Pan Birmingham NHS
Cancer Network

Guideline for the Assessment, Management and Referral of Patients with Suspected Ovarian Cancer

Version History

Version	Date	Summary of Change/Process
2.0	February 2008	Endorsed by the Governance Committee
2.1	November 2010	Circulated at NSSG meeting
2.2	July 2011	Reviewed and updated by Suhail Anwar
2.3	July 2011	Reformatted by Lara Barnish
2.4	August 2011	Reviewed and updated by Suhail Anwar
2.5	August 2011	Reviewed and commented upon by members of the Gynae Network Site Specific Group
2.6	September 2011	With Lara Barnish comments
2.7	October 2011	Following discussion between Suhail Anwar and Lara Barnish
2.8	October 2011	Following review by Suhail Anwar and circulated to the Gynae NSSG for comment
2.9	November 2011	Following consultation with the NSSG – with comments from Raji Ganesan and Tony Head
2.10	November 2011	Reviewed and updated by Network Guidelines Sub Group
2.11	22.11.11	With changes by Suhail Anwar following the Network Guidelines Sub Group
3.0	24.11.11	Endorsed by Network Guidelines Sub Group

Date Approved by Network Governance	**November 2011**

Date for Review	**November 2014**

Changes Made During Review in 2011

- NICE Clinical Guideline 122 was published in April 2011 which updates and replaces recommendation 1.7.4 in referral guidelines for suspected cancer specifically in relation to referral from primary care see section 3.1 (NICE CG 27; Published 2005).

- This emphasises the need for assessment and early investigation of symptoms compatible with diagnosis of ovarian cancer in primary care with the use of CA-125 measurement and pelvic\abdominal ultrasound especially in women above the age of 50. This is likely to increase the number of referrals of suspected ovarian cancer to secondary care.

- The guideline recommends no chemotherapy for optimally staged grades 1 and\or 2, Figo stages 1a and 1b epithelial ovarian cancers. It recommends discussion in multi disciplinary team (MDT) meeting and with the patient regarding chemotherapy in suboptimally staged early ovarian cancers. Patients with stage 1c or grade 3 should be offered 6 cycles of carboplatin.

1 Scope of the Guideline

This guidance has been produced to support the following:

- the procedures required when making a diagnosis of ovarian cancer.
- the preferred place of treatment for patients diagnosed with ovarian cancer.
- the procedures that should take place in the event that a patient is diagnosed with ovarian cancer following an emergency admission.
- the referral of patients for assessment where genetic risk is to be considered.

2 Guideline Background

2.1 All Trusts undertaking gynaecological surgery in the Pan Birmingham Cancer Network are recognised as cancer units. Sandwell and West Birmingham Hospitals NHS Trust (City Hospital site) is the recognised the Gynaecological Cancer Centre.

2.2 All patients with a CA125 > 250 in pre menopausal, an RMI >250 in postmenopausal women and those patients whose imaging would suggest a malignant process should be discussed at the cancer centre specialist multi disciplinary team (SMDT) *before* their definitive management is started. All other patients with a diagnosis of ovarian cancer are discussed at the SMDT once surgery has been performed.

2.3 Work is in progress by the NICE topic expert team to provide guidance on additional issues such as bevacizumab in combination with paclitaxel and carboplatin which are undergoing NICE technology appraisal at the moment. Publication date to be confirmed.

Guideline Statements

3 Referral (please see appendix 3)

3.1 <u>2 week wait referrals</u>

3.1.1 The following patients should be referred using the 2 week wait pathway:

i. Women reporting having any of the following symptoms persistently or frequently – particularly more than 12 times per month (especially if they are 50 or over):

a) persistent abdominal distension (‘bloating’).
b) feeling full (early satiety) and/or loss of appetite.
c) pelvic or abdominal pain.

d) increased urinary urgency and/or frequency.

ii. Women aged 50 or over with symptoms within the last 12 months that suggest irritable bowel syndrome.

