West Yorkshire & Harrogate Cancer Alliance

Guidelines for the Management of Gynaecological Cancers

Version 4.3

Updated September 2018

i Document Control

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Author(s)	Gynaecology MDT Leads across West Yorkshire & Harrogate Cancer Alliance
Owner	West Yorkshire & Harrogate Cancer Alliance

Version Control		
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Contributors to current version		
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Sub Regional Palliative & EoLC Group	Sub Regional Palliative & EoLC Group	Appendix 2 - Palliative & EOLC Chapter 12
Gynaecology NSSG	Gynaecology NSSG	Revision to section 3.6.2 (LLETZ biopsies)
Individual	Cheng Choy	Full review and update
Individual	Sandeep Sharma	Updates to section 1.4.1 & 4.1, plus update of FIGO Ovarian Cancer Staging
Individual	Claire Parkinson & Chen Choy	Update to section 1.3

ii Information Reader Box

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1 Introduction

1.1 National Guidance for Gynaecological Cancers

The 'Improving Outcomes in Gynaecological Cancers' document, produced by the National Cancer Guidance Steering Group in July 1999, highlights the following key recommendations:

Dedicated diagnostic and assessment services should be established in Cancer Units to which all women with possible or suspected gynaecological cancers should be referred. This includes women with symptoms and those who present through the cervical screening programme.

There should be specialist multiprofessional gynaecological oncology teams based in Cancer Centres. These teams should be responsible for the management of all women with ovarian cancer and the majority of women with other gynaecological malignancies.

The specialist gynaecological oncology and palliative care teams in each Cancer Centre and associated Cancer Units should agree clear local policies for the management of women with advanced or progressive disease. These policies should be designed to ensure the co-ordination of high quality care between Cancer Centres, Cancer Units, palliative care, primary care and community services.

There should be rapid and efficient communication systems for liaison and cross-referral between all levels of service. Audit should take place across the entire service delivery network, including the Cancer Centre and all related Units.

1.2 Purpose and Scope of these Guidelines

These are based on the national Improving Outcomes in Gynaecological Cancers guidance, and accompanying research evidence, with appropriate interpretation for our local service. Contained in this document are guidelines for the management of cervical, ovarian, endometrial and vulval cancers.

The guidelines were originally written by members of the former YCN Gynaecology Network Site Specific Group and have been reviewed by the West Yorkshire & Harrogate Cancer Alliance Gynaecology MDT Leads.

They will be reviewed every three years. The guidelines will be available online

1.3 All Gynaecological Malignancies

Individual gynaecological cancers are uncommon. A general practitioner could expect to see one new case of ovarian cancer every 5 years, and one new case of cervical cancer every 7 years.(Statistics from Cancer Research UK)

1.3.1 Endometrial Cancer

Statistics

- Approximately 9,100 new cases in the UK every year
- 2360 deaths 2016
- 78% survival 10 years (2010 – 11England and Wales)
- 34% preventable
- Incidence highest in females aged 75 to 79
- Not associated with deprivation

Risk factors

- Overweight(34% caused by obesity)
- Taking HRT
- Taking Tamoxifen
- Lynch Syndrome

1.3.2 Ovarian Cancer

Statistics

- Approximately 7,400 new cases in the UK every year
- 4227 deaths 2016
- 35% survival 10 years (2010 -2011 England and Wales)
- 11% preventable
- Peak rate of ovarian cancer between ages of 75 - 79
- Almost 70-75% of patients are diagnosed at a late stage
- Not associated with deprivation

Risk factors

- 80 - 85% sporadic
- Genetically BRCA 1 & 2 mutations & Lynch Syndrome –Hereditary non-polyposis colorectal cancer (HNPCC)
- Family history
- 7% caused by obesity
- Less than 1% caused by smoking
- Less than 1% caused by workplace exposure

1.3.3 Cervical Cancer

Statistics

- Approximately 3,200 new cases in the UK every year
- 854 deaths in 2016
- 63% survive for 10 years or more
- 99.8% of cases are preventable
- Incidence is highest in females aged 25 to 29 years.
- More common in females living in the most deprived areas

Risks factors

- Smoking almost doubles the risk of developing squamous cell carcinoma (48%)
- Human papilloma virus is present in 98.8%
- Cervical cancer risk among parous women is 77% higher in those under 17 years old at their first full-term pregnancy, compared with those aged 25 or older

1.3.4 Vulval Cancer

Statistics

- Approximately 1300 new cases in the UK every year
- 460 deaths 2016
- 53% survival 10 years (2009 -2013 England)
- 69% preventable
- Incident rates for vulval cancer are in females aged 90+
- More common in people living in the most deprived areas.

Risk factors

- Human papillomavirus (HPV) type 16
- 69% caused by HPV infections

1.3.5 Vagina Cancer

Statistics

- Approximately 240 new cases in the UK every year
- 100 deaths 2016
- 53% survival 10 years (2009-2013 England)
- 75% preventable

Risk factors

- HPV type 16
- DES(Diethylstilbestrol) exposure in utero

1.4 Gynaecological Cancer Services in the Yorkshire WY&H CA

The West Yorkshire & Harrogate Cancer Alliance (WY&H CA) has a resident population of approximately 2.6 million and there are 11 Clinical Commissioning Groups and 6 Acute Hospital Trusts within the Network. The Cancer Centre is based at Leeds Teaching Hospitals NHS Trust.

1.4.1 Local Gynaecology MDT Teams table

Updated 09.05.17

Trust (Hospital Site)	MDT Lead
Airedale NHS Trust (Airedale General Hospital)	Mr Stephen Porter
Bradford Teaching Hospitals NHS Foundation Trust (Bradford Royal Infirmary)	Dr Moiad Alazzam
Calderdale & Huddersfield NHS Foundation Trust (Calderdale Royal Hospital)	Mr Cheng Choy
Harrogate & District NHS Foundation Trust (Harrogate District Hospital)	Mr Adrian Barnett
Leeds Teaching Hospitals NHS Trust (St. James's University Hospital)	Mr Richard Hutson
Mid Yorkshire Hospitals NHS Trust (Pinderfields Hospital)	Mr Sandeep Sharma
York Hospitals NHS Foundation Trust ** (York Hospital)	Mr Robert Hunter

** Please note that the York Teaching Hospitals NHS Foundation Trust is now part of the Humber Coast and Vale Cancer Alliance

The National Cancer Peer Review Programme in their publication "Manual for Cancer Services 2008: Gynaecology Measures" provided the detailed specification for both core and extended membership of a local gynaecology MDT.

1.4.2 Specialist Gynaecology Team Configuration

Trust (Hospital Site)	MDT Lead
Leeds Teaching Hospitals NHS Trust (St. James's University Hospital)	Mr R Hutson

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1.5 Local Clinical Pathways

The gynaecological pathways:

- Cervical Cancer Pathway
- Endometrial Cancer Pathway
- Ovarian Cancer Pathway
- Vulval Cancer Pathway

Are supported by generic and tumour specific information pathways and supportive and palliative care pathways

Teenage & Young Adult Services

a) TYA aged 16 – 18 must be referred to the TYA principle treatment centre (PTC) for their initial treatment
b) TYA between age 19 -24 should be offered place of care either in a TYA designated hospital or the TYA PTC

The TYA Team will always consult with the gynaecological team managing the patient before an approach to the patient is made.

A former YCN Soft Tissue Sarcoma Shared Care Pathway for Gynaecology MDT to access the Leeds Sarcoma MDT (recognising high level expertise in diagnostic and local management of gynaecological sarcoma) has been agreed

1.6 Patient Information

Clinical teams offer all newly diagnosed cancer patients information specific to their site, treatment and relevant to their individual need. Patients can also access NHS choices for an information prescription and clinical teams will offer help to do this, if required.

2 GP Referral Guidelines for Suspected Gynaecological Malignancies

2.1 Cervical Cancer

2.1.1 Pre malignant cervical cancer

The premalignant phase of the disease, cervical intraepithelial neoplasia, is not associated with any symptoms or signs, hence the importance of the screening smear.

Patients with severe dyskaryosis, invasive cancer or glandular changes are treated as suspected cancer and should be referred as an urgent suspected cancer (2 week wait).

2.1.2 Symptoms of invasive cervical cancer

Early symptoms

- Irregular bleeding, particularly postcoital bleeding, bleeding noted after micturition/defaecation, or post-menopausal bleeding. However, the majority of women with irregular bleeding will not have cancer.
- Vaginal discharge - initially non-specific, but often becoming blood-tinged or offensive.

Later symptoms

- are related to local spread, e.g. malaise due to renal failure (due to ureteric obstruction), haematuria, leg oedema (commonly unilateral), rectal bleeding, low back and sacral pain.

2.1.3 Signs: the examination of symptomatic patients

- In order to diagnose early invasive cervical cancer it is important to have a high index of suspicion and a willingness to carry out a FULL PELVIC EXAMINATION for relatively minor symptoms.
- Speculum examination: The appearance of the normal cervix can vary considerably depending on parity, the pill and the presence of inflammation and nabothian follicles. Any other lesion on the cervix, e.g. nodule, small ulcer, or an inflamed cervix that bleeds easily on gentle examination should be regarded with suspicion.
- On digital examination the cervix may feel indurated or firm or soft and friable.

2.1.4 Referral

- Women with the above signs and symptoms should be referred to a gynaecologist for investigation.
- If the suspicion of cancer is high the woman should be referred directly to the gynaecological assessment service at a Cancer Unit, using the two-week wait fast track referral system. A cervical smear may be done but the wait for a result should not delay referral.

- Cytological examination of cervical smears has a detection rather than a diagnostic accuracy. A negative cytology report does not exclude cervical cancer and can cause both delay in diagnosis and provide false reassurance.
- The referral letter should include details of relevant medication.

2.2 Endometrial Cancer

2.2.1 Symptoms

- Post-menopausal bleeding (PMB) (bleeding after 12 months amenorrhoea is the cardinal symptom of endometrial cancer)
- Pre-menopausal women over the age of 40 with persistant or heavy intermenstrual bleeding (This group have a low risk of endometrial cancer. Nonetheless, 15% of endometrial cancers present in this way)
- Persistent unexpected bleeding with hormone replacement therapy
- Persistent unexplained vaginal discharge in a postmenopausal woman
- Risk factors such as diabetes and obesity, a history of prolonged unopposed estrogen therapy, breast cancer and Tamoxifen treatment have low specificity but may raise the level of suspicion
- Less than 4% of endometrial cancers occur in women under 40 and these are usually associated with predisposing factors such as anovulatory menstrual cycles secondary to polycystic ovary syndrome and/or infertility.

2.2.2 Signs: the examination

- Endometrial cancers usually present early with PMB in the absence of any other physical signs.
- Uterine cancer must be excluded before accepting signs of postmenopausal atrophy or cervical polyps as the cause of unexpected bleeding.
- PMB may be due to vaginal or cervical cancer and women with this symptom should have a vaginal and pelvic examination performed.
- If there is any doubt about the source of bleeding rectal examination should be considered.

2.2.3 Referral

Women at high risk

Women with a single heavy episode or persistent PMB are at high risk and should be referred using the two-week wait fast track referral system or to a direct access hysteroscopy clinic.

Symptoms suggesting possible endometrial cancer

Women with unexpected vaginal bleeding who do not fall into the high risk category should be referred for direct access hysteroscopy or urgently to designated gynaecologists, identified in each Cancer Unit according to an agreed protocol.

Referral should not be delayed by requests for a vaginal ultrasound scan. If a vaginal ultrasound scan has been requested prior to the referral, GPs should state on the request form that urgent gynaecological assessment has been arranged, and that the results should

be available at the time of the appointment. It should also be stated on the referral letter if an ultrasound has been arranged. An abdominal ultrasound scan is not indicated

2.3 Ovarian Cancer

2.3.1 Symptoms

A woman who is found on examination to have:

- ascites
- a pelvic or abdominal mass (which is not obviously uterine fibroids)
- or both

should be referred as a suspected gynaecological cancer to an appropriate clinic.

Ovarian cancer is characterised by non-specific symptoms. It is therefore necessary to explore the possibility of this diagnosis in women with the following:

- persistent abdominal distension (women often refer to this as “bloating”)
- feeling full (early satiety) and/or loss of appetite
- pelvic or abdominal pain
- increased urinary urgency and/or frequency
- symptoms suggestive of irritable bowel syndrome in a woman over the age of 50

For all these symptoms, the suspicion of ovarian cancer is enhanced if the woman is over 50, if symptoms occur more than 12 times per month or if there is a family history of ovarian cancer.

The diagnosis should also be considered among other causes if a woman reports unexplained weight loss, fatigue or changes in bowel habit.

2.3.2 Tests

The features above should prompt investigations as follows:

- Measure serum CA125. **This should be requested from primary care**.

If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis.

If the ultrasound suggests ovarian cancer, the patient should be referred as a suspected gynaecological cancer to an appropriate clinic.

If the ultrasound is normal in a premenopausal woman she may be reassured that mild elevations may frequently be found in due to benign conditions; the test can be repeated after 2 months.

2.3.3 Safety Netting

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
- If the clinical features listed above persist it will be helpful to discuss the case with the lead clinician of the local gynaecological cancer diagnostic service.

2.3.4 Incidental finding of a possible ovarian mass

In the event of an ovarian mass with features suspicious of malignancy being discovered on an ultrasound examination performed in primary care for some other indication, the patient should be referred as a suspected gynaecological cancer to an appropriate clinic, together with measurement of serum CA 125.

2.3.5 Small ovarian cysts

Simple cysts less than 10cm in diameter in premenopausal women or less than 5cm in diameter in post-menopausal women are unlikely to be malignant and do not represent an indication for urgent referral. A serum CA 125 in the normal range, especially if <20 IU/ml gives additional reassurance.

2.4 Vulval Cancer

These Guidelines for Vulval Cancer have been adapted from the Royal College of Obstetricians and Gynaecologists “Management of Vulval Cancer” (2006)[1].

2.4.1 Basic considerations

- The disease is most common in post-menopausal women.
- Vulval cancer may be asymptomatic.
- Vulval pain, itching, burning and soreness may all be associated with vulval cancer.
- Any vulval symptom in a post-menopausal woman should prompt examination of the vulva, vagina and cervix. This should also apply to pre-menopausal women if there has been no response to simple first line therapy such as antifungal treatment.
- Warts are uncommon in elderly women and should, therefore, be treated with suspicion. They are much more common in pre-menopausal women and should initially be managed as condylomata acuminata.
- Only a minority of suspicious vulvas will have confirmed malignancy.

2.4.2 Recommendations

Any of the following changes in vulval epithelium should prompt referral:

- A swelling, polyp or lump.
- An ulcer.
- Colour change (whitening, pigment deposition)
- Elevation and or irregularity of the surface contour.
- A clinical "wart".
- Irregular fungating mass.
- An ulcer with raised, rolled edges.
- Enlarged groin nodes.

Persistent "warts" in the pre-menopausal woman should be referred for excisional biopsy to the local unit/centre.

In pre-menopausal women all other vulval signs and symptoms should be managed as for those in post-menopausal women unless there is an obvious and confirmed infectious cause such as candidiasis, herpes, etc.

2.4.3 Referral

Patients should be referred using the two-week wait fast track referral system.

2.5 Referral Form

2.5.1 Contents of a 2ww Referral Form

Referrals should be made by fax with hard copy sent by post. The hard copy should also state the date that the faxed copy was sent.

The following information should be contained in the GP referral form: -

- Full demographic patient details including daytime and evening telephone numbers.
- Age.
- Symptoms and signs on physical examination.
- Family history of cancer – specifically ovary/breast/endometrial/colon.
- Date of last normal smear and if most recent smear is abnormal.
- Dates of any investigations recently organised (enclosing copies of all reports).
- Date and time of any imaging, including tests arranged (enclosing copies of all reports).
- Details of previous medical and surgical history, especially previous gynaecological surgery.
- Explanation given to the patient.

Other information which may be useful includes:-

- Parity.
- LMP/Menstrual cycle.
- Use of oral contraceptive pill/current contraceptive.
- Use of HRT/Tamoxifen/Fertility drugs.
- Other relevant medication.

A specialist will see urgent referrals within 2 weeks. Unit Lead Clinicians will co-ordinate designated referral clinics.

2.5.2 Communication

General Practitioners will receive a communication from the relevant Cancer Unit within two weeks of the patient being seen. This will include any available investigation results, a provisional diagnosis, and what the patient has been told.

