ltd

- Sanofi
- Scottish Clinical Biochemistry Managed Diagnostic Network
- Scottish Intercollegiate Guidelines Network
- Sheffield Teaching Hospitals NHS Foundation Trust
- Shropshire & Mid Wales Cancer Forum
- SNDRi
- Social Care Institute for Excellence
- Society for the Protection of Unborn Children
- South Asian Health Foundation
- South Eastern Health and Social Care Trust
- South London & Maudsley NHSFT
- South Tees Hospitals NHS Trust
- South Wales Cancer Network
- South West Thames Regional Genetics Service
- South West Yorkshire Partnership NHS Foundation Trust
- Southend Hospitals NHS Foundation Trust
- Southern Health & Social Care Trust
- Southport and Ormskirk Hospital NHS Trust
- St Mary's Hospital
- Staffordshire and Stoke on Trent Partnership NHS Trust
- Step4Ward Adult Mental Health
- Stockport Clinical Commissioning Group
- Teenage Cancer Trust

- Teenagers and Young Adults with Cancer
- Teva UK
- The British Association of Gynaecological Pathologists
- The British In Vitro Diagnostics Association
- The Eve Appeal
- The Institute of Cancer Research
- The National LGB&T Partnership
- The Patients Association
- The Rotherham NHS Foundation Trust
- The Surrey Park Clinic
- The University of Birmingham
- UCL Partners
- UCL/UCLH Institute for Women's Health
- UK Clinical Pharmacy Association
- UK National Screening Committee
- UK NSC
- United Kingdom National External Quality Assessment Service
- United Lincolnshire Hospitals NHS
- University Hospital Birmingham NHS Foundation Trust
- University Hospitals Birmingham
- University of Nottingham
- Walsall Local Involvement Network
- WellBeing of Women

- Welsh Cancer Services Coordinating Group
- Welsh Government
- Welsh Scientific Advisory Committee
- Western Health and Social Care Trust
- Western Sussex Hospitals NHS Trust
- Whitehouse Consultancy
- Wirral University Teaching Hospital NHS Foundation Trust
- Women’s Support Network
- Women's Health Alliance
- Wrightington, Wigan and Leigh NHS Foundation Trust
- York Hospitals NHS Foundation Trust