3.1.2 All patients suspected of ovarian cancer should be referred to their local gynaecological unit using the 2 week wait form (see appendix 1).

3.2 Emergency referral

3.2.1 The following patients should be referred to the SMDT as an emergency:

a. patients presenting as an emergency; and have suspected ovarian cancer.
b. incidental unexpected findings compatible with ovarian or primary peritoneal cancers during planned or emergency pelvic surgery.

3.2.2 Where cancer is suspected the patients should be transferred to City Hospital before surgery where it is safe to do so.

3.2.3 In the unusual situation that a patient suspected of having ovarian cancer requires emergency surgery out of hours then the on call gynaecological oncologist for the Pan Birmingham Cancer Network (at City Hospital) should be contacted with a view to a joint procedure. This is done via City Hospital switchboard on 0121 507 4000.

3.2.4 Any patient diagnosed incidentally via these routes should be referred to the SMDT at City Hospital within 1 working day of the diagnosis. All should be discussed at the SMDT.

3.3 Other referrals

All patients with ovarian cancers and those with suspected ovarian cancer (and a risk of malignancy index (RMI) of more than 250) should be referred to the specialist gynaecological oncologist urgently. See appendix 2 for more information on RMI.

3.4 Referral for family history assessment

3.4.1 Individuals (affected or unaffected with cancer) who meet the guidelines below, should be referred to the West Midlands Regional Clinical Genetics Unit, Birmingham Women's Hospital for risk assessment.

Ovarian Cancer	○ Two or more cases of ovarian cancer in first degree relatives.
Breast AND Ovarian Cancer	○ One ovarian cancer and at least one breast cancer diagnosed below 50yrs in first degree relatives.

	○ One ovarian cancer and two breast cancers at 60 or below in first degree relatives.
Other cancers	○ One ovarian cancer and three colorectal cancers with one cancer being diagnosed below the age of 50yrs. ○ Three or more close relatives, with other gastrointestinal, renal, urinary tract, uterine or ovarian cancer at any age. ○ Three or more relatives with a combination of cancers of breast, ovary, prostate, pancreas, melanoma or thyroid. ○ A known mutation in a predisposing gene.

3.4.2 Individuals who are requesting risk-reducing surgery should also be referred for risk assessment.

3.4.3 Individuals with an Eastern European/Jewish origin who do not meet the above criteria could still be considered because of their increased risk of BRCA1 and BRCA2 mutation.

3.4.4 The individuals will be assessed and managed using the West Midlands Family Cancer Strategy guidelines. Further details about the strategy are available at http://www.bwhct.nhs.uk/genetics-index/genetics-wmrcgs-howrefer.htm. Taking part in population surveillance programmes is recommended and healthy lifestyle information can also be provided.

4 Assessment

4.1 All patients irrespective of their source of referral should undergo the following assessment:

a. clinical history including menopausal status and family history.
b. clinical examination.
c. trans-vaginal ultrasound is appropriate in most cases. Trans-abdominal scan is required to assess larger pelvic masses and distant spread to the upper abdomen.
d. CA125 should be used to calculate the RMI.
e. CA19.9, CA15.3 and CEA may be indicated in some patients but should not be routine because of their poor specificity.
f. women below the age of 40 should have HCG, AFP and LDH checked in addition to CA125.
g. CT scan of abdomen and pelvis to assess patients with suspected metastatic disease in the abdomen and pelvis.
h. there is no evidence to support the routine use of colour Doppler in isolation.
i. all patients having surgery should have a chest x-ray. A CT scan of the thorax should only be undertaken if this is clinically indicated, or the chest x-ray is abnormal i.e. should not be routine.

4.2 For those patients with adnexal cysts, there should be standardised reporting of the morphology of these cysts in order for the clinician to determine the RMI.