3 Cervical Cancer

3.1 National Guidance

All women whose tumours appear to be more advanced than Stage Ia and all those with adenocarcinomas should be referred to the specialist gynaecology oncology team at the Cancer Centre. These guidelines are written to be consistent with the National Guidance.

3.2 Local Implementation of National Guidance

It is intended that all patients with proven malignancy or where malignancy is strongly suspected, will be referred urgently by the Cancer Unit by fax, phone or via the appropriate Centre Consultant to the Cancer Centre in accordance with the National Guidance. Designated Cancer Units may treat certain patients in close co-operation with the Centre i.e. Stage 1A1 patients.

All patients must be discussed at a MDT meeting.

When a patient is referred to the Cancer Unit for urgent gynaecological assessment, she should be seen within two weeks of receipt of the referral.

3.3 Diagnosis

When a patient appears to have superficial invasion, a loop or cone biopsy should be carried out.

A designated pathologist with a special interest in malignant gynaecological disease should examine the biopsy specimen. If invasive carcinoma is present the specimens should be sent to the Specialist Pathologist at the Cancer Centre for review in a MDT meeting. Referral for micro-invasive disease is not necessary unless a further opinion about histology is required.

All women whose tumours appear to be more advanced than Stage Ia and all those with adenocarcinomas should be referred to the specialist gynaecological oncology team at the Cancer Centre. Magnetic Resonance Imaging should be available to assess the local extent of early disease.

3.4 Imaging

3.4.1 MRI in Cervical Carcinoma

- Staging
- Histologically proven Ca Cervix
- Clinical Stage 1bi or greater disease
- Assessment of non-surgical treatment response
- Suspected local disease relapse
- Reassessment.
- 3 months post completion of chemo-radiotherapy, reviewed in conjunction with clinical findings.
- Repeat examination after a further 3 months for patient's with visible residual disease or an equivocal MRI abnormality.

Technique

- Avoid vaginal tampon
- Intravenous anti-peristaltic agent – Glucagon or Buscopan
- Sagittal SFOV (20 cm) T2W sequence through the pelvis
- 'Inclined axial' SFOV T2W sequence perpendicular to the endocervical canal
- LFOV axial FISP (or equivalent overview sequence depending on Manufacturer) and coronal T1W sequences through the retroperitoneum and pelvis to assess nodal disease and hydronephrosis

Currently there is no role for the routine use of Gadolinium in MRI staging of Cervical Carcinoma.

3.4.2 CT in Cervical Carcinoma

Where MRI is available there is no role for CT in initial staging

With known advanced disease, CT is the modality of choice to provide information about disease spread beyond the pelvis, i.e. for assessment of the thorax and upper abdomen.

3.4.3 PET - CT in Cervical Carcinoma

PET - CT is indicated in all patients with local disease recurrence, or failure of local disease control, who are being considered for exenterative surgery.

3.5 Surgery

3.5.1 Management of Stage Ia disease

Stage 1a1

Loop excision may be adequate treatment provided there is complete excision of both the invasive and pre-invasive element. If excision is incomplete, a further loop or cone biopsy should be performed to exclude further invasion. The pathology should be discussed in the local MDT in the presence of the centre surgeon but referral to the centre MDT is not necessary unless a further opinion about the histology is required.

Stage 1a2

Management should be carried out by the appropriate centre surgeon following discussion in the centre MDT. The standard treatment is radical hysterectomy with bilateral pelvic lymphadenectomy. However, in some circumstances following MDT review, a simple hysterectomy with bilateral pelvic lymphadenectomy may be appropriate, performed as an open, vaginal or laparoscopic procedure. If there is a desire to retain fertility, then a cone biopsy or radical trachelectomy, with bilateral pelvic lymphadenectomy may be considered.

3.5.2 Management of Stage Ib or IIa disease

All patients should undergo staging with MRI and CXR. Routine staging with EUA and cystoscopy is not necessary unless there is discrepancy between clinical findings and MRI. Each case should be discussed in the centre MDT meeting.

Stage 1b1

Treatment can be with radical surgery or radical radiotherapy. This will depend on the patients age, suitability for major surgery and the womans preference. In general though, if the patient is fit, surgery is usually the preferred option.

Stage 1b2 disease

Careful discussion should take place in the centre MDT with regards to the best mode of treatment which could be either radical surgery or radiotherapy.

Stage 11a disease

Depending upon the extent of spread onto the vagina, treatment with either radical surgery or radical radiotherapy may be appropriate. In this situation, it may be necessary to perform a formal EUA to assess the best mode of treatment prior to discussion in the centre MDT.

Radical Trachelectomy

This procedure may be considered where there is a strong desire to retain fertility but should only be performed for tumours <2cm. The patient should be carefully counselled, including the implications for future pregnancies.

The operation can be performed via the vaginal or abdominal route with bilateral pelvic lymphadenectomy.

3.6 CWT Guidelines for LLETZ Biopsy

If LLETZ biopsy is performed for diagnostic intent only then this cannot be classed as first treatment for gynaecological cancer (i.e. cannot end the 62 day pathway).

If LLETZ biopsy is performed for therapeutic intent (i.e. if the intention of the procedure was to remove the tumour) then this would count as first treatment irrespective of whether the margins are clear.

If the intention was diagnostic but the tissue was found to be malignant, the procedure could count as first treatment if the tumour had been removed by this excision.

3.7 Histopathology

3.7.1 Cervical biopsy

Handling of specimen

Biopsies are to be examined at three levels initially with further levels if appropriate. A full face must be examined of the tissue within the block.

Histological reporting

A diagnosis of invasive squamous carcinoma may be made on a punch biopsy but it must be emphasized that in many cases staging will not possible on the biopsy material.

Adequate assessment of neoplastic glandular lesions can rarely be made on punch biopsy alone and LLETZ biopsy may be required.

3.7.2 Cone/LLETZ Biopsy

Macroscopic description

The three dimensions of the cone biopsy are to be measured in millimetres. Comment is to be made if the cone biopsy is orientated, whether it is incomplete or disrupted and in how many pieces it was received.

Handling of specimens

If the cone/LLETZ biopsy has been orientated the specimen is marked to permit assessment of location of abnormal foci and photographed if facilities permit.

The specimen is sliced at 3mm intervals at right angles to the cervical os and one slice blocked per cassette.

Care should be taken with the first and last slices to enable the handling pathologist to comment on the ectocervical and lateral soft tissue, excision margin.

One tumour block should be examined with a mucin stain in cases of invasive carcinoma to enable the distinction between a poor differentiated, invasive squamous cell carcinoma from an adenocarcinoma.

Histological reporting

If the cone/LLETZ biopsy has been received in more than one piece comment on excision is limited.

If the invasive carcinoma has been completely excised in the cone/LLETZ biopsy accurate staging is permitted in accordance with FIGO 1995. If excision is incomplete accurate staging is not possible though minimum dimensions are reported and the case discussed at the weekly gynaecological cancer MDT when the patients can be accurately staged.

Check List

- Histological type of invasive tumour
- Histological grade
- Size of tumour in three dimensions/stage (see above)
- Lymphovascular permeation
- Excision margins
- Presence and excision of associated intraepithelial neoplasia +/- wart viral change
- CIN (cervical intra-epithelial neoplasia)
- CGIN (cervical glandular intraepithelial neoplasia)
- SMILE (stratified mucin-producing intra-epithelial lesion)

Minimum Dataset

Please also complete the form “Reporting Proforma for Cervical Cancer in Excisional Cervical Biopsies” (Appendix B1 in the RCPath dataset publication).

3.7.3 Hysterectomy specimens

Hysterectomy specimens for cervical cancer will be either a routine hysterectomy or a Wertheim’s hysterectomy. The latter includes vaginal cuff, paracervical and parametrial soft tissues, a variable proportion of broad, round and uterosacral ligaments and lymph node dissection.

Bilateral salpingo-oophorectomy may be included.

Macroscopic description

Hysterectomy:	Dimensions of uterus Appearances of cervix
Wertheim’s:	Dimensions of uterus including medial to lateral dimension of the cervical tissues Appearance of cervix with macroscopic assessment of tumour size Macroscopic description of additional tissues received

Handling of Specimens

Hysterectomy	Amputation of the cervix with orientation and treatment as a cone/LLETZ biopsy

	Complete examination is usually required to permit comment on residual/neoplasia and excision A transverse block, from the high endocervix may be informative The body of the uterus, if uninvolved, is sampled as for non-neoplastic uteri.
Wertheim's	Cervix treated as above If the tumour is macroscopically visible representative sections may be sufficient to give the information required (detailed below). If the tumour is not visible complete examination of the cervical tissues may be required. Examine all paracervical and parametrial soft tissues. The vaginal cuff may be amputated if necessary.
Lymph nodes	Groups of nodes will be received in separate pots. Document number in each group. All lymph nodes are to be examined being sectioned at right angles to the longest axis of the lymph node at 3mm intervals.
Fallopian tubes & Ovaries	Examine as for non-neoplastic disease in the absence of a macroscopic abnormality.

Check List

- Histological type
- Histological grade.
- Tumour size, three dimensions.
- Figo Stage.
- Lymphovascular permeation/
- Lymph node status. (Number of nodes and number involved).
- Presence or absence of extracapsular spread.
- Involvement of paracervical and parametrial soft tissues.
- Surgical margin status including lateral/paracervical margin and vaginal resection margin.
- Extension to uterine body.

In cases of trachelectomy the specimen should be treated as the amputated cervical portion of a Wertheim's hysterectomy specimen with additional consideration of the margin status of the proximal resection margin.

Additional information can be acquired from "Standard Operating Procedures" held in CPA Accredited Histopathology laboratories.

Minimum Dataset

Please also complete the form "Reporting Proforma for Cervical Cancer in Hysterectomy Specimens" (Appendix B2 in the RCPath dataset publication).

The patient is to be registered with the Northern and Yorkshire Cancer Registry and Information Service

3.8 Radiotherapy

3.8.1 Management of Stage IIb -IVa disease

Radical chemoradiotherapy or radiotherapy should be offered as outlined below.

3.8.2 Pre-radiotherapy assessment

All patients should be carefully assessed prior to radiotherapy. The following tests should be performed:

- FBC and biochemical profile
- EDTA creatinine clearance (where concurrent chemotherapy is to be given)
- Chest X-ray
- MRI of the pelvis
- Examination under anaesthetic (EUA) and insertion of markers
- Cystoscopy where the MRI indicates bladder involvement (to confirm stage IVa disease)
- Hydronephrosis may require ureteric stenting prior to the commencement of RT.

3.8.3 Pelvic radiotherapy

The standard treatment for locally advanced cervix cancer will combine pelvic radiotherapy with intracavity brachytherapy.

Pelvic radiotherapy encompasses the primary tumour, uterus, parametrial tissue, upper vagina and pelvic nodes including the parametrial, pre-sacral, obturator, internal, external and common iliac nodes. All patients are planned conformally. Full details are included in the Radiotherapy protocols.

A dose of 48Gy in 24 fractions over 32-35 days. Unscheduled gaps or prolongation of the total treatment time should be avoided as this reduces local control.

The maintenance of haemoglobin ≥ 12g/dl has been shown in a retrospective study to improve both pelvic control and survival rates[2].

3.8.4 Concurrent chemotherapy

Where patients are fit enough they should receive cisplatin 40mg/m2 weekly (maximum dose 76mg) for a total of 5 treatments. Full details are included in the Radiotherapy protocols.

3.8.5 Brachytherapy following external beam radiotherapy.

Brachytherapy following pelvic radiotherapy should be used when possible. Brachytherapy should be timed so that there is no or minimal gap between the end of external beam treatment and brachytherapy. Following pelvic radiotherapy the usual dose is 21Gy in 3 weekly fractions. This is prescribed to point A or conformally planned following MRI imaging with applicators in place. Full details are included in the Radiotherapy protocols.

Intracavity brachytherapy is normally given under a spinal anaesthetic. The St James's Institute of Oncology uses the High Dose Rate MicroSelectron (Ir192, dose rate 1.5Gy/min).

[2] Grogan M et al. The importance of haemoglobin levels during radiotherapy for carcinoma of the cervix. Cancer 1999; 86: 1528-36.

3.8.6 Brachytherapy alone

When brachytherapy alone is used as a radical treatment in early stage disease a dose of 35 – 37.5Gy in 5 fractions to point A or conformally planned in 5 fractions is given at weekly intervals over 29 days

3.8.7 External beam boost

When brachytherapy is not possible patients should be considered for a conformal external beam boost of 16.2-18Gy in 9-10 fractions over 11-12 days.

3.8.8 Parametrial boost

Parametrial boosts are occasionally given for disease extending out to the pelvis side wall not covered by the brachytherapy boost. A dose of 5-10 Gy in 3-5 fractions over 3-7 days should be considered.

3.8.9 Treatment by stage

Stage Ib1

Women who are not medically fit for radical surgery or who refuse surgery should be considered for radical intracavitary treatment (brachytherapy) alone.

Stage Ib2-IVa

Women with stage Ib2 -IVa disease should be considered for radical chemo-radiotherapy or radiotherapy followed by intracavitary treatment. All women with positive nodes on MRI, irrespective of stage should be considered for radical pelvic chemo-radiotherapy or radiotherapy followed by intracavitary treatment.

Radiotherapy, chemotherapy and brachytherapy should be administered as outlined above.

In patients who have had a poor response to chemoradiotherapy prior to brachytherapy, or where brachytherapy is not possible due to inability to cannulate the cervix 3 further cycles of weekly cisplatin at 50mg/m2 can be considered prior to a further attempt at brachytherapy. Alternatively patients can proceed to an external beam boost as outlined above.

Stage IVb, and all other stages of disease in women who are not suitable for radical radiotherapy

Local pelvic control is important in the management of all women with cervical cancer. Radical treatment should be considered for all patients however where patients are unfit or the disease is regarded as too extensive (either locally or widespread metastases) then palliative radiotherapy should be considered.

Appropriate schedules include

- 40Gy in 15 fractions followed by ICT 8.5Gy to point A
- 30Gy in 10 fractions

- 10Gy 1fraction repeated if symptoms persist no more than once every 4-6 weeks for a maximum of 3 times[3],[4],[5],[6]

3.8.10 Follow-up following radical chemoradiotherapy

Clinical examination and direct inspection are mandatory in the routine follow-up of patients who have had radical radiotherapy.

Patients should have an initial MRI at 3 months to assess response. Further imaging should be guided by the results and clinical examination / patients symptoms.

Cervical smears following radiotherapy are not recommended, as they are difficult to interpret.

Hormone replacement therapy should be offered to all patients who are pre-menopausal prior to treatment. An oestrogen and progestogen combination should be prescribed as women given an unopposed oestrogen may experience uterine bleeding despite a high dose of radiation to the endometrium.

3.8.11 Adjuvant Radiotherapy Following Radical Surgery

Adjuvant radiotherapy is recommended for patients whose primary therapy is surgical, but whose surgical specimen reveals unfavourable prognostic features.

These include:

- Positive or close resection margins <3mm and/or evidence of microscopic parametrial spread
- One or more positive pelvic nodes
- Bulky cervical tumour >4 cm and/or deep stromal invasion >10mm
- Lymphovascular space permeation is a relative indication for RT

Adjuvant pelvic radiotherapy (or chemoradiotherapy) 45Gy in 25F given daily total treatment time 32-35days. Concurrent chemotherapy, weekly Cisplatin 40mg/m2 x5should be considered for patients with positive pelvic nodes especially if two or more nodes are involved.

3.8.12 Follow-up

Clinical examination and direct inspection are mandatory in the routine follow-up of patients who have had adjuvant radiotherapy.

Vault smears following radiotherapy are not recommended, as they are difficult to interpret.

Hormone replacement therapy should be offered to all patients who are pre-menopausal prior to treatment. An unopposed oestrogen should be prescribed in this situation.