4.3 There is no evidence to support the routine use of or CT, MRI or PET scanning[6] in early disease. However, all of these modalities have value in some patients. If extra pelvic disease is suspected then a CT will be considered in the first place. Decisions regarding imaging should be based on the results of clinical findings, the initial USS and CA125 marker. The results should be discussed at the multi disciplinary team (MDT) meeting.

4.4 It is expected that the primary care teams would adopt NICE guidelines[11] for the early detection of suspected ovarian cancer.

4.5 Clinical Guidance CG122[11] (http://www.nice.org.uk/nicemedia/live/13464/54268/54268.pdf) has suggested a pathway to be followed in primary care which is outlined in appendix 3.

5 Definitive diagnosis and staging

5.1 Diagnosis and staging is achieved through surgery (laparotomy) and histology of the tissue removed.

5.2 Methods of tissue diagnosis other than laparotomy:

5.2.1 Other methods of tissue diagnosis are likely to be used where neo-adjuvant chemotherapy is being considered. (Please see Guideline for the Medical Management of Gynae Cancers with Chemotherapy)

5.2.2 Where surgery has not been performed, histology rather than cytology should be used to obtain a tissue diagnosis. To obtain tissue for histology, percutaneous image-guided biopsy should be used if this is feasible. Laparoscopic biopsy should be considered if percutaneous image-guided biopsy is not feasible or has not produced an adequate sample. Histology should always be sought where feasible.

5.3 Cytology should be used if histology is not appropriate.

5.4 If histology or cytology is not available prior to chemotherapy this should be discussed in the SMDT meeting and with the patient outlining risks and benefits[11].

5.5 All patients

Risk should be assessed as high, medium or low according to the RMI

All patients should then be identified as one of the following:

a) low risk RMI <25 (may have surgery by any gynaecologist in the unit).
b) medium risk RMI 25 – 250 (should have surgery by the designated gynae oncologist within the unit or be referred to the centre).
c) high risk RMI >250 (should be referred to the cancer centre for surgery, or following local agreement, managed by the designated gynae-oncologist within the cancer unit).

5.5.1 All initial assessment and diagnostic tests should be carried out at the patient's local hospital.

5.5.2 All patients from units diagnosed with ovarian cancer should have their management discussed/agreed at the SMDT meeting. All patients with a CA125 > 250 in pre menopausal, an RMI >250 in postmenopausal women and those patients whose imaging would suggest a malignant process should be discussed at the cancer centre specialist multi disciplinary team (SMDT) *before* their definitive management is started. All other patients with a diagnosis of ovarian cancer are discussed at the SMDT once surgery has been performed.

5.5.3 If the pre-operative assessment finds the patients to be in the high-risk group then the SMDT discussion should be **PRIOR** to surgery, in order that neo-adjuvant chemotherapy can be discussed.

5.5.4 All medium and high risk patients will have their surgery carried out at the gynaecological cancer centre. See appendix 4.

5.5.5 All patients classed as low risk should have their initial surgery/be managed conservatively at their local hospital by a designated gynaecologist. If diagnosed with ovarian cancer these patients should be discussed at the SMDT meeting at the centre; from where future treatment will be co-ordinated.

5.5.6 Patients identified as being moderate or high risk should be considered for an available clinical trial.

5.5.7 The site of chemotherapy should follow the existing routes of treatment, that is:

- For treatment (under the care of a medical/clinical [gynae] oncologist) at City Hospital patients travel from the following Hospitals:
  - City Hospital
  - Birmingham Women's Hospital

- Patients from Heartlands Hospital, Good Hope Hospital, Solihull Hospital, Walsall Hospital, and Sandwell Hospital will have their chemotherapy delivered locally.

5.5.8 Patients requiring transfer to the cancer centre should experience minimum delays ensuring that treatment times do not exceed those outlined in the waiting times guidance; that is a maximum of 2 months wait from urgent G.P. referral to treatment.