[3] Hodson DJ, Krepart GV. Once-monthly radiotherapy for the palliation of pelvic gynaecological malignancy. Gyncol Oncol 1983; 16:112-6.
[4] Stehman FB, et al. Radiation therapy with or without weekly cisplatin for bulky stage 1B cervical carcinoma: follow-up of a GOG trial. Am J Obstet Gynecol 2007, 197:503e1-e6.
[5] Lanciano R, et al. Randomized comparison of weekly cisplatin or protracted venous infusion of fluorouracil in combination with pelvic radiation in advanced cervix cancer; GOG study. J Clin Oncol 2005, 23:8289-95.
[6] Eifel PJ et al Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of RTOG90-01. 2004,22:872-80

3.9 Chemotherapy

3.9.1 Introduction

All patients with advanced primary, or recurrent/persistent carcinoma of the cervix should be considered for clinical trials. Such trials are likely to be co-ordinated by the Leeds Cancer Centre at St James's Institute of Oncology.

3.9.2 Adjuvant

- No evidence of benefit
- Treatment considered within clinical trial if available

3.9.3 Locally advanced disease

- Chemoradiotherapy, with cisplatin

3.9.4 Palliative

- Incompletely resected; metastatic; recurrent.
- Depending on : peformance status; comorbidity; patient choice.
- Treatment considered within clinical trial if available

First line

- Cisplatin & Topotecan
    - Cisplatin naÏve or >180 days post previous cisplatin
- Cisplatin
- Paclitaxel & carboplatin - 3 weekly
- Paclitaxel & carboplatin - weekly
- Carboplatin - 3 weekly
- Carboplatin - weekly
- Topotecan - 3 weekly
- Topotecan - weekly

Second line

Depending on:

- peformance status; comorbidity; patient choice, first line agents used
- treatment considered within clinical trial if available

- Paclitaxel & carboplatin – 3 weekly
- Paclitaxel & carboplatin – weekly
- Paclitaxel – 3 weekly
- Paclitaxel - weekly
- Topotecan - 3 weekly
- Topotecan - weekly

For details of regimens, please contact local Gynaecology MDT Teams

3.10 Special Situations

Patients with the following at the time of diagnosis must be referred to the Cancer Centre MDT team for further management:

- Rare histological types, e.g. small cell cancer
- Incidentally diagnosed invasive cervical cancer
- Cervical stump carcinoma
- Cervical cancer diagnosed in pregnancy

3.10.1 Small cell cancer of the cervix

Patients with small cell cancer of the cervix should be referred to the Cancer Centre for management.

Patients where a pre-operative diagnosis of small-cell carcinoma is made should be considered for 2 cycles of cisplatin/etoposide, chemoradiotherapy with concurrent cisplatin followed by 2 cycles of cisplatin/etoposide. This should be the standard of care for all patients with stage Ib2 and above. For patients with Stage Ib1 and below can be considered for primary chemotherapy (regimens for small cell cancer of the lung are used) followed by surgery. Patients who have primary surgery with a subsequent diagnosis of small cell should receive chemotherapy post-operatively with or without adjuvant radiotherapy. Currently, there is no indication for prophylactic cranial irradiation.

Adjuvant

- Fully resected disease any stage
- Accepting that evidence for benefit is uncertain
- Depending on peformance status and comorbidity
- Treatment considered within clinical trial if available

    - Cisplatin & etoposide
    - Carboplatin & etoposide
    - Carboplatin
    - CAV

Palliative

- Incompletely resected; metastatic; recurrent
- Depending on peformance status, comorbidity and previous adjuvant treatment;
- Treatment considered within clinical trial if available

    - Cisplatin & etoposide
    - Carboplatin & etoposide
    - Carboplatin
    - CAV

3.10.2 Incidentally diagnosed invasive cervical cancer

Patients who are diagnosed, as having an invasive cancer of the cervix following a simple hysterectomy should be discussed at the Cancer Centre for consideration of further surgery or radiotherapy / chemoradiotherapy.

3.10.3 Cervical stump carcinoma

Patients who have had a previous sub-total hysterectomy and who are diagnosed as having cervical cancer should be discussed at the Cancer Centre for consideration of radical surgery or radiotherapy depending on the stage of disease. External beam radiotherapy is given to the pelvis – 48Gy in 24F. It is sometimes possible to give brachytherapy using a short intracavity applicator or alternatively an conformal external beam radiotherapy boost of 16.2-18Gy in 9-10 fractions over 11-12 days may be given.

3.10.4 Cervical cancer diagnosed in pregnancy

The management of cervical cancer in pregnancy depends on the stage of both the pregnancy and the cancer, and the wishes of the patient. If it is decided that the pregnancy is to proceed the patient is usually jointly managed by the department of feto-maternal medicine in Leeds, and the gynaecological oncologist/non-surgical oncologist.

4 Endometrial Cancer

4.1 Endometrial Hyperplasia with atypia

The clinical importance of endometrial hyperplasia largely relates to the risk of progression to type 1 endometrial carcinoma.

The revised 2014 World Health Organization (WHO) classification is recommended. This separates endometrial hyperplasia into two groups based upon the presence of cytological atypia: i.e. (i) hyperplasia without atypia and (ii) atypical hyperplasia.

Simple hyperplasia without atypia is unlikely to progress to malignancy and progestogen therapy is usually recommended.[7]

20-50% of women with complex hyperplasia with atypia have or develop malignancy[8][9] and thus TAH, BSO and washings would usually be the recommended management.

In view of the significant risk of an underlying malignancy it is recommended that cases of endometrial hyperplasia with atypia are discussed in a gynaecological MDT meeting (Local or Central).

Certain pathological features (see separate pathology section) make the diagnosis of malignancy more likely and if there is diagnostic uncertainty central pathological review should be requested. It may on occasion be useful to perform a formal radial curettage under GA if there is ongoing diagnostic uncertainty.

MRI is no longer advised based on a local audit presented and discussed at the NSSG study day held at St James's University Hospital on 11th May 2017.

Surgery should be performed by Unit Cancer Lead preferably Laparoscopic hysterectomy with removal of both tubes and ovaries.

Special situations:

The main clinical situations in which definitive surgery may not be considered appropriate would be if the patient wishes to maintain fertility and/or when significant medical co-morbidities are present.

These cases should be discussed in a MDT setting to agree appropriate management and there is a requirement for close surveillance with repeat biopsies during progestogenic therapies.

[7] Kurman, RJ et al. Cancer 1985; 56: 403-12
[8] Zaino, R et al. Cancer 2006; 106: 804-11
[9] Trimble, CL et al. Cancer 2006; 106: 812-9.

4.2 Diagnosis

All patients with PMB should have trans-vaginal ultrasound performed with measurement of endometrial thickness and assessment of the adnexal structures. (see section 4.4 for the ultrasound protocol for suspected endometrial cancer). When endometrial thickness exceeds 4mm an endometrial biopsy should be obtained, either by Pipelle aspiration or at the time of hysteroscopy. Failure to obtain a biopsy using the Pipelle device is an indication for hysteroscopy and curettage.

In pre-menopausal women where malignancy is suspected this should be excluded either by Pipelle aspiration biopsy or hysteroscopy and biopsy. If there is suspicion of cervical involvement at the time of the hysteroscopy, or on imaging a cervical wedge or cone biopsy should also be performed. The grade of tumour in a curettage specimen often correlates poorly with that in the hysterectomy specimen. This is even more apparent when pipelle biopsy is used for diagnosis.

A designated pathologist with a special interest in malignant gynaecological disease should examine the biopsy specimen.

All patients should have an MRI to assess the depth of invasion which in conjunction with histology will dictate whether the surgery is local or central. However it is recognised that MRI may not be appropriate in some cases e.g. claustrophobic or extreme obese patients.

The pathology should be discussed in the local MDT in the presence of a Centre surgeon but referral to the Centre MDT is not necessary unless a further opinion is required or treatment is going to take place at the Centre.

4.3 Imaging

4.3.1 Ultrasound protocol for suspected endometrial cancer

Indications

- Gynaecological symptoms
- Post menopausal bleeding
- No role in asymptomatic screening.
- There is also no role for ultrasound if the woman is going to have hysteroscopy and guided biopsy anyway.

Preparation

- Women should attend with a full bladder.
- The menstrual state should be recorded, as well as any history of gynaecological surgery, IUCD and any medications such as Tamoxifen, HRT etc.
- If cyclical HRT is being taken, the scan should be timed for the withdrawal bleed.

Scan procedure

A transvaginal scan is essential to assess the endometrium and should always be offered in addition to a transabdominal scan.

If the woman has attended with a full bladder the transabdominal scan is done first. This is so that large masses that extend out of the pelvis, omental cake or ascites are not overlooked. The kidneys should be examined as an integral part of any pelvic scan.

The woman then empties her bladder prior to a transvaginal scan. The woman should lie supine with her bottom at the end of the couch and her legs supported by a chair or stirrups. This enables adequate space to manoeuvre the transducer without the couch preventing the handle from being depressed enough to visualise anterior pelvic structures. The alternate method of placing a pillow under the woman's buttocks to elevate them has the disadvantage that pelvic fluid will tend to drain away to the upper abdomen and be missed.

A transvaginal scan is a dynamic investigation in that the relative mobility of the pelvic structures can be assessed. The free hand can also be used to press gently on the lower abdomen to bring structures into view.

Minimum imaging protocol of the endometrium

- Uterus in longitudinal and transverse sections (LS and TS)
- Endometrium in LS and TS
- Measure double layer thickness of endometrium in LS (excluding any fluid)
- Both ovaries
- Any adnexal lesion
- Both kidneys

Extended protocol if abnormality found

- Is the endometrium uniformly or focally enlarged, is it cystic or not?
- Is there any fluid in the endometrial cavity?
- Any submucosal fibroids or endometrial polyps identifiable
- Relative width of endometrium compared to uterus. Is the subendometrial darker halo intact?
- Colour Doppler of the endometrium and uterine arteries
- Search for distant spread in abdomen

Criteria

- A postmenopausal endometrial double layer thickness of 4mm or less effectively excludes endometrial cancer
- Colour flow Doppler signal present within the postmenopausal endometrium raises the likelihood of cancer.
- Low impedance flow (RI less than 0.5) and high peak systolic velocities (over 40cm/s) in a postmenopausal fibroid raise the possibility of sarcomatous change.

Hard copy imaging

- This is recommended in all cases. It is accepted that there is a practice of not taking images of a normal examination in some institutions.

Follow up imaging

- Hysteroscopy and guided biopsy are required for women with postmenopausal bleeding and a thickened endometrium.
- If hysteroscopy is not readily available, then saline infusion sonohysterography and pipelle biopsy may help select those who need further intervention.
- MRI should be performed following a confirmed diagnosis.
- CXR

Conclusion

- The main role of ultrasound, in women suspected of having endometrial cancer, is to identify those that do not require hysteroscopy and biopsy.

4.4 Surgery

4.4.1 Endometrioid carcinoma

Following histological diagnosis, an MRI should be performed to assess the presence of myometrial invasion, which along with the grade of tumour, will determine where surgery is performed.

Stage 1a; G1/2 disease

Discussion of management should occur in the unit MDT in the presence of the centre surgeon. As the risk of lymph node metastasis is very small in this group, routine pelvic lymphadenectomy is not justified, but the pelvic sidewall should be explored and any suspicious nodes removed. Surgery can be performed as an open or laparoscopic procedure and should comprise:-

- Peritoneal washings
- Total Hysterectomy + BSO
- Exploration of pelvic sidewalls with removal of any suspicious lymph nodes

This surgery can take place in the units by the unit surgeon, preferably laparoscopically, but routine removal of pelvic lymph nodes is not required.

Stage 1b (any grade); G3 (any stage) disease

Discussion of the histology and MRI should occur in the centre MDT. Surgery should be carried out in the centre as detailed below and can be performed as an open or laparoscopic procedure. The value of lymph node dissection remains controversial with no national or international consensus. However, whilst it is recognised that it provides no therapeutic benefit, the opinion of the West Yorkshire & Harrogate Gynacology MDT Leads is that the risk of nodal metastasis in this group is sufficient to warrant pelvic lymphadenectomy which should be undertaken to help identify those who may benefit from adjuvant treatment:-

- Peritoneal washings
- Total Hysterectomy + BSO
- Bilateral pelvic lymphadenectomy

Stage 2 disease

In some circumstances, a radical hysterectomy with pelvic lymphadenectomy may be appropriate to avoid subsequent adjuvant radiotherapy but many patients will have a body habitus or comorbidity preventing such an approach, in which case surgery as for 1b disease should be performed. This should be discussed with the clinical oncologist in the centre MDT.

Stage 3 / 4 disease

Surgical treatment should be individualised following discussion in the centre MDT but may involve the following:-

- Peritoneal washings
- TAH + BSO
- Bilateral pelvic lymphadenectomy
- Para-aortic lymph node sampling

- Omentectomy

4.4.2 Clear cell / serous papillary carcinoma

Following histological diagnosis, a CT scan of the chest, abdomen and pelvis should be performed to stage the disease. The pathology and radiology should be discussed in the centre MDT. Surgery should take place in the centre and in the absence of apparent disease outside the uterus, a laparoscopic approach may be used. The procedure should involve:-

- Total Hysterectomy + BSO
- omentectomy
- pelvic lymphadenectomy & para-aortic lymph node sampling
- peritoneal biopsies of suspicious areas
- peritoneal washings

However, some patients may not be fit enough for adjuvant combination chemotherapy that could be potentially required (see chemotherapy treatment) and following discussion in the MDT, just TH + BSO to provide local control of disease may be appropriate, thereby avoiding morbidity from additional staging biopsies that are not going to alter management or outcome.

4.5 Histopathology

The Royal College of Pathologist's publication "Minimum dataset for the histopathological reporting of atypical hyperplasia and adenocarcinoma in endometrial biopsy and curettage specimens and for endometrial cancer in hysterectomy specimens" was last updated in 2001 and an update is due imminently.

This section of the guidelines will be updated following the RCPath guideline update.

4.6 Radiotherapy

4.6.1 No radiotherapy

The following disease stages/grades are not indicated for radiotherapy.

Stage	Histology	Grade	PORTEC3 Trial Eligibility
1A	Endometrioid	1-3	No
1B	Endometrioid	1-2	No
1A	Serous/Clear cell		No

4.6.2 Consider External Beam RT or Vaginal Bracytherapy

Stage	Histology	Grade	PORTEC3 Trial Eligibility
1B	Endometrioid	3	Yes
1B	Serous/clear cell		Yes
2	Endometrioid	3	Yes
2	Serous/clear cell		Yes

4.6.3 Vaginal Brachytherapy

Stage	Histology	Grade	PORTEC3 Trial Eligibility
2	Endometrioid	1-2	Yes

4.6.4 External Beam RT +/- Vaginal Brachytherapy

Stage	Histology	Grade	PORTEC3 Trial Eligibility
3A	Endometrioid	1-3	Yes
3A	Serous/clear cell		Yes
3C1	Endometrioid	1-3	Yes
3C2	Endometrioid	1-3	Yes
3C (1 & 2)	Serous/clear cell		Yes

4.7 Chemotherapy

4.7.1 Introduction

All patients with advanced primary, or recurrent/persistent endometrial cancer should be considered for clinical trials. Such trials are likely to be co-ordinated by the Leeds Cancer Centre at St James's Institute of Oncology.

4.7.2 Adjuvant

- Fully resected stage 3a, 3c or 4 disease
- (Considered for early stage disease with incomplete surgical staging)
- Depending on peformance status; comorbidity; morphology
- Treatment considered within clinical trial if available
    - Paclitaxel/carboplatin - 3 weekly
- If contraindicated consider
    - Cisplatin/doxorubicin
    - Carboplatin/doxorubicin
    - Cisplatin/paclitaxel
- If combination therapy contraindicated, single agent therapy should NOT be used

4.7.3 Palliative

- Incompletely resected; metastatic; recurrent
- Depending on peformance status; comorbidity; morphology and previous adjuvant treatment
- Treatment considered within clinical trial if available
    - Paclitaxel & carboplatin - 3 weekly
    - Paclitaxel & carboplatin – weekly
    - Paclitaxel & carboplatin - weekly dose-dense
    - Cisplatin/Doxorubicin
    - Carboplatin/Doxorubicin
    - Carboplatin - 3 weekly
    - Carboplatin - weekly
    - Cisplatin
    - Paclitaxel - 3 weekly
    - Paclitaxel - weekly

4.8 Hormone therapy

Progestogens have been used in the management of recurrent endometrial cancer after the original report by Kelly and Baker in 1961 of the use of parenteral hydroxyprogesterone caproate. Beneficial results from this and similar trials were mostly confined to a subset of patients with well-differentiated tumour, metastases to the lung, and a long disease-free interval between diagnosis of the primary tumour and the development of metastases. Subsequent trials, using MPA or megestrol acetate, explored the use of high-dose progestogen therapy on better-selected patients through the study of hormone receptor content of tumours and limiting therapy to receptor-positive cases, paralleling breast cancer strategies.

Overall, fewer than 30% of patients (even with the best selection) show objective responses, and the survival of patients with metastatic disease is disappointingly short, except for the rare, extremely hormone-responsive patient. Earlier series reporting very long median survival rates reflect carefully selected patients or loose criteria of response. No dose-response effect for progestogens has been proven. Although some responders have very long survival rates, the median duration of response in most studies does not exceed 10 months. The results of treatment with tamoxifen are generally inferior to those obtained with progestogens. It remains to be seen whether tamoxifen in sequential combination with progestogens (to modulate receptors) will have an advantage over progestogen therapy alone.

Other hormonal manipulations are increasingly under study. These include combinations of tamoxifen and MPA, and other selective oestrogen receptor modulators such as raloxifene, luteinizing hormone–releasing hormone (LHRH) agonists and antagonists, and aromatase inhibitors. It is likely that the same subset of patients responds to these hormonally directed therapies, and no obvious advantage of one agent over another has emerged to date. Moreover, results from small studies may be discordant, reflecting the importance of patient selection in maximizing the probability of response.

Hormone receptors should be measured in patients with recurrent or advanced endometrial cancer, to provide prognostic information and to direct therapeutic strategies.

Patient selection:

Factors predicting for response to hormonal therapy include:

- Endometrioid histology
- Well differentiated
- Long disease free interval
- ER/PR status
- Extra pelvic disease
- Low tumour burden
- Slow progression
- Asymptomatic
- Performance status/co-morbidity

- First choice
    - Alternating Megestrol acetate & Tamoxifen
- Alternatives
    - Megestrol acetate
    - Anastrazole (If progestogens contraindicated)

4.9 Recurrent disease

Patients who originally presented with Stage I disease and who did not receive adjuvant radiotherapy post-operatively are potentially curable by pelvic radiotherapy if they relapse locally within the pelvis. Radical radiotherapy is given:

- 45Gy in 25 fractions to intersection point (ICRU), over 35 days, to whole pelvis followed by phase II boost to site of residual disease, 18 Gy in 10 fractions over 14 days. A further intravaginal boost of 9-12 Gy in 3-4 fractions could be considered where appropriate.

Patients who have previously received pelvic radiotherapy or intravaginal therapy alone are potentially salvageable by surgery but outcomes are often poor.

Patients with distant metastases should be considered for systemic therapy with hormones and/or chemotherapy.

4.10 Uterine sarcomas

Uterine sarcomas comprise fewer than 5% of all uterine malignancies. They can arise from the endometrium or the myometrium. Uterine sarcomas occur primarily in women 40 to 60 years of age. There is an approximately three-fold increase in risk among black women compared to white women. A history of pelvic irradiation is a risk factor, noted in 5-10% of patients with this disease.

Patients with uterine sarcomas should be referred to the specialist team for management.

The histological classification of uterine sarcomas is based upon the type of cells and their site of origin:

- Carcinosarcomas- mixed homologous and heterologous types
- Leiomyosarcoma
- Endometrial stromal sarcoma
- Adenosarcoma

Diagnosis and staging

Whilst the diagnosis of carcinosarcoma can be made on the basis of uterine currettings, the diagnosis of other uterine sarcomas is made from histological examination of the entire uterus, since endometrial sampling alone may be negative.

With the increasing use of pre-operative imaging such as MRI, the suspicion of an underlying uterine sarcoma may be raised. Staging of is the same as for endometrial cancer.

4.10.1 Carcinosarcoma

These account for over 40% of uterine sarcomas. Both carcinomatous and sarcomatous elements must be present in this type of sarcoma. Mixed homologous carcinosarcomas contain only tissue elements that are indigenous to the uterus. Mixed heterologous

carcinosarcomas contain exogenous tissue not normally found in the uterus e.g. bone and cartilage. Carcinosarcomas tend to be aggressive in nature. They metastasise early via haematogenous and lymphatic pathways.

Surgery

Following histological diagnosis, a CT scan of the chest, abdomen and pelvis should be performed to stage the disease. The pathology and radiology should be discussed in the centre MDT. Surgery should take place in the centre, can be open or laparoscopic and should involve:-

- Total Hysterectomy + BSO
- omentectomy
- pelvic lymphadenectomy & para-aortic lymph node sampling
- peritoneal washings

Chemotherapy

Adjuvant

- Accepting that evidence for benefit is uncertain
- Fully resected stage 3a, 3c or 4 disease
- Considered for early stage disease with incomplete surgical staging
- Depending on peformance status; comorbidity
- Treatment considered within clinical trial if available

- Sequential doublet

Palliative

- Incompletely resected; metastatic; recurrent
- Depending on peformance status; comorbidity and previous adjuvant treatment
- Treatment considered within clinical trial if available

- Sequential doublet
- Paclitaxel & carboplatin - 3 weekly
- Paclitaxel & carboplatin - weekly
- Cisplatin/Doxorubicin
- Carboplatin/Doxorubicin
- Carboplatin - 3 weekly
- Carboplatin - weekly
- Paclitaxel - 3 weekly
- Paclitaxel - weekly

Radiotherapy

Indications for the use of adjuvant radiotherapy continue to evolve. Adjuvant radiotherapy has been shown to improve pelvic control but have little effect on overall survival or disease-free survival[101112].

[10] Reed, Nicholas S. The management of uterine sarcomas. Clinical Oncology 2008, 20:470-478.
[11] Reed, NS et al. First results of a randomised trial comparing radiotherapy versus observation postoperatively in patients with uterine sarcomas, an EORTC GCG study. Int J Gynecaol Cancer 2003, 13:4 (abstract).
[12] Wolfson et al A GOG randomised trial of whole abdominal irradiation (WAI) vs cisplatin-ifosfamide and mesna (CIM) as post surgical therapy in stage I-IV carcinosarcoma (CS) of the uterus. Gynecol Oncol 2007, 107:177-185.

In carcinosarcomas the rate of local relapse in stage I and II disease is about 25%; adjuvant pelvic radiotherapy reduces this rate by about a half. In the EORTC 55874 trial the local relapse for patients with carcinosarcoma was 39% with EBRT versus 53% without. However, there was no significant impact on survival. The role of pelvic radiotherapy remains controversial and should probably parallel the indications for high grade endometrial cancer as outlined above.

4.10.2 Adenosarcoma

Adenosarcomas of the uterus have malignant stromal and benign epithelial components. They present as polypoid masses. They have low malignant potential.

4.10.3 Leiomyosarcoma

These account for one-third of uterine sarcomas. Macroscopically, they appear as large (>10cm) yellow solitary masses with soft, fleshy cut surfaces exhibiting haemorrhage and necrosis. Benign leiomyomas and malignant leiomyosarcomas often coexist in the same uterus. However, they are independent entities; leiomyomas probably do not degenerate into leiomyosarcomas. The three main criteria for the diagnosis of leiomyosarcomas are frequent mitotic figures, significant nuclear atypia and the presence of coagulative necrosis of tumour cells. Using these criteria, a risk of malignancy >10%, is identified in those that show diffuse significant atypia, no coagulative necrosis, and a mitotic count >10 mitoses per 10HPF.

Surgery

Following histological diagnosis, a CT scan of the chest, abdomen and pelvis should be performed to stage the disease. The pathology and radiology should be discussed in the centre MDT. As leiomyosarcomas tend not metastasise to lymph nodes, lymphadenectomy is not required but surgery should take place in the centre and should involve:-

- TAH + BSO
- Omentectomy may be considered

Chemotherapy

Adjuvant

- No evidence of benefit
- Treatment considered within clinical trial if available
- Cases should be discussed with the sarcoma MDT

Palliative

- Incompletely resected; metastatic; recurrent
- Treatment considered within clinical trial if available
- Cases should be discussed with the sarcoma MDT

First line

- Doxorubicin

Second line

- Ifosfamide

Radiotherapy

High-grade leiomyosarcomas predominantly relapse by distant spread with a lower incidence of lymph node spread compared to carsinosarcomas however local relapse can be as high as carcinosarcoma. However, in the EORTC 55874 study there was no significant effect of pelvic radiotherapy on local control or survival and therefore pelvic radiotherapy is not recommended following complete excision[1011]. For cases with residual disease after surgery radiotherapy should be discussed.

4.10.4 Endometrial stromal tumours

Endometrial stromal tumours arise from the endometrium and infiltrate the myometrium. They are divided into low and high-grade sarcomas. High-grade stromal sarcomas demonstrate moderate to marked atypical cellular atypia with prominent chromatin clumps and nucleoli. They have >10 mitoses per 10HPF. These tumours are poorly differentiated, without specific features. Their infiltrating pattern suggests that they may originate from endometrial stromal cells. They enlarge and metastasise quickly and are often fatal.

Surgery

Following histological diagnosis, a CT scan of the chest, abdomen and pelvis should be performed to stage the disease. The pathology and radiology should be discussed in the centre MDT. Surgery should take place in the centre, can be open or laparoscopic and should involve:-

- Total Hysterectomy + BSO
- pelvic & para-aortic lymph node sampling may be considered

Evidence is lacking due to the rarity of this tumour. However, in some studies, those in whom the ovaries were preserved had an increased rate of recurrence. Furthermore, following removal of the ovaries, HRT should not be given as this may stimulate recurrent disease. As most cases are diagnosed following an incidental hysterectomy, there is insufficient evidence regarding lymph node sampling for it to be recommended as a routine, although it may be considered in some circumstances.

Hormonal therapy

- Low grade ESS
- Incompletely resected; metastatic; recurrent
- Treatment considered within a clinical trial if available

- Consider hormonal therapy:

- Anastrazole
- Consider GnRH agonist if pre-menopausal
- Megestrol acetate

Radiotherapy

Low-grade endometrial stromal sarcomas have been noted for a protracted clinical course an improved 5-year survival over high-grade endometrial stromal sarcoma. However, there is a high local relapse rate despite an indolent clinical course. The overall rate of pelvic relapse for endometrial stromal sarcomas is about 55%. It is recommended that following complete macroscopic removal pelvic radiotherapy is reserved for relapse.

5 Ovarian Cancer

5.1 National Guidance

The National Guidance states that women with pelvic masses which are judged likely to be malignant on the basis of age, raised CA125 levels, and ultrasound findings, should be referred without delay to the specialist gynaecological oncology team at the Cancer Centre. These Guidelines are written to be consistent with the National Guidance.

5.2 Local Implementation of National Guidance

It is intended that all patients with obvious malignancy or where malignancy is strongly suspected will be referred urgently by fax, phone or via the appropriate Centre Consultant to the Cancer Centre in accordance with the National Guidance. Designated Cancer Units may treat these patients in close co-operation with the Centre.

All patients must be discussed at a MDT meeting locally and then if necessary centrally.

5.3 Initial Clinical Assessment

When a patient is referred to the Cancer Unit for urgent gynaecological assessment, she should be seen within two weeks of receipt of the referral fax.

A thorough clinical history should be taken and the patient should be physically examined. All patients should have blood taken for CA125 (CEA, CA 19.9, CA15.3, Beta HCG, LDH, Inhibin and AFP may also be considered)

Imaging should be arranged – ultrasound, CT or MRI (see section 5.6).

5.4 Emergencies

Whenever possible patients who present as emergencies and who are suspected to have ovarian cancer should be stabilised and transferred to the Cancer Centre. If emergency surgery is necessary and transfer is not feasible the Unit Lead Clinician should if possible be part of the team undertaking surgery.

5.5 Patients unfit for surgery

There will be group of patients considered unfit for surgery, either by age or co-morbidity. These patients should be discussed at the Cancer Centre MDT meeting for an opinion as to whether primary chemotherapy would be an appropriate treatment option.

If primary chemotherapy is contemplated then an image guided core biopsy should be considered if immunocytochemistry on a cell block is not conclusive, using US or CT guidance, and reported by an expert gynaecological pathologist to ensure that the diagnosis is as accurate as possible.

If patients respond to chemotherapy as assessed by repeat CT after 3 cycles, interval debulking surgery should be considered.

5.6 Imaging

Patients with obvious malignancy should proceed to CT of abdomen and pelvis and chest x-ray.

The role of CT is to identify bulky supracolic or suprarenal disease and those with involvement of the GI tract and/or ureters. This group is likely to need a joint surgical approach with colleagues in urology or general surgery. In some cases the extent of disease shown by CT will suggest that primary chemotherapy is more appropriate. In such cases biopsy proof of the diagnosis may be obtained by laparoscopy or image core guided biopsy.

CT will usually provide all the information required to plan surgery.

5.6.1 Ultrasound protocol for suspected ovarian cancer

Indications

- Gynaecological symptoms
- Suspected mass or ascites
- Raised tumour markers
- Family history (within guidelines for screening only and referred by geneticists)

Preparation

- Women should attend with a full bladder.
- The stage of menstrual cycle should be recorded as well as any history of gynaecological surgery

Scan procedure

A transabdominal scan should always be done as well as a transvaginal scan. If the woman has attended with a full bladder the transabdominal scan is done first. This is so that large masses that extend out of the pelvis, omental cake or ascites are not overlooked.

The kidneys should be examined as an integral part of any pelvic scan. The woman then empties her bladder prior to a transvaginal scan. The woman should lie supine with her bottom at the end of the couch and her legs supported by a chair or stirrups. This enables adequate space to manoeuvre the transducer without the couch preventing the handle from being depressed enough to visualise anterior pelvic structures.

The alternate method of placing a pillow under the woman's buttocks to elevate them has the disadvantage that pelvic fluid will tend to drain away to the upper abdomen and be missed. A transvaginal scan is a dynamic investigation in that the relative mobility of the pelvic structures can be assessed. The free hand can also be used to press gently on the lower abdomen to bring structures into view.

Minimum imaging protocol

- Uterus, longitudinal section (LS) and transverse section (TS). Include view of endometrial thickness in LS. Identify any free fluid and search the adnexae out to the iliac vessels
- Both ovaries, in both LS and TS. Measure size.
- Both kidneys

Extended protocol if abnormality found

- Lesion location
- Cystic or solid
- Thickness of walls and septae if any
- Any nodules or echogenic, shadowing plugs
- Mobile or adherent
- Tender or not
- Colour Doppler, describe distribution of any flow found (i.e. peripheral or Central)
- Spectral trace of areas of abnormal flow. Calculate RI, PI and PSV

- Look for distant spread, ascites, pleural effusions, omental cake and serosal deposits around the liver and spleen.

Hard copy imaging

- This is recommended in all cases. It is accepted that there is a practice of not taking images of a normal examination in some institutions.

Follow up imaging

Ovarian cysts of less than 2.5cm in diameter in a woman still having menstrual cycles are regarded as normal physiological follicles or lutea and are not reported.

Most isolated ovarian cysts larger than 2.5cm, even those that appear complicated, in a woman who is still having menstrual cycles will spontaneously resolve during the next two menstrual cycles. Consequently, the best imaging strategy is to repeat the ultrasound in 6 to 8 weeks. Simple ovarian cysts of less than 5cm in a postmenopausal woman can also be safely followed with further ultrasound exams. These lesions are often stable and do not regress for long periods of time.

If ovarian cancer is diagnosed by ultrasound, then staging and follow up should be done with CT.

If an adnexal mass presents a conundrum then MRI should be used for problem solving rather than CT.

Intervention

Ultrasound is ideally suited to guiding aspiration of pleural effusion or ascites. It also enables guided biopsies to be taken either transabdominally or transvaginally. Indications would be to determine the primary tumour in someone who otherwise is not suitable for surgery or to differentiate recurrent tumour from residual fibrosis in those on follow up.

Conclusion

Ultrasound should be readily available without restriction for gynaecological symptoms. It is an excellent first imaging tool that will often provide a diagnosis without recourse to other imaging tests. If an abnormality is found the ultrasound examination should be extended to look for other likely sites of disease. Time solves many problems.

5.6.2 CT protocol for ovarian cancer

Indications

- Staging at diagnosis to determine disease extent.
- Definition of the safety and options for image guided core biopsy.

- After surgery to document residual disease and to monitor response to chemotherapy.
- Monitoring of response to primary chemotherapy.
- Assessment of suspected recurrence.
- CT is not indicated in the further investigation of small adnexal masses detected by ultrasound and MRI is the preferred investigation for suspected benign disease e.g. dermoid, endometrioma (Section 5.6.3).