5.6 All patients undergoing laparotomy should be fully staged as described below:

5.6.1 Staging should be carried out by an appropriately trained surgeon: For patients with an RMI < 25 any gynaecologist, an RMI 25 –250 by the designated gynaecological oncologist for the cancer unit, and RMI >250 a gynaecological oncologist in the designated centre (City Hospital) as part of a SMDT.

5.6.2 Working through an extended midline incision the surgery should include:

a. cytology of ascitic fluid.
b. laparotomy with clear documentation of liver, diaphragm, GI tract, omentum, peritoneal and para-aortic nodes.
c. representative biopsies of the omentum, peritoneum, retro peritoneal and para-aortic nodes.
d. total abdominal hysterectomy, bilateral salpingo-oophorectomy and omental biopsy.

5.7 <u>Patients with obvious metastatic disease</u>

5.7.1 RMI score is inappropriate when obvious metastatic disease is present. All of these patients should be referred to the centre as soon as cancer is suspected. A scan (CT or MRI as appropriate) is required to assess retroperitoneal, omental and peritoneal disease.

5.7.2 Patients who present with advanced disease at diagnosis (that is, with ascites, omental cake or widespread peritoneal disease) should have their management discussed at the SMDT meeting and be considered for entry into clinical trials. If the SMDT meeting decision is for palliative care only then this may be delivered locally.

6 Patient information and counselling

6.1 All patients, and with their consent, their partners will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a

clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the gynae team at all times.

6.2 Access to psychosocial and psychosexual support will be available if required. All patients should undergo a holistic needs assessment and onward referral as required.

7 Palliative care

7.1 Palliative care services will be made available to all patients as deemed appropriate by the MDT.

7.2 Patients with limited life expectancy of less than a year should be referred to end of life care pathway.

8 Clinical trials

8.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.

8.2 Where a study is only open at one Trust in the Network, patients should be referred for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network. Email: PBCRN@westmidlands.nhs.uk .

8.3 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol.

Monitoring of the guideline (from RCOG guideline 34 see reference 6)

1. The proportion of women undergoing preoperative investigations with ultrasound and serum CA125 levels with use of RMI.
2. The proportion of women managed at the correct location (gynaecological unit, cancer unit, cancer centre) according to the risk of malignancy index.
3. The proportion of women in the cancer network with ovarian cancer referred to the cancer centre from the cancer or gynaecological units *before* surgery.

References

1. 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.

2. 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.
3. 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.
4. Tailor 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.
5. Antonic J, Rakar S. Colour and pulsed Doppler US and tumour marker CA125 in differentiation between benign and malignant ovarian masses. Anticancer Res 1995:15 (4) 1527-32.
6. RCOG October 2003, *Ovarian Cysts in Post Menopausal Women, Guideline Number 34*, Royal College of Obstetricians and Gynaecologists, London.
7. Website for details of the chorus trial.
8. Department of Health, 2004, *Manual for Cancer Services 2004.* Department of Health, London.
9. National Institute for Clinical Excellence 1998, *Improving Outcomes in Gynaecological Cancers The Manual.* NICE, London.
10. SIGN (Scottish Inter-Collegiate Guidelines Network). Epithelial Ovarian Cancer www.sign.ac.uk(2003)
11. www.nice.org.uk/guidance/CG122

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Approval Signatures

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URGENT

Pan Birmingham NHS Cancer Network

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URGENT REFERRAL FOR SUSPECTED GYNAECOLOGICAL CANCER

If you wish to include an accompanying letter, please do so. **On completion please FAX to the number below.** (Version 2.0)

These forms should only be used for suspected cancer and in conjunction with the NICE Referral Guidelines for Suspected Cancer, June 2005

Patient Details	**GP Details (inc Fax Number)**
Surname Forename D.O.B. Gender Address Postcode Telephone NHS No Hospital No Interpreter? Y / First Language:	**Date of Decision to Refer** **Date of Referral** **GP Signature**