Patient preparation

Oral contrast e.g. 1L of 3% Gastrografin over 1 hour prior to examination with the final cup taken just before scanning to refill the stomach. Large bowel opacification is improved by 'overnight' preparation e.g. 5mls of Gastrografin taken in 200ml water 6 to 8 hours before scanning from an ampoule which can be sent out with other patient instructions.

Some patients prefer other oral contrast agents e.g. dilute barium agents.

Areas to be covered

Abdomen and pelvis following intravenous contrast should be used unless there is a contraindication e.g. 100 mls of 300 strength injected at 3ml/sec. The liver and spleen should be imaged commencing at about 65 seconds after the start of the injection.

Image inspection and display

Liver images should be displayed at appropriate pre-settings (recommended WW200, WC 70) , the whole abdomen and pelvis at soft tissue settings (WW350-400, WC 40-50) and the lung bases should be displayed at WW1000, WC-700.

Multislice CT allows high quality reformatted images in the coronal and sagittal planes and these can be useful to assess structures such as the subdiaphragmatic spaces and the mesenteries.

Reporting

The CT report of a pre-surgical study should give an indication of disease bulk, sites of potential surgical difficulty and the likely stage at diagnosis with reference to the FIGO classification.

Post-operative baseline studies should identify sites of residual disease when present with measurement in two dimensions. Clear anatomic location of such lesions using table position or slice number is desirable.

Hydronephrosis, likely cause and site, should be indicated for consideration of stenting. The presence of impending or actual bowel obstruction and venous thrombosis should also be highlighted.

Problem solving

It is preferable to review images before the patient gets off the CT table to ensure adequate bowel opacification to allow distinction of disease from unopacified bowel. Use of additional oral contrast, supine or decubitus positions or delayed imaging may help to distinguish between disease and pseudotumour.

Masses may be seen following surgery at the vaginal vault, pelvic sidewall and other sites of biopsy or debulking which may mimic disease. Ultrasound guided transvaginal biopsy or drainage may be valuable in distinction of residual disease from infection/ haematoma. Occasionally MR imaging may be of value but its use should follow multidisciplinary discussion.

Image guided biopsy and drainage

Ultrasound is the primary imaging modality for ascitic drainage and a wide variety of biopsy procedures.

Indications for omental / peritoneal core biopsy in the diagnosis of peritoneal carcinomatosis

- history of malignancy which may mimic ovarian cancer e.g. breast, colon
- uncertain diagnosis e.g. with no adnexal mass (as in primary peritoneal cancer)
- patients unfit for primary debulking surgery
- patients with extensive disease considered beyond the scope of debulking surgery

Image guided core biopsy, using US or CT, of omental or peritoneal masses is an alternative to surgical biopsy as a primary diagnostic test and may avoid the need for endoscopy, barium studies to look for a primary site. This should follow multidisciplinary discussion. Core biopsy with cytokeratin analysis achieves a complete diagnosis including subtype and grade in more than 90% of cases.

Biopsy and palliative drainage may be performed as a combined procedure.

It is reasonable to biopsy an ovarian mass if after MDT discussion this is the safest site for biopsy in a woman with established peritoneal carcinomatosis. US offers the option of the transvaginal route for some pelvic masses.

Reassessment

The abdomen and pelvis should be re-examined using an identical technique. Previous studies should be available at the time of CT examination to ensure that known sites of disease are adequately assessed.

When possible an indication of disease response should be given. Patients within clinical trials may require more detailed response assessments using WHO / SWOG or RECIST criteria. Size and site of new disease or specific complications should be clearly indicated as above.

For most patients with adequately debulked ovarian cancer CT should be performed at baseline after surgery and at the end of chemotherapy. For patients with inadequately debulked disease, otherwise at high risk of progressive disease or difficult to monitor clinically/biochemically, e.g non CA-125 producers, a repeat CT examination midway through treatment is a reasonable policy.

5.6.3 MR imaging of the indeterminate adnexal mass

MR imaging allows correct diagnosis as benign or malignant in about 90% of indeterminate masses.

Basic technique:

- Use of a 1.0 to 3.0T machine
- Placement of an IV cannula
- Administration of a smooth muscle relaxant
- T2W sagittal imaging of the pelvis
- A pair of T1W and T2W sequences in the same plane to assess the mass
- T2W imaging along the long axis of the uterus

This allows identification of the mass, its signal characteristics and usually its site of origin i.e. uterine or ovarian.

Masses are either:

- T1 bright
- T2 solid, either very dark or intermediate in signal
- Complex cystic or cystic-solid

Additional problem solving sequences are then used:

- T1 bright masses require fat suppressed T1W imaging to see if this bright component is fat or blood
- T2 dark solid masses are often defined as uterine fibroids or ovarian fibromas by these basic sequences which show the presence or absence of a stalk from the uterus
- Some T2 dark solid masses require additional oblique T2W images to look for such a stalk
- Complex cystic or cystic-solid masses require contrast-enhannced T1W images to look for enhancing mural nodules, abnormally thickened septa or walls or frankly solid areas with or without necrosis
- T2 solid masses which are not obvious fibroids or fibromas also require CET1W images

Outcome

- Haemorrhagic masses, fat containing dermoid tumours, fibroids and ovarian fibromas are the commonest indeterminate masses. These can be managed on the basis of symptoms.
- All complex cystic, cystic-solid or enhancing solid masses should be discussed in the Centre MDT.
- Probable cancers require additional CT staging.
- Solid enhancing adnexal masses may represent metastases to the ovary from the GI tract and these sites need careful review on the staging CT.

5.6.4 When to perform chest CT

There is no indication for routine chest CT. Absence of pleural or mediastinal disease on the lung base images effectively excludes supradiaphragmatic metastasis. For patients with Stage IV disease - pleural, supraclavicular nodal metastasis - it is reasonable to perform chest CT.

Women in remission

There is no justification for surveillance CT.

Women with suspected recurrence

CT may be helpful but should only be performed after expert clinical assessment. CT may be rendered useless if barium studies of the GI tract are performed. Imaging options should be discussed with a radiologist. Symptom investigation and palliation are as important as disease restaging. Biopsy of suspected recurrent pelvic sidewall and retroperitoneal masses is rarely indicated as most women have raised CA-125 or other features of recurrence.

Women with suspected recurrence and normal CT

In certain situations treatment may be recommenced without further imaging. In others further symptom investigation is required. With asymptomatic CA-125 elevation and normal CT a repeat study in 2 months may identify progression.

5.6.5 Other imaging

All patients should undergo chest x-ray, to exclude a pleural effusion or parenchymal pulmonary metastasis. If a pleural effusion is detected, this should be aspirated either clinically or under ultrasound-guided control, and fluid sent for cytological examination.

Staging CT should then include the chest.

As radiological investigation results become available they should be reviewed in the Cancer Centre Gynaecology MDT but this should not delay patient assessment or referral.

5.6.6 Imaging the treated patient

There is no requirement for serial CT examinations of women believed to be in remission. Follow up is based on serial CA125 measurements and clinical review with CT performed in response to clinical concern.

As minority of women are CA125, marker, negative (MN). These women may benefit from serial CT at 6, 12 and 24 months after complete remission with an early 3 month post-treatment scan for women with CT measurable residual disease at the end of treatment.

5.7 Surgery

5.7.1 Early Stage Disease

Discussion of management should occur in the unit MDT in the presence of the centre surgeon. For disease that appears confined to the ovary, a staging laparotomy through a midline incision should be performed which should comprise :-

- TAH + BSO
- omentectomy
- pelvic & para-aortic lymph node sampling
- peritoneal biopsies of suspicious areas
- peritoneal washings
-

All cysts with RMI > 250 and all cysts with MRI < 250 with suspicious features on the MRI scan should be discussed at the centre MDT. If the Centre review suggests malignancy, surgery will be undertaken in the centre but if not, surgery can be performed locally. All cases of suspected ovarian cancer and their management will be ratified by the specialised Gynae MDT. The outreach model for gynaecological cancer, where a visiting surgeon is present at the local MDT allows for local decision making to speed the patient pathway followed by central endorsement of these decisions.

The presence of ascites may indicate peritoneal disease not detectable on imaging and such patients should should be considered for surgery in the centre.

Fertility Sparing Surgery

In some circumstances e.g. young age; family not complete, it may be appropriate to remove only the ovarian mass and perform staging biopsies but leave the uterus and normal ovary in situ.

5.7.2 Advanced Disease

Primary Cytoreductive Surgery

Following review of the CT scans in the centre MDT, if it is felt that the patient can be optimally debulked i.e. to nodules <1cm, then primary surgery should be undertaken to remove as much of the tumour and its metastases as possible, before subsequent chemotherapy is instituted. On occasion, bowel surgery may be required and as part of the multidisciplinary approach, it may be appropriate to involve the colorectal surgeons in the operation.

Whilst the CHORUS study is running, such patients should be considered for this trial but if they decline, primary surgery should be undertaken.

If optimal debulking is not possible at the time of surgery, a second attempt may be appropriate after 3 cycles of chemotherapy but should be discussed in the MDT.

Interval Debulking Surgery

This is an operation performed after a short course of chemotherapy (usually 3 cycles) with the intention to remove as much primary and metastatic disease as possible. Primary chemotherapy with a view to IDS should be considered in the following situations:-

- Disease not amenable to optimal debulking with primary surgery
- Where there is a high chance of stoma
- Where there is poor performance status or has low or rapidly falling albumin
- Where there is significant acute or chronic co-morbidity leading to increased risks from surgery

Although not all these patients will ultimately undergo IDS, they should be considered for it through the MDT.

Laparoscopic Surgery

Laparoscopic surgery has a limited role in ovarian cancer but may be considered in the following circumstances:

- For diagnostic purposes when image guided biopsy has been unsuccessful
- For staging of disease when the histology results have shown an unexpected ovarian carcinoma
- For removal of indeterminate ovarian masses

Secondary Cytoreductive Surgery

This operation is usually reserved for those with persistent disease on the completion of a planned course of chemotherapy or for localised recurrence. Such surgery is uncommon and whether it is appropriate should be discussed in the central MDT.

Palliative Secondary Surgery

In general, surgery should be kept to a minimum. Correction of intestinal obstruction should be reserved for patients who appear most likely to benefit, such as tumours that have been chemosensitive, where further chemotherapy is appropriate and for single sites of obstruction. It would be anticipated that patients who undergo such procedures would live for several month or longer.

5.8 Histopathology

Macroscopic description

Dimensions	The dimensions of the tumour are to be measured in millimetres. The measurement should be given in three dimensions. If the mass is cystic and collapsed then the measurements must be made and appended with the comment “in the collapsed state”.
Weight	The specimen should be weighed in grams or kilograms as appropriate.
Capsule	A comment on the integrity of the capsule is important i.e. intact or ruptured, smooth or irregular. The presence of any papillary or solid areas protruding from the capsular surface should be commented on. If the lesion is intact the capsular surface should be dried and the capsular surface painted with ink and this should be fixed with acetic acid. (Alcian blue or coloured paint may be used instead of ink).
Cyst structure	Unilocular or multilocular – quote range of size of locules.
Cyst contents	These may be watery fluid or mucoid material. The presence of hair or blood should be commented upon.
Cyst lining	A description of any papillary or solid areas, areas of haemorrhage, necrosis or yellow tan areas. The thickness of the cyst wall should also be remarked upon and maximum thickness measured.

Sampling of tumour

Tumour	It is generally accepted sampling protocol to take one block for every 10mm diameter of the ovarian neoplasm. Where the lesion is a thin-walled cyst more than one portion of tissue can be fitted into a cassette. Blocks should be taken preferentially from solid areas, finely cystic areas, papillary areas and soft fleshy areas i.e. any abnormal area. Extensive sampling of the capsule is vital, as it will influence subsequent management of the patient. A note of these blocks should be made. Blocks must include any capsular breach or areas where there are capsular irregularities and adhesions. Sample any residual ovary away from tumour.
Fallopian Tube (if present)	Sample as for non-neoplastic disease. Blocking any irregular areas.

Hysterectomy and bilateral salpingo-oophorectomy as part of a staging procedure for malignant disease of the ovary

Ovarian neoplasms will arrive as part of a total hysterectomy specimen accompanied by omentum, peritoneal biopsies and lymph nodes. It is important that the sites are identified on the specimen containers upon receipt and checked with the special request form. These headings must appear on the macroscopic and microscopic part of the report.

Hysterectomy specimen	The uterus is described and blocked as for non-neoplastic uteri. Additional blocks must be taken to include pouch of Douglas or cornual serosa to seek evidence of metastatic disease. Also additional blocks must include any abnormality.
Omentum	When there are focal abnormalities within the omentum these are sampled and their size is recorded. When there is no visible abnormality the omentum is laid flat, measured and sliced at 1cm intervals and a full thickness strip is taken every 3 to 5cm through the full width of the tissue.
Peritoneal biopsies Dimensions	Presence or absence of any macroscopic tumour deposits. Any other abnormality. They are blocked in their entirety and two levels examined.
Lymph nodes	The piece of tissue submitted as lymph nodes is measured in three dimensions. Any palpable lymph nodes are removed and sectioned transversely and embedded in one cassette per lymph node using more cassettes per lymph node if the lymph node is large. After the palpable nodes are identified and removed, the remained of the fatty tissue is processed in its entirety.

Histological reporting

Checklist

- Histological type
- Histological grade (grade 1-3)
- Capsular penetration
- Presence of any metaplasia
- The tumour may predominantly be of a certain histological type with a smaller component of another type. This must be recorded in the report.
- Lymphovascular space permeation by tumour
- The state of the non-neoplastic ovary and in particular if there are areas of endometriosis relevant in associated with clear cell and endometrioid adenocarcinoma
- A comment about the fallopian tube and paratubal tissues

5.8.1 Prophylactic Oophorectomy for Familial Ovarian Cancer

Dissection and sampling

The ovaries are carefully measured, external appearance noted and then serially blocked.

The ovaries should be handled with care to preserve as much as possible of the surface epithelium.

The fallopian tubes are examined in their entirety. The tubal blocks may be taken transversely but the fimbrial end must be sampled longitudinally to facilitate recognition of in-situ neoplasia. Facilitation of this may require p53 and Ki67 immunohistochemistry.

If the uterus has been removed as part of this procedure, examine routinely as for non-neoplastic disease, but in addition blocks must be taken to allow full examination of pelvic peritoneum to include pouch of Douglas, meso-ovarium, mesosalpinx, broad ligament and round ligament.

5.8.2 Minimum Dataset

Please also complete the form “Reporting Proforma for non-benign epithelial ovarian tumours” (Appendix C in the RCPath dataset publication).

5.8.3 Additional Information

Additional detailed notes for specimen handling and reporting are available in the Royal College of Pathologists publication “Datasets for the histopathological reporting of neoplasms of the ovaries and fallopian tubes and primary carcinomas of the peritoneum” which is available via this website link http://www.rcpath.org/index.asp?PageID=1605

5.9 Chemotherapy

For epithelial ovarian carcinoma and including primary peritoneal carcinoma and fallopian tube carcinoma. Ovarian carcinosarcoma should also be treated according to the following algorithm.

5.9.1 First line

- Treatment considered within clinical trial if available
- Stage 1c or above (Surgical stage 1c only if other adverse features)
- Any stage with adverse features (G3 or clear cell)
- Early stage if surgical staging incomplete
- Depending on performance status; comorbidity; patient choice; developing toxicity or allergy

- Paclitaxel & carboplatin - 3 weekly
- Paclitaxel & carboplatin - weekly
- Paclitaxel & carboplatin - weekly dose-dense
- Carboplatin - 3 weekly
- Carboplatin – weekly

- Cisplatin – 3 weekly
- Paclitaxel & cisplatin
- Docetaxel & carboplatin

5.9.2 Second & subsequent line

- Treatment considered within clinical trial if available

Depending on
- performance status; comorbidity; patient choice
- previous response; duration of response
- time since previous exposure
- previous toxicity; allergy

- Paclitaxel & carboplatin - 3 weekly
- Paclitaxel & carboplatin - weekly
- Paclitaxel & carboplatin - weekly dose-dense
- Carboplatin - 3 -4 weekly
- Carboplatin - weekly
- Cisplatin
- Paclitaxel & cisplatin
- Paclitaxel - 3 weekly
- Paclitaxel - weekly
- Carboplatin & gemcitabine
- Docetaxel & carboplatin
- Cisplatin & etoposide
- Liposomal doxorubin
- Topotecan - 3 weekly
- Topotecan - weekly
- Tamoxifen
- Anastrazole
- Etoposide

5.9.3 Supportive drugs

- Darbepoietin
    - platinum induced anaemia (According to NICE guidance)
- GCSF
    - Secondary prophylaxis for treatment with curative intent

5.10 Radiotherapy

This does not form part of the standard management of women with ovarian cancer. However, it may be indicated in selected cases where disease is localised, following discussion in the specialist MDT.

There is a group of patients with ovarian cancer who has a history of persistent disease in the pelvis or a tendency to relapse in the pelvis following primary surgery and chemotherapy, with no evidence of disease radiologically outside the pelvis. The standard treatment for such patients is further chemotherapy. Radiotherapy is recognised to as an effective treatment modality in the management of ovarian cancer but its use is limited by its toxicity when given to large abdomino-pelvic fields to a dose required to control disease.

In the St James's Institute of Oncology we have evolved a protocol for patients with pelvic disease who have previously received chemotherapy who have relapsed in the pelvis for the first or second time, that involves either further chemotherapy and/or debulking surgery followed by high dose pelvic radiotherapy. This is given in two phases with 30 Gy in 15 fractions given daily, mid-plane dose to the whole pelvis, followed by a CT planned boost to the site of residual disease of 20 Gy in 10 fractions given daily to ICRU intersection point. Alternatively, as the aim of the treatment is high grade palliation a single phase treatment encompassing the primary tumour plus margin of 50 Gy in 25 fractions can be considered.

Radiotherapy is useful in the palliation of symptomatic pelvic disease in the context of widespread disease (extra-pelvic sites). Commonly used regimens include:

- 40 Gy in 15 fractions to pelvis
- 20 Gy in 5 fractions
- 10 Gy 1 fraction repeated if symptoms persist no more than once every 6 weeks for a maximum of 3 times

5.11 Recurrent Disease

The specialist gynaecology oncology MDT at the Cancer Centre should review all patients who develop recurrent disease. Their case should be discussed in the Centre MDT meeting and an appropriate individualised treatment plan formulated.

Patients should be offered entry into clinical trials whenever appropriate.

Many women with recurrent ovarian cancer will appropriately be treated with a further course of chemotherapy. The choice of drug depends on the agent(s) previously used and the time-period before relapse. The possibility of chemotherapy-resistant disease should be considered if women fail to respond to two different types of chemotherapeutic agents.

5.12 Germ cell tumours

5.12.1 Chemotherapy

- Should be considered for all cases
- Stage I disease may be considered for intensive surveillance

- First line
    - BEP/EP

- Second line
    - TIP

5.13 Granulosa cell tumours

5.13.1 Chemotherapy

- Incompletely resected; metastatic; recurrent
- May be considered as adjuvant therapy in high risk early stage disease
    - BEP (Granulosa)
    - Paclitaxel – weekly

6 Vulval Cancer

6.1 National Guidance

The National Guidance states that all patients with vulval cancer should be referred without delay to the specialist gynaecological oncology team at the Cancer Centre. These Guidelines are written to be consistent with the National Guidance.

6.2 Local Implementation of National Guidance

It is intended that all patients with histologically confirmed or obvious clinical malignancy will be referred urgently by fax, phone or via the appropriate Centre Consultant to the Cancer Centre.

All patients must be discussed at a MDT meeting.

6.3 Initial Clinical Assessment

When a patient is referred to the cancer Unit for urgent gynaecological assessment, she should be seen within two weeks of receipt of the referral letter.

Patients will fall into 2 categories: -

1. Obvious malignancy
   - These patients should be referred directly without further investigation to the specialist team MDT.

2. Malignancy suspected
   - These patients require urgent biopsy.

6.4 Biopsy for vulval cancer

The diagnosis of vulval cancer should be based on a representative biopsy of the tumour that should include the area of epithelium where there is a transition of normal to malignant tissue. Biopsies should be referred to a pathologist with a specialist interest in gynaecological pathology. The type of biopsy will depend upon the site, size and symptoms associated with the lesion and the general condition of the patient.

In lesions measuring two centimetres or less in diameter a wide local excision biopsy may be an appropriate first procedure (should include a surrounding zone of normal tissue 1 cm in width and depth). It should confirm the diagnosis and provide additional data regarding the need for further treatment.

The remainder should have diagnostic biopsies that are of a sufficient size and orientation to allow quality pathological interpretation. Diagnostic biopsies should also contain the zone of transition from normal to abnormal epithelium (see Section 6.11)

There may be exceptions to these rules. If, for instance an elderly woman with major medical problems and a severely symptomatic lesion presented, wide local excision of the primary lesion will achieve diagnosis and symptom relief although may not be adequate total treatment for the lesion.

All pathology specimens should be retained and reviewed by a specialist in gynaecological pathology.

Although not essential, pre-biopsy photographs are of value in planning treatment, particularly if the diagnostic phase and treatment phases are conducted in separate units.

6.5 Referral Pathways – Local MDT and Specialist MDT

When the clinical findings are suggestive of a vulval malignancy, the patient should be referred to a local gynaecologist with experience in gynaecological oncology or to the nearest specialist MDT.

If the diagnosis is suspected or confirmed outwith a specialist MDT, referral to the nearest specialist MDTshould take place.

The patient should be seen within two weeks of referral and definitive treatment commenced no later than 6 weeks following diagnosis.

Referral should include sending all relevant histopathological material to the specialist gynaecological pathologist in the specialist MDT.

6.6 Confirming the Diagnosis

The diagnosis of vulval cancer should usually be confirmed by biopsy prior to definitive surgery. In certain situations where the clinical diagnosis is apparent and the patient very symptomatic, i.e. heavy bleeding and or pain, definitive surgery to the vulval lesion may be performed. Surgery to the groin nodes should only be performed once a histological diagnsosis has been confirmed.

When the lesion is small, less than 2 cm, it may be appropriate to excise the entire lesion. In this situation a clinical photograph taken prior to surgery can be helpful when the patient is referred for further treatment.

6.6.1 Milestones

Once the diagnosis is confirmed the patient should be seen within two weeks of first visit. Referral to the lead clinician for gynaecological cancer should occur and if such a service is not available within the hospital, referral to the nearest specialist MDT should be arranged.

The patient should be informed of the diagnosis and counselled as to the proposed management plan. Results of previous investigations should be available at this visit. Management options will include surgery, and/or radiotherapy (with or without concurrent chemotherapy).

The appointment should allow for adequate time to counsel and support the patient and if at all possible the patient should be introduced to the Gynaecological CNS at this stage.

Surgery should be undertaken within four weeks of the second visit although in exceptional circumstances a six week interval may be acceptable.

If a surgical approach is not an option the patient should be referred to a clinical oncologist with a specific interest in gynaecological malignancy and should expect to receive an appointment within two weeks. Treatment should commence within four weeks of the decision to treat by radiotherapy although in exceptional circumstances a six week interval may be acceptable.

The patient's general practitioner should be informed of the diagnosis and management plan within seven working days of the clinic visit.

6.7 Communication and Counselling

Patients should be provided with as much relevant information as possible in both a timely and sensitive manner. Some will require more time to come to terms with their diagnosis and may require access to the team during the interval between diagnosis and planned treatment. Ideally the patient should be counselled in the presence of a family member, friend or other advocate unless she does not wish this. The patient should have access to gynaecological oncology nurse specialists, lymphoedema specialists and psychosexual counselling during this pre-treatment phase.

It is vitally important to ensure adequate communication with the primary care team as well as the other disciplines involved in the care of the patient.

General practitioners should receive information regarding their patient within seven working days of visit/treatment.

All women should be informed of their diagnosis, the consequences of the disease and the management plan. There may be rare exceptions where this is either not possible or not in keeping with the wishes of the patient.

It should be clear as to which team is responsible for primary follow-up after treatment. The patient should be informed of the likely pattern and duration of follow up. The general practitioner should be kept informed of all follow-up visits.

Centres managing vulval cancer should be able to provide suitable written material for patients.

6.8 Investigations

6.8.1 Biopsies

After confirming the diagnosis, the objectives of further investigations are to:

- Determine the extent of the disease
- Determine suitability for treatment

The following investigations are suggested for the majority of patients although one must accept that in a predominantly elderly population this cannot be considered either complete or prescriptive, as each case must be fully assessed according to individual need:

- Full blood count.
- Biochemical profile.
- Chest X-ray.
- Cervical smear if not done and cervix in situ.
- Locally available and appropriate imaging to assess for concurrent pelvic pathology and retroperitoneal nodes.
- MRI is the best test to assess local disease extension.
- CT is the single most useful test for advanced metastatic disease.
- US may help to assess the groin nodes.
- Biopsy of any clinically suspicious nodes or other metastases where the result will alter management (i.e. may elect for radiation prior to surgery).

6.9 Management and Treatment

6.9.1 Rationale

The management of this rare cancer may vary considerably from quite simple to very complex. Each case should be considered on its merits and an agreed plan of management devised by the gynaecological cancer team. Factors such as tumour size, location, medical fitness and the wishes of the patient will all influence management. The management of the nodes and the primary tumour should be considered on their own merits.

6.9.2 Early stage disease

Small tumours in the absence of clinically suspicious or involved groin nodes should usually be managed surgically. Surgery to the primary tumour should be radical to remove the tumour yet conservative to avoid unnecessary surgical and psychological morbidity. Wide radical local excision with a minimum margin of I cm of disease free tissue is often sufficient. Excision of atypical skin (Lichen sclerosus or VIN) affecting the remainder of the vulva should be considered as these areas might contain separate foci of invasion. A pre-operative vulvoscopy may help in the planning of surgery. Removal of any lichen sclerosus or VIN skin need not be to the same depth as that for invasive disease unless occult invasion is suspected.

6.9.3 Factors influencing surgical management

Depth of invasion

Dissection of the groin nodes should be performed when the depth of invasion is greater than I mm (Stage Ib or worse) or the maximum diameter of the tumour is greater than 2 cm (Stage II or worse). This surgery can often be undertaken through separate incisions (triple incision technique) as the incidence of skin bridge recurrence in early stage disease is very low.

Lateral vulval tumours

Extensive crossover of lymphatic channels of the vulva may result in nodal involvement of the contralateral groins in addition to the ipsilateral groin nodes. Therefore bilateral groin node dissection is usually required. However in very lateral tumours (the medial edge of the tumour must be at least 2 cm lateral to the midline of the vulva) only an ipsilateral groin node dissection need initially be performed. If the ipsilateral nodes are subsequently shown to be positive for cancer, the contralateral nodes should also be excised or irradiated (research recommended) as the nodes are more likely to be positive in this scenario.

Groin node dissection

Appropriate groin node dissection is the single most important factor in decreasing mortality from vulval cancer. However, groin node dissection should be omitted if the patient has Stage Ia disease. It is recommended that the superficial groin node as well as the deep femoral nodes be removed. Superficial groin node dissection alone is associated with a higher risk of groin node recurrence. There is no specific recommendation about the need to remove the long saphenous vein.

6.9.4 Factors influencing the need for adjuvant radiotherapy

Surgical margins

The incidence of vulval recurrence is related to the measured disease free surgical margin as measured in the histopathological specimen. The risk of recurrence increases as the disease free margin decreases (L8 mm 0%, 8-4.8 mm 8%; <4.8 mm 54%). Eight millimetres is usually taken as the minimum margin for not prescribing adjuvant radiotherapy.

Groin node positivity

Adjuvant radiotherapy should be considered when two or more lymph nodes are involved with metastastic disease or there is extra capsular spread in any node. Adjuvant radiotherapy should be given to the affected side and should include the pelvic nodes. Whether both sides should be irradiated is a subject for further research.

6.9.5 Other pathological factors influencing outcome

The presence of infiltrative growth patterns, compared with a pushing pattern, is associated with a higher local recurrence rate. Lymphovascular space involvement (LVSI) is also associated with an increased local recurrence rate. LVSI has not been associated with an increased risk of groin node metastasis. Both factors are markers of poor prognosis, but these factors do not indicate the need for adjuvant treatment.

Research is required to establish the influence of these factors on the outcome of this disease.

6.9.6 Advanced Vulval Cancer

Multimodality treatment is of increasing importance in the management of advanced vulval cancer. The use of pre-operative radiotherapy may allow for sphincter preserving surgery. Radiotherapy may also be of use in place of surgery for histologically proven involved groin lymph nodes. It is unknown whether post radiation groin node removal is advantageous in terms of outcome.

Surgery to the primary lesion

The size and location of the tumour will influence the surgical approach. Wide radical local excision with a minimum of I cm disease free margin may be used however, some tumours will require a radical vulvectomy. If these surgical approaches risk sphincter damage, leading to urinary or faecal incontinence, treatment by radiotherapy should be considered either with curative intent or to reduce tumour volume to permit less destructive surgery. Two studies have suggested that preoperative chemoradiation in advanced vulval cancer reduced the need to perform defunctioning stomas. Reconstructive surgical techniques should be employed to enable primary surgical closure and reduce morbidity due to scarring.

Management of the groin nodes

Groin node dissection should be undertaken when there are clinically suspicious groin nodes present. In cases with large primary lesions and clinically suspicious nodes, a radical vulvectomy with 'en bloc' groin node dissection may be warranted. In cases with fixed or ulcerated groin nodes radiotherapy to the affected groin and pelvic nodes should be considered rather than surgery. Pathological assessment of these nodes should be undertaken prior to radiotherapy either by open biopsy or fine needle aspiration cytology.

6.10 Surgical management of non squamous vulval cancer

6.10.1 Carcinoma of the Bartholins gland

This is a rare vulval cancer. Histologically it can be either a squamous carcinoma or adenocarcinoma. The current evidence base is insufficient to suggest different management from squamous tumours.

6.10.2 Basal cell carcinoma, Verrucous carcinoma and Superficially invasive squamous carcinoma (up to 1mm invasion)

These squamous variants are rarely associated with lymph node metastases and can be managed by wide local excision. Basal cell carcinomas are also amenable to treatment by radiotherapy, which should be the preferred treatment if resection would compromise function (i.e. sphincter damage).

6.10.3 Malignant melanomas

This group of tumours have not been shown to benefit from block dissection of the groin. Wide local excision is preferred. Relapse in this subgroup is high and closely correlates with the depth of invasion (Clarke's levels) and as yet there are no new strategies to minimise the risk of relapse in melanomas.

6.11 Histopathology

6.11.1 Clinical information

The clinician should provide an accurate description of the site and appearance of the gross lesion. This can be important if the suspected diagnosis is, for example, carcinoma of Bartholin's gland or verrucous carcinoma. The request should also indicate whether the biopsy was excisional or diagnostic.

6.11.2 Indications for biopsy

Suspected intraepithelial neoplasia (squamous, Paget's disease, melanocytic)
Tumour or suspected tumour

6.11.3 Types of specimen

- Punch biopsy
- Small ellipse
- Excision biopsy
- Local/radical excision with or without nodes

6.11.4 Sampling the types of specimen

Punch Biopsy	The size of the biopsy should be recorded. Usually taken in the context of VIN or other dermatological disorder. The sample should be examined in its entirety at several levels. Care should be taken to ensure that the sections are cut at right angles to the surface of the skin.
Small ellipse of skin	The biopsy should be measured in three dimensions, care being taken to indicate which is the depth of the specimen. The skin should be cut at right angles to the long axis of the specimen at approximately 2-3 mm intervals. All the tissue should be examined histologically.
Excision biopsy	The tissue should be measured. The size of the lesion and the distance of the lesion from the resection margins should be reported. The sample should be cut so that the pathologist can identify the nature of the lesion, the condition of the adjacent skin, the distance of the tumour and associated intraepithelial neoplasm from the resection margins (lateral and deep).
Local/radical excision with or without lymph nodes	The vulval specimen should be carefully described. Blocks should be taken to identify the type of tumour (or residual tumour), the size and adequacy of excision, the proximity of the resection margins, associated dermatological disease (for example lichen sclerosus) and the presence or absence of lymphovascular permeation. The lymph nodes should be counted and unless they are macroscopically infiltrated by tumour, should be cut into slices which should all be examined histologically.