CANCER TYPE SUSPECTED (Check as appropriate)		**ABDOMINAL SYMPTOMS** (Check as appropriate)			
OVARY	☐	Bloating	☐	Upper GI Pain	☐
CERVIX	☐	Lower GI	☐	Altered bowel habit	☐
ENDOMETRIUM	☐	Urinary symptoms	☐		
VAGINA / VULVA	☐				
BLEEDING PV		**EXAMINATION FINDINGS**			
Persistent intermenstrual	☐	Abdominal mass			☐
Post Coital	☐	Pelvic mass			☐
Post Menopausal	☐	Visible cervical lesion			☐
Tamoxifen user	☐	Visible vulval lesion			☐
Single Heavy Episode	☐	Ascites			☐
>1 Episode **and** pattern of bleeding	☐	Type of examination conducted			
Duration of bleeding weeks _____		Abdominal ☐	Bi-manual ☐	Speculum ☐	
MENOPAUSAL STATUS					
Premenopausal	☐	Postmenopausal (>1 year since LMP)			☐
Hysterectomy	☐	On HRT			☐

Clinical Details: History/Examination/Investigations ……
Medication ……

For Hospital Use

Appointment Date Clinic Attending

Was the referral appropriate Yes No (if no please give reason)

GYNAECOLOGICAL CLINICS WITH RAPID ACCESS FACILITIES

Hospital	**Tel**	**Fax**
City and Sandwell	**0121 507 5805**	**0121 507 5075**
Birmingham Women's	**0121 623 6845**	**0121 627 2768**
Good Hope	**0121 424 5000**	**0121 424 8952**
Heart of England	**0121 424 5000**	**0121 424 8952**
Walsall Manor	**01922 721172 ext 7110 or 7785**	**01922 656773**

- Please discard all other Gynaecological Urgent Referral Forms -

ENDORSED BY THE GOVERNANCE COMMITTEE

Why Have I Been Given a 'Two Week Wait' Hospital Appointment?

What is a 'two week wait' appointment?
The 'two week wait' or 'urgent' appointment was introduced so that a specialist would see any patient with symptoms that ***might*** indicate cancer as quickly as possible. The two week wait appointment has been requested either by your GP or dentist.

Why has my GP referred me?
GPs diagnose and treat many illnesses but sometimes they need to arrange for you to see a specialist hospital doctor. This could be for a number of reasons such as:

- The treatment already given by your GP has not worked.
- Your symptoms need further investigation.
- Investigations arranged by your GP have shown some abnormal results.
- Your GP suspects cancer.

Does this mean I have cancer?
Most of the time, it doesn't. **Even though you are being referred to a specialist, this does not necessarily mean that you have cancer**. More than 70% of patients referred with a 'two week wait' appointment do not have cancer.

What symptoms might need a 'two week wait' appointment?

- A lump that does not go away.
- A change in the size, shape or colour of a mole.
- Abnormal bleeding.
- A change in bowel or bladder habits.
- Continuous tiredness and/or unexplained weight loss.
- Other unexplained symptoms.

What should I do if I'm unable to attend an appointment in the next two weeks?
This is an important referral. Let your GP know immediately (or the hospital when they contact you) if you are unable to attend a hospital appointment within the next two weeks.

What do I need to do now?

- Make sure that your GP has your correct address and telephone number, including your mobile phone number.
- The hospital will try to contact you by telephone to arrange an appointment. If they are not able to make telephone contact, an appointment letter will be sent to you by post.
- **Inform your GP surgery if you have not been contacted by the hospital within three working days** of the appointment with your GP.
- You will receive further information about your appointment before you go to the hospital. It is important you read this information and follow the instructions.
- Please feel free to bring someone with you to your appointment at the hospital.

It is important to remember that even though you will receive a 'two week wait' appointment, being referred to a specialist does not necessarily mean that you have cancer. Remember, 7 out of 10 patients referred this way do not have cancer.