6.11.5 Reporting the specimens

Punch biopsy	The report should describe the condition of the epidermis (e.g. acanthotic, hyperkeratotic, parakeratotic), the presence of features suggesting HPV infection (e.g. koilocytes, dyskeratotic cells, multinucleated cells), the presence or absence of a dermatopathological condition, the presence or absence of cytological atypia, and the presence or absence of invasive neoplasia.
	Cytological atypia should be graded and the report should include a statement saying whether the abnormality is in squamous epithelium, is adenocarcinoma in situ (Paget's disease) or a melanocytic abnormality.
	If invasion is present the depth of invasion and the presence or absence of lymphovascular permeation should be stated.
	In a punch biopsy it is expected that both intraepithelial and invasive neoplasia will have been incompletely excised.
Small ellipse of skin	The content of the report will be similar to that for a punch biopsy. It may be possible, however, to say whether a focal lesion has been completely excised or not.
Excision biopsy	In the case of an area of intraepithelial neoplasia, the report should confirm the presence of intraepithelial neoplasia, grade it if appropriate, state whether invasion is present or not and say whether the lesion has been completely excised or not.
	In the case of a solid neoplasm, the report should confirm: • The presence of tumour • Identify and grade it • Include its measurements • State how close it comes to the resection margins (including the deep margin) • State if it has been incompletely excised or not • State if lympho-vascular permeation is present or not The report should also include a description of the adjacent epidermis and should indicate if any intraepithelial neoplasm has been completely excised or not.

Local/radical excision with or without lymph nodes	In the case of intraepithelial neoplasia, the report should be similar to that for an excision biopsy. In the case of a solid neoplasm, the report should be similar to that for an excision biopsy. The presence or absence of metastatic carcinoma in the lymph nodes should be recorded. The total number of lymph nodes and the number containing metastases should be given.

6.11.6 Histology Summary

These follow the known factors that influence both management and outcome:

Primary tumour:

1. The total dimensions of the specimen
2. The dimensions (x3) of the tumour(s)
3. The total number of tumours.
4. The histological type.
5. Any abnormalities in the adjacent epithelium (i.e. VIN, maturation disorder).
6. The maximum depth of invasion.
7. Whether or not there is lymphovascular space involvement.
8. The minimum clearance from the excision margins.

The nodes:

1. The total number of lymph nodes.
2. The presence or absence of tumour in the lymph nodes.
3. Whether the node or nodes are totally replaced by tumour.
4. Whether there is evidence that tumour has broached the node capsule.

6.11.7 Minimum Dataset

Please also complete the form “Reporting Proforma for Vulval Cancer Resection Specimens” (Appendix C in the RCPath dataset publication).

6.11.8 Additional Information

Additional detailed notes for specimen handling and reporting are available in the Royal College of Pathologists publication “Dataset for histological reporting of vulval neoplasms (2nd edition)”

6.12 Radiation and Chemotherapy

Radiotherapy (with or without concurrent chemotherapy) is indicated in vulval cancer and in patients with locally advanced disease not amenable to surgery or where surgery would require an APER. Increasingly, regimens used to treat cervical cancer are being employed in cervical cancer.

Radical treatment will usually require that a prophylactic dose (45-50 Gy) be delivered to the primary and nodal sites and the tumour then be boosted by a second phase of treatment by electrons, conformal radiotherapy or brachytherapy to a total dose of 63-5 Gy. The total prescribed dose is determined by the clinical context.

6.12.1 Adjuvant radiotherapy

Radiotherapy to the primary site

This is indicated where surgical margins are close (<8 mm).

- Dose, 45 Gy in 25fractions given daily, as a direct field, over 35 days. See radiotherapy protocols for details.

Adjuvant treatment to the pelvic nodes

This is indicated where there are ≥2 positive nodes or extra capsular in one or more nodes. Chemoradiotherapy should be considered for patients with multiple nodal involvement and an adequate performance status and renal function.– see radiotherapy for protocols. Radiotherapy should be to the ipsilateral side +/- the contralateral side.

- Dose, 45 Gy in 25 fractions given daily, as a planned volume over 3 5days. See radiotherapy protocols for details.

Radical (chemo) radiotherapy in advanced vulval cancer

All patients should be carefully assessed prior to radiotherapy. The following tests should be performed:

- FBC and biochemical profile
- EDTA creatinine clearance (where concurrent chemotherapy is to be given)
- Chest X-ray
- MRI of the pelvis
- Examination under anaesthetic (EUA) might be necessary for some patients

Pelvic radiotherapy

Pelvic radiotherapy encompasses the primary tumour, inguinal and pelvic nodes including the inguinal, obturator, internal, external and common iliac nodes where indicated. All patients are planned conformally. The patients treatment position should be carefully considered and bolus over the primary and involved nodes used where appropriate. Full details are included in the Radiotherapy protocols.

- A dose of 45 Gy in 25 fractions over 35 days. Unscheduled gaps or prolongation of the total treatment time should be avoided as this reduces local control.

6.12.2 Concurrent chemotherapy

Where patients are fit enough they should receive cisplatin 40mg/m2 weekly for a total of 5 treatments. Full details are included in the Radiotherapy protocols.

Consideration of resection

Patients can be considered for resection after 45 Gy. Where appropriate all patients should be discussed with the treating surgeon to discuss the possibility of resection, especially if patients are responding well. Where resection is still deemed not appropriate patients should continue to phase II.

6.12.3 Neoadjuvant chemotherapy

In patients with very advanced disease, 2 courses of neoadjuvant combination chemotherapy (5-Fu and cisplatin) can be considered prior to radical chemoradiotherapy.

For full details please refer to the radiotherapy protocols.

6.12.4 Palliative radiotherapy

Radiotherapy is useful in the palliation of symptomatic pelvic disease in the context of widespread disease (extra-pelvic sites) or where the patients' performance status precludes radical surgery or radiotherapy. Commonly used regimens include:

- 40 Gy in 15 fractions
- 30 Gy in 10 fractions
- 20 Gy in 5 fractions
- 10 Gy 1 fraction repeated if symptoms persist no more than once every 6 weeks for a maximum of 3 times

6.12.5 Chemotherapy

Palliative chemotherapy for recurrent or metastatic disease.

This is a rare patient group and there is currently no evidence of benefit of chemotherapy for this group of patients.

Treatment should be considered in the context of clinical trial when available.

Outside the context of the clinical trial dependant on patient fitness and co-morbidity, treatment options include:

- Paclitaxel/Carboplatin - 3 weekly
- Paclitaxel/Carboplatin - weekly:

- Cisplatin & fluoropyrimidine combinations may also be considered.

6.12.6 Carcinoma of the Bartholins gland

If the disease is localised a radioactive implant can be employed to control disease:

Interstitial boost to vaginal mass 60 Gy to the 85% reference isodose (ICRU) at 60c Gy/h – total treatment time 100 hours.

All other stages of disease should be treated in the same way as a vulval or lower vaginal treatment is given.

6.13 Treatment Summary

Disease Extent	Description	Treatment Principle
Early disease	Small lesions with less than I mm invasion (FIGO Stage Ia)	Wide local excision. Groin node dissection unnecessary
	Truly lateralised squamous lesions (FIGO Stage l and II)	Initially only require wide local excision and ipsilateral lymphadenectomy
	Centrally located tumours where excision is possible without sphincter compromise	Requires wide local excision and bilateral lymphadenectomy initially
Advanced disease	Extensive vulval involvement	Primary radiotherapy to the vulva with groin node dissection. May also require surgical excision and reconstruction of the vulva.
	Clinically advanced nodes	Excision and or chemoradiation therapy
Metastatic disease		Palliation may still require appropriate management of the primary tumour

6.14 Morbidity

Morbidity associated with the management of vulval cancer is well recognised. It comprises two groups:

1. Resulting from relapsed disease.
2. Structural damage consequent upon the treatment.

6.14.1 Morbidity related to Relapse

Local relapse

This usually occurs as a result of inadequate surgical margins. A minimum clearance of I cm on all aspects of the tumour is recommended. This should be the target even if such an attempt would compromise urethral or anal function. Reconstruction of these structures is a far more acceptable alternative to local relapse. In selected cases small lesions confined to the tissues adjacent to such structures might be equally well managed by radiation thus reducing the risk of structural damage.

Regional relapse

Relapse in the regional nodes or intervening skin bridges is a much more difficult situation. This usually arises as a result of not having performed an inguinal node dissection or more rarely, only a superficial inguinal lymphadenectomy. Survival following regional relapse is poor and thus all attempts to prevent it must be made at the time of primary treatment.

6.14.2 Morbidity related to surgery

The primary objectives of less radical surgery are to reduce morbidity whilst maintaining high cure rates for early vulval cancers. The complications associated with vulval and inguinal surgery are:

- Wound breakdown
- Wound infection
- Deep vein thrombosis and pulmonary embolism
- Pressure sores
- Introital stenosis
- Incontinence
- Rectocele
- Faecal incontinence
- Lymphocyst
- Lymphoedema
- Hernias
- Psychosexual issues

6.14.3 Recurrent disease

In local recurrence irradiation should be the first choice if excision would impair sphincter function. If irradiation has already been given to maximum dose, then excision should be considered.

Groin recurrence is much more difficult to manage. In patients who have not received radiation and who have histologically confirmed recurrence, radiotherapy should be performed first. Resection should be considered if the response to radiotherapy is not complete. Patients who have been irradiated should be offered palliative resection if possible.

6.14.4 Community care

Patients who have received successful curative therapy will require little community care. Those undergoing palliative or non-curative treatment who may be symptomatic and expectant of relapse should receive regular support and surveillance from the general practitioner and community nursing services. Pain control should be monitored regularly. Careful hygiene and dressing of fungating lesions will require very close nursing supervision.

7 Vaginal Cancer

All the preinvasive and invasive forms of vaginal cancer are uncommon, comprising 1-2% of gynaecological malignancies. Many cases have a prior history of gynaecological malignancy, most commonly cancer of the cervix. 50% will have had a previous hysterectomy. The most common primary site is the posterior wall of the upper two-thirds of the vagina.

The vagina, however, can be a common site for metastatic disease either by direct extension of cervical or vulval tumours or through lymphatic or vascular spread as seen in endometrial and gestational trophoblastic disease. Metastatic tumours can also occur from the bladder, urethra or periurethral glands and rarely breast, renal and lung cancer.

The histological distinction between squamous cell carcinoma and adenocarcinoma is important because the two types represent distinct diseases, each with a different pathogenesis and natural history.

Squamous cell carcinomas (~85% of cases) initially spread superficially within the vaginal wall and later invade paravaginal and parametrial tissues. Distant metastases occur most commonly in the lungs and liver.

Adenocarcinomas (~15% of cases) are commoner in younger women, and differ from squamous cell carcinomas by an increased incidence of pulmonary metastases, supraclavicular and pelvic node involvement. Melanomas, sarcomas and adenosquamous carcinomas are rare.

7.1 National Guidance

The National Guidance states that all patients with vaginal cancer should be referred without delay to the specialist gynaecological oncology team at the Cancer Centre. These Guidelines are written to be consistent with the National Guidance.

7.2 Local Implementation of National Guidance

It is intended that all patients with histologically confirmed or obvious clinical malignancy will be referred urgently by fax, phone or via the appropriate Centre Consultant to the Cancer Centre.

All patients must be discussed at a MDT meeting.

7.3 Vaginal intraepithelial neoplasia (VAIN)

Treatment options include:

- Surgical excision
- Laser vaporisation with a CO2 laser
- Topical 5-fluorouracil
- Brachytherapy - This would be intravaginal treatment only and would normally be administered using a vaginal cylinder. A dose of 30Gy prescribed to 5mm from the surface of the applicator (ICRU[13]) in 10fractions given daily over 12-14days can be used. At the St James's Institute of Oncology we use the High Dose Rate MicroSelectron (Ir^{192}, dose rate 1.5Gy/min).

7.4 Invasive cancer of the vagina

Radiotherapy is generally the treatment of choice for invasive vaginal cancers. Radical surgery is sometimes useful in primary cancers of the lower third of the vagina.

Treatment planning is important, where not only the extent of the tumour, i.e. its stage, but the volume and the tumour location are also critical in determining which radiation techniques and doses are to be used. Lesions involving the apex or upper vagina are often treated in a similar approach to primary cervical lesions using similar doses and treatment fields.

7.4.1 Radiotherapy

Intravaginal treatment only

Patients are usually treated using either the Miami applicator or vaginal cylinder with or without a central tube.

A dose of 42 Gy in 6 fractions 2 fractions per week over 17-19 days is prescribed to the tumour and high risk region and 27 Gy in 6 fractions 2 fractions per week to the intermediate risk region. All treatments are conformally planned.

Pelvic radiotherapy

Pelvic radiotherapy encompasses the primary tumour, uterus, vagina and pelvic nodes including the obturator, presacral, internal, external and common iliac nodes. Inguinal nodes should be included for patients with lower third tumours. All patients are planned conformally. Full details are included in the Radiotherapy protocols.

A dose of 45 Gy in 25 fractions over 32-35 days is prescribed. Unscheduled gaps or prolongation of the total treatment time should be avoided as this reduces local control.

[13] International Committee on Radiation Units

The maintenance of haemoglobin ≥ 12g/dl has been shown in a retrospective study to improve both pelvic control and survival rates[14].

Phase 2 boost

Following pelvic radiotherapy a boost to the primary should be given. This can either be in the form of an external beam boost or brachytherapy boost.

- Interstitial boost to vaginal mass 30 Gy to the 85% reference isodose (ICRU) at 60cGy/h – total treatment time 50hours.
- Intracavity boost 20 Gy in 4 fractions 2 fractions per week to the high risk region and 12 Gy in 4 fractions 2 fractions per week to the intermediate risk region over 12-14 days. All treatments are conformally planned.
- Conformally planned external beam radiotherapy boost 18 Gy in 10 fractions over 12-14days.

Concurrent chemotherapy

Where patients are fit enough they should receive cisplatin 40mg/m2 weekly for a total of 5 treatments. Full details are included in the Radiotherapy protocols.

7.4.2 Treatment by stage

Stage I & II

If of small volume they may be amenable to primary surgical treatment in selected patients. Surgery generally should consist of a radical-type hysterectomy, parametrectomy and upper vaginectomy together with pelvic lymphadenectomy. Stage I lesions involving the lower third of the vagina may also be amenable to primary surgical therapy. Surgery will generally require some vulval excision

Stage I superficial lesions ≤ 0.5cm thick can be treated with radical brachytherapy alone.

Bulky stage I & II lesions of the upper vagina can often be treated using the same protocols as carcinoma of the cervix.

Bulky stage I and II lesions involving the middle and lower third of the vagina are treated by using a combination of external beam therapy combined with chemotherapy +/- intravaginal brachytherapy.

Stage III & IV

Radiotherapy / chemoradiotherapy treatment is the modality of choice for Stage III and IV. Exenteration-type procedures are selectively employed and would generally be used in recurrence or contraindications to radiotherapy (e.g. previous pelvic radiotherapy).

[14] Grogan M et al. The importance of haemoglobin levels during radiotherapy for carcinoma of the cervix. Cancer 1999; 86: 1528-36.

7.4.3 Palliative radiotherapy:

Radical treatment should be considered for all patients however where patients are unfit or the disease is regarded as too extensive (either locally or widespread metastases) then palliative radiotherapy should be considered. Appropriate schedules include

- 40 Gy in 15 fractions.
- 30 Gy in 10 fractions
- 10 Gy 1 fraction repeated if symptoms persist no more than once every 4-6 weeks for a maximum of 3 times[15]

7.4.4 Chemotherapy

Palliative chemotherapy for recurrent or metastatic disease.

This is a rare patient group and there is currently no evidence of benefit of chemotherapy for this group of patients.

Treatment should be considered in the context of clinical trial when available.

Outside the context of the clinical trial dependant on patient fitness and co-morbidity, treatment options include:

- Paclitaxel/Carboplatin - 3 weekly
- Paclitaxel/Carboplatin - weekly:
- Cisplatin & fluoropyrimidine combinations may also be considered.

7.4.5 Follow-up following radical (chemo)-radiotherapy

Clinical examination and direct inspection are mandatory in the routine follow-up of patients who have had radical radiotherapy.

Patients should have an initial MRI at 3 months to assess response. Further imaging should be guided by the results and clinical examination / patients symptoms.

Cervical / vault smears following radiotherapy are not recommended, as they are difficult to interpret.