Publication date: October 2009

Review date: October 2012

Patient Information adapted from Harrow Primary Care Trust

Appendix 2

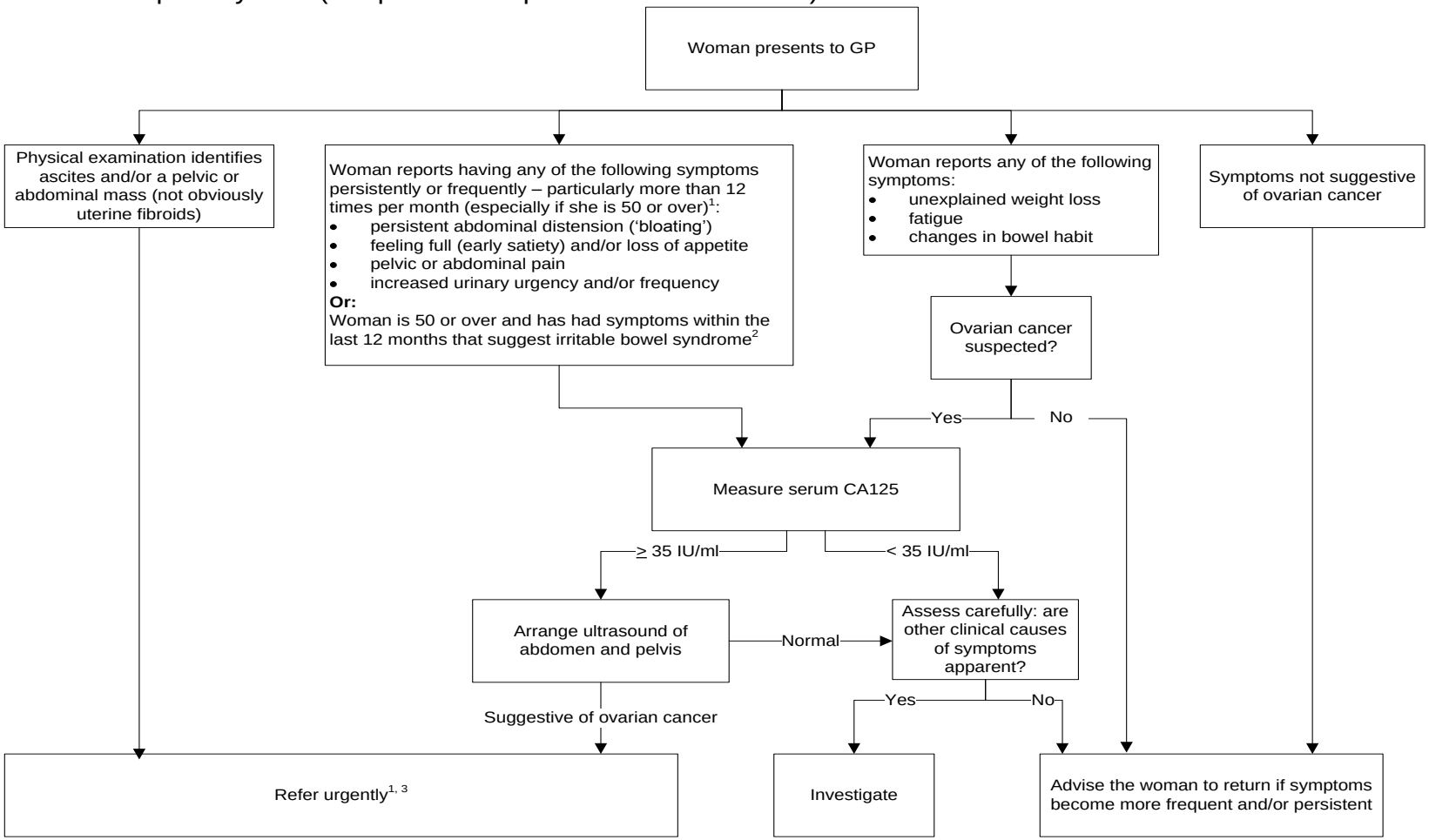
Risk of malignancy index (RMI I)

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

RMI = U x M x CA125

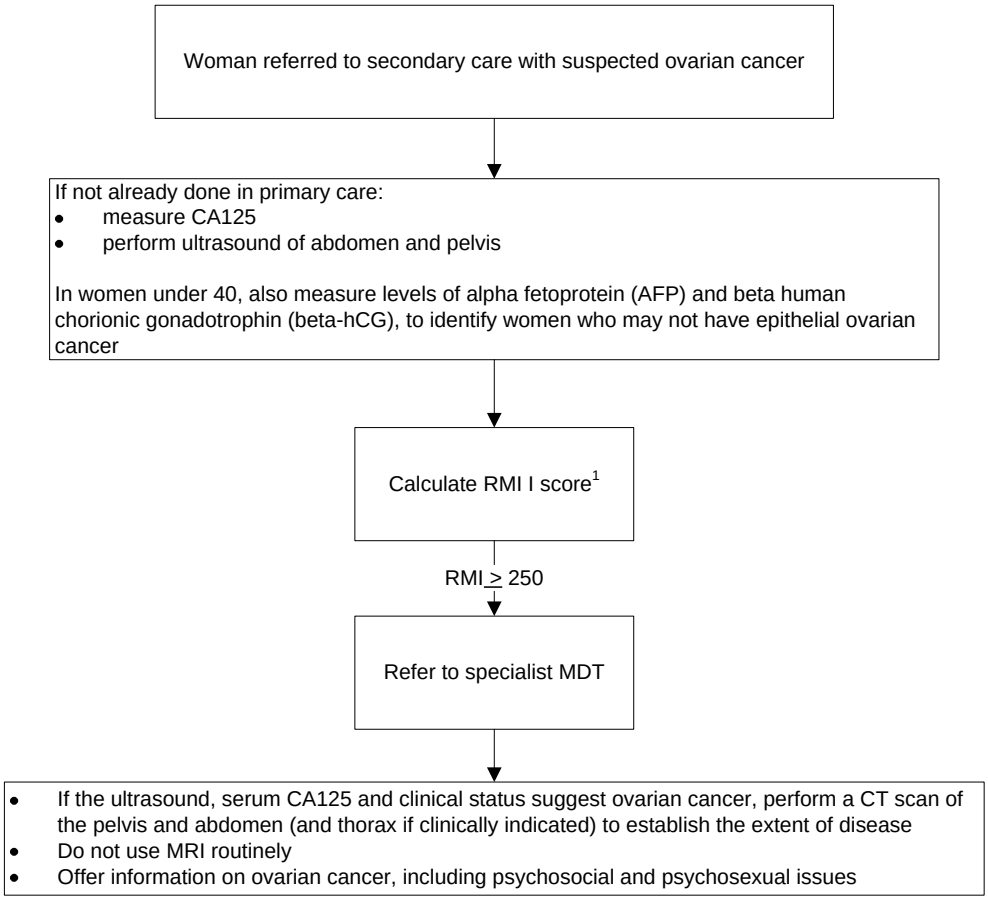
- The ultrasound result is scored 1 point for each of the following characteristics: multi-locular cysts, solid areas, metastases, ascites and bilateral lesions. U = 0 (for an ultrasound score of 0), U = 1 (for an ultrasound score of 1), U = 3 (for an ultrasound score of 2–5).
- The menopausal status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

Detection in primary care (Adapted and copied from NICE CG122)[11]



Appendix 4 triage and referral to the Gynaecological Cancer Centre

(Adapted and copied from NICE CG122)[11]



Appendix 5 overview of pathway (adapted and copied from NICE CG122)[11]