Hormone replacement therapy should be offered to all patients who are pre-menopausal prior to treatment. An oestrogen and progestogen combination should be prescribed as women given an unopposed oestrogen may experience uterine bleeding despite a high dose of radiation to the endometrium.

[15] Hodson DJ, Krepart GV. Once-monthly radiotherapy for the palliation of pelvic gynaecological malignancy. Gyncol Oncol 1983; 16:112-6.

7.5 Clear cell carcinoma of the vagina

Maternal diethylstilboestiol (DES) exposure is a risk factor for clear cell carcinoma. Small lesions ≤ 2.5cm, and ≤ 0.5cm thick, can be treated with interstitial or transvaginal radiation alone thus sparing the uterus and ovaries in an attempt to maintain fertility[16]. Larger lesions are treated based on their volume and location.

[16] Low-lying ovaries will receive a significant dose from scattered irradiation and fertility will be compromised.

8 Support

Women whose cancer is in remission are likely to need aftercare and support during the recovery period after primary treatment, and should have continuing access to appropriate services.

Radical treatment by surgery or radiotherapy can be appropriate for a small proportion of women who develop recurrent disease. Early detection of recurrence and management of such patients will require the combined skills of the specialist gynaecological oncology team at both the Cancer Centre and Cancer Unit.

8.1 Support for patients

All women with a diagnosis of a gynaecological malignancy may benefit from additional care and support, due to the effects of treatment on their physical, psychological and social well being.

Psychosocial support should be available at every stage to help patients and their families to cope with the effects of the disease and its treatment. From the time of diagnosis each patient should be made aware of, and have access to the Clinical Nurse Specialist for Gynaecology, either locally, or at the Cancer Centre. Clinical Nurse Specialists have training to enhance their ability to recognise the psychological needs of patients and to deal with them appropriately.

The clinical nurse specialist can offer and provide the following:

- Specialist nursing support for staff, patents and carers.
- Assessment of patient/carer needs.
- Emotional support from time of diagnosis.
- Formulation of action plans re future care.
- Make recommendations re medication.
- Provide information about gynaecological cancers and their treatment.
- Help with controlling side effects of treatment, or symptoms of the illness.
- Discuss issues of altered body image, fertility, and sexuality.
- Discuss discharge advice and work alongside other members of the ward team and other specialist teams where appropriate.
- A contact and link with other staff and services involved in an individuals care.
- Continuity of care between different disciplines.
- Refer to other specialist teams as required.

8.2 Psychosocial support

Patients should be encouraged to bring a partner, relative or close friend to provide support at diagnostic clinics and appointments at which distressing news may be communicated.

Adequate provision should be made to ensure that women have privacy and are able to maintain their dignity. Health service staff must be sensitive to potential embarrassment and to the needs of women from cultures with strong taboos about female sexuality and nudity.

8.3 Psychosexual counselling

All women who have treatment that is likely to affect sexual activity should be aware that advice is available on minimising adverse effects on their sexual experience and relationships. Specialist interventions should be available for women and their partners to help them to understand and cope with the effects of treatment on sexual relationships.

8.4 Post-treatment Support and Follow-up

Treatment for gynaecological cancers can lead to physical, psychosocial and sexual adverse effects. There should be a documented local policy which ensures that all women who have undergone such treatment can receive help, support and appropriate treatment without delay, and that women and their GPs are given full information about how they can access these services. Provision of such services is likely to be shared between Cancer Units and Centres; local arrangements may vary, and there must be effective communication and co-ordination between different levels.

Women should be informed about specific problems that may develop some time after treatment (such as lymphoedema, bowel or bladder dysfunction) and should have clear routes for access to appropriate specialist help if signs or symptoms appear.

9 Follow-Up

9.1 Background

There have been numerous reasons as to why patients following treatment for a gynaecological cancer are followed-up at the hospital by clinicians at regular intervals for many years. These have included:

Detection of disease recurrence
Regular clinic follow-up may enable early detection of disease recurrence. Depending on the disease site, stage and previous treatment this may improve the chance of salvage. It is generally acknowledged that recurrence beyond 3 years post treatment is uncommon in any gynaecological oncology disease sites.

Symptom management
Gynaecological cancer follow-up clinics enable expert management of symptoms associated with treatment side effects as well as symptoms of active diseases. It must not be forgotten that this is also performed in the community utilising specialist personnel such as palliative care and lymphoedema specialists.

Patient reassurance
Many patients feel they benefit from regular follow-up and are reassured when no evidence of recurrent disease is found. Some patients however become anxious prior to their follow-up appointment.

Outcome Data
Reviewing patients regularly in follow-up clinics enables accurate outcome data to be measured.

Benefit of clinician
Oncology clinicians benefit from reviewing successfully treated patients in clinic. Trainees also benefit from seeing living proof of effective treatments.

Historically gynaecological cancer patients have been followed up in out patient clinics by clinicians generally for a period of at least 5 years and for ovarian patients 10 years. The Network had guidelines in place which units and the centre were thought to be following. A snap shot audit of the regimes of follow-up at each unit discovered that guidelines were not being followed and different follow-up regimes were being carried out at different units.

British publications addressing the value of regular follow-up for gynaecology oncology patients with endometrial, cervical and vulval carcinoma have suggested there may be little or no benefit from regular follow-up[17,18,19,20]. It has also been suggested that regular routine clinic follow-up may even be harmful for patients in terms of delaying their presentation for review at the onset of symptoms suggesting possible recurrence. Unfortunately there is no high quality evidence as to the value of follow-up in gynaecological oncology. A recent piece

[17] Nordin, et al., Mode of detection of recurrent gynecological malignancy: does routine follow-up delay diagnosis and treatment? International Journal of Gynecological Cancer. 16(5):1746-1748, September/October 2006
[18] Fung-Kee-Fung, et al., Follow-up after primary therapy for endometrial cancer: a systematic review. Gynecol Oncol. 2006 Jun;101(3):520-9.
[19] Kew, et al., The role of routine follow-up after gynecological malignancy. Int J Gynecol Cancer. 2005 May-Jun;15(3):413-9.
[20] Olaitan, et al., A critical evaluation of current protocols for the follow-up of women treated for gynecological malignancies: a pilot study. Int J Gynecol Cancer. 2001 Sep-Oct;11(5):349-53.

of research undertaken at a unit revealed that patients and staff felt that follow-up should be individual, holistic and based on patient choice.

There are several Government documents and initiatives suggesting that routine follow-up should be changed in order to improve services. Below is a list of a selection of documents and what they recommended / suggested with regard to follow-up.

- Improving Outcomes in Gynaecological Cancer (1999) – There is no evidence to support routine follow-up for women whose cancer is in remission.
- Improving Communication in Cancer Care (2003) – Improvements regarding communication are required.
- NHS Cancer Plan (2004) – Services should be patient centred.
- Ten High Impact Changes for Service Improvement and Delivery (2004) – Avoiding unnecessary follow-up and for it to be in the most appropriate setting.
- Applying High Impact Changes to Cancer Care (2005) – It should be clinically appropriate & patients' experiences should be improved.

An alternative model of follow up has been commenced at Pan-Birmingham and Kent & Medway Cancer Network in the form of patient initiated follow-up. Detailed patient information is provided at an "exit" interview at the end of treatment (surgery, chemotherapy or radiotherapy). The patient is educated regarding symptoms suggestive of a possible disease recurrence. Contact details of the nurse specialist are given and the patient is encouraged to telephone her at any time to discuss any concerns they may have regarding recurrence of disease or side effects related to treatments. The nurse specialist can then triage the patient appropriately, for urgent review by a clinician, to the General Practitioner, to a special service such as lymphoedema clinic or for discussion at the next multidisciplinary team meeting.

The model of care is attractive in that it empowers patients and enables them to access care at short notice when required. It also helps patients to progress beyond the "sick role" as soon as they have recovered from treatment.

Most patients develop a relationship with the clinical nurse specialist that begins at the time of diagnosis and usually continues throughout the patient's treatment. The CNS usually becomes an essential link with the clinical team. This resource should be incorporated when planning changes to follow- up guidelines and their link and knowledge regarding the patients should be used harnessed.

9.2 Policy

At the NSSG meeting 08/05/09 it was suggested that in the absence of quality evidence we should continue with routine regular follow-up in the clinical setting for the majority of gynaecological patients but with a maximum follow-up of 3 years.

All patients will be followed up at the referring cancer unit in conjunction with the cancer centre personnel on completion of treatment (see section 1.6.1 for local team configuration).

At the same time rationalise the schedule of routine clinic reviews, and supplement this with an integrated model of patient initiated follow-up. The follow-up schedule should be discussed with each patient and their wishes taken into consideration. Each plan of follow-up should be recorded in the notes, the GP informed and patients given a copy of the plan.

In order to help patients understand the rationale for changing follow-up and encourage them to progress beyond the sick role completion of treatment interviews are being suggested. These could be run by the nurse specialists and allow time for issues regarding recovery such as physical emotional, sexual, body image or social aspects to be discussed. Detailed information should be given regarding symptoms that may suggest a recurrence of disease and contact details given regarding who and how to contact personal in order to be seen quickly at the next available follow-up clinic.

Leaflets should also be produced explaining the follow-up procedures within the network.

9.2.1 Range of routine clinic review which can be considered as reasonable

- Initial post treatment clinic review
- 3 – 6 monthly review post completion of treatment (1st year)
- 3 - 6 monthly review 1 year after completion of treatment (2nd year)
- 3 – 12 monthly review 2 years after completion of treatment (3rd year)

The above are suggestions only and clinicians should negotiate with patient times and frequency of follow-up acceptable to patient and clinician.

Where patients have undergone treatment by more than one speciality (e.g. surgery and radiotherapy) it is suggested that the initial post treatment follow-up is performed by the surgeon after treatment and then by the clinical oncologist after completion of radiotherapy. The consultant providing the last treatment should then follow-up the patient but have the option of sharing or transferring the follow-up if more appropriate.

Clinical nurse specialists would be able to arrange for the patient to be reviewed at any time on an urgent basis, in addition to the standard regime as described.

Patients would be given contact details of other members of the team at the completion of treatment interview enabling them to instigate their own follow-up if required in between the scheduled appointments.

9.2.2 Patients requiring chemotherapy

- Initial post treatment clinic review
- As the minimum standard routine clinic review
- To increase follow-up dependent on how patient is clinically
- To negotiate with patient times and frequency of follow-up acceptable to patient and clinician

These patients are likely to have more advanced disease and have a higher risk of local, regional and distant relapse, their follow-up may need to be adjusted to assess the treatments morbidity and relapse status. These patients should be seen by the medical oncology team.

Patients should also be given the opportunity to attend a completion of treatment interview following their initial treatment in order to be given details of symptoms that would indicate a recurrence, contact details of whom and how to contact the team urgently if required and to discuss any physical emotional, sexual, body image or social aspects following their initial treatment.Patients could instigate their own follow-up in between scheduled appointments if required.

9.2.3 Patients requiring radiotherapy or chemo-radiotherapy

- Initial post treatment clinic review
- As the minimum standard routine clinic review
- To see patient as frequently as required dependent on treatment related morbidity
- To increase follow-up dependent on response to treatment
- To negotiate with patient times and frequency of follow-up acceptable to patient and clinician

These patients are likely to have more advanced disease and have a higher risk of local, regional and distant relapse, their follow-up may need to be adjusted to assess the treatments morbidity and relapse status. These patients should be seen by the clinical oncology team.

Patients should also be given the opportunity to attend a completion of treatment interview following their initial treatment in order to be given details of symptoms that would indicate a recurrence, contact details of whom and how to contact the team urgently if required and to discuss any physical emotional, sexual, body image or social aspects following their initial treatment.

Patients could instigate their own follow-up in between scheduled appointments if required.

9.2.4 Disease and treatment related morbidity

Review in follow-up clinic will remain available on a basis of need. In addition to patient initiated review more frequent review can be initiated by any members of the multidisciplinary team on the basis of need. For example patients with treatment-related morbidity may require more frequent regular review in a follow-up clinic.

Patients could instigate their own follow-up in between scheduled appointments if required.

9.2.5 Clinical Trials

Patients involved in clinical research and trials should undergo follow-up as prescribed by the trial protocol. They should be encouraged to participate in a completion of treatment interview in order to progress beyond the sick role. It would also give them the opportunity to discuss any physical emotional, sexual, body image or social problems. They would be given information regarding symptoms that would indicate a recurrence and contact details so they could access the follow-up clinic at any time in between scheduled follow-up if required.

9.2.6 Very Low Risk Patients

- Endometrial cancer FIGO 1A grade 1 or 2
- Adequately staged FIGO stage 1 ovarian tumours of borderline malignant potential.
- These groups should be managed with patient initiated follow-up alone.
- Carcinoma of the cervix FIGO stage 1A

Disease recurrence in these particular patient groups above is so rare that they do not require any structured routine clinic reviews beyond the initial post treatment appointment. It is likely that these patients would also benefit from a completion of treatment interview with the CNS to allow time for discussion regarding any physical, emotional, sexual and body image issues following treatment. At the same interview details of how to contact any member of the team urgently could be given along with symptoms that could suggest a recurrence. Any patients who feel there is a need for concern could instigate follow-up by liaising with a relevant member of the team in order for them to be seen in a timely manner.

10 Palliative Treatment and Care

10.1 All Gynaecological Malignancies

10.1.1 National Guidance for Gynaecological Cancer Management

Most women with advancing cancer are likely to wish to remain at home for much of the duration of their illness, under the care of general practitioners. Multiprofessional palliative care teams should also be involved. These teams should aim to provide both optimal relief from symptoms and social and psychological support for patients and their carers. They should, at a minimum, include a specialist in palliative medicine, a specialist palliative care nurse and social worker support; they should meet regularly and liaise closely with primary care teams.

The main role of the palliative care specialist is likely to be in the provision of education and advice for other health professionals, but he or she may take on the role of lead clinician and have overall responsibility for the management of care for the patient.

When palliative surgery, chemotherapy, or other specialist procedures may be appropriate for symptom control, the palliative care specialist should discuss management options with the specialist gynaecology oncology team at the Cancer Centre. Interventions may be delivered at Cancer Centres or Cancer Units, depending on the type and degree of expertise required, and the patient's condition and preferences. Cancer Centres and Cancer Units should jointly agree local arrangements. Efficient systems to ensure rapid and effective communication between each of these levels and teams are essential.

The palliative care team should have access to other skills including counselling for patients with advanced incurable disease, spiritual guidance, dietary advice, and practical support. All health care professionals who deal with these patients should be encouraged to take training in communication and in understanding the needs of women with incurable illness.

All women with advanced disease, whether in hospital or in the community, should have access to specialist palliative care on a 24 hour basis and there should be local arrangements to ensure continuity of care. Patients should be helped to remain in the place they prefer, whether this is their home, hospital, or hospice, and should, whenever possible, be allowed to choose where they wish to die.

10.1.2 Local Implementation of National Guidance

See Appendix 2: Palliative Care Guidelines

11 Appendix 1 : Guidelines for Ovarian Screening

11.1 Introduction

Although developments in tumour marker and ultrasound technologies have provided tests, which can detect the majority of ovarian cancers before they cause symptoms, there is as yet no evidence that routine screening will reduce mortality from this disease. Population screening is not therefore recommended at least until the results of clinical trials are known.

11.2 High risk women

Any survival advantage conferred by ovarian cancer screening is most likely to be evident in women known to be at high risk.

This high risk group can be identified by the following:

- Women with a proven BRCA1, BRCA2, hMLH1 or hMSH2 mutation
- Two or more first or second degree relatives with ovarian cancer on the same side of the family.
- One first or second degree relative with ovarian cancer, plus one or more first or second degree relatives on the same side of the family with breast cancer diagnosed under the age of 60 years.
- One first or second degree relative with both breast and ovarian cancer.
- One first or second degree relative with ovarian cancer, plus two first or second degree relatives with colorectal cancer, one of which was diagnosed under the age of 50 years.

Asymptomatic women with a family history of ovarian cancer, particularly if they clearly fit into a high-risk group, should be referred to Dr Carol Chu, Consultant in Clinical Genetics at St James's Hospital. A risk assessment will then be carried out by questionnaire. Low risk women and their referrer will be informed that no screening is indicated. High risk women should be offered screening according to the protocol. A referral pathway is enclosed (section 11.4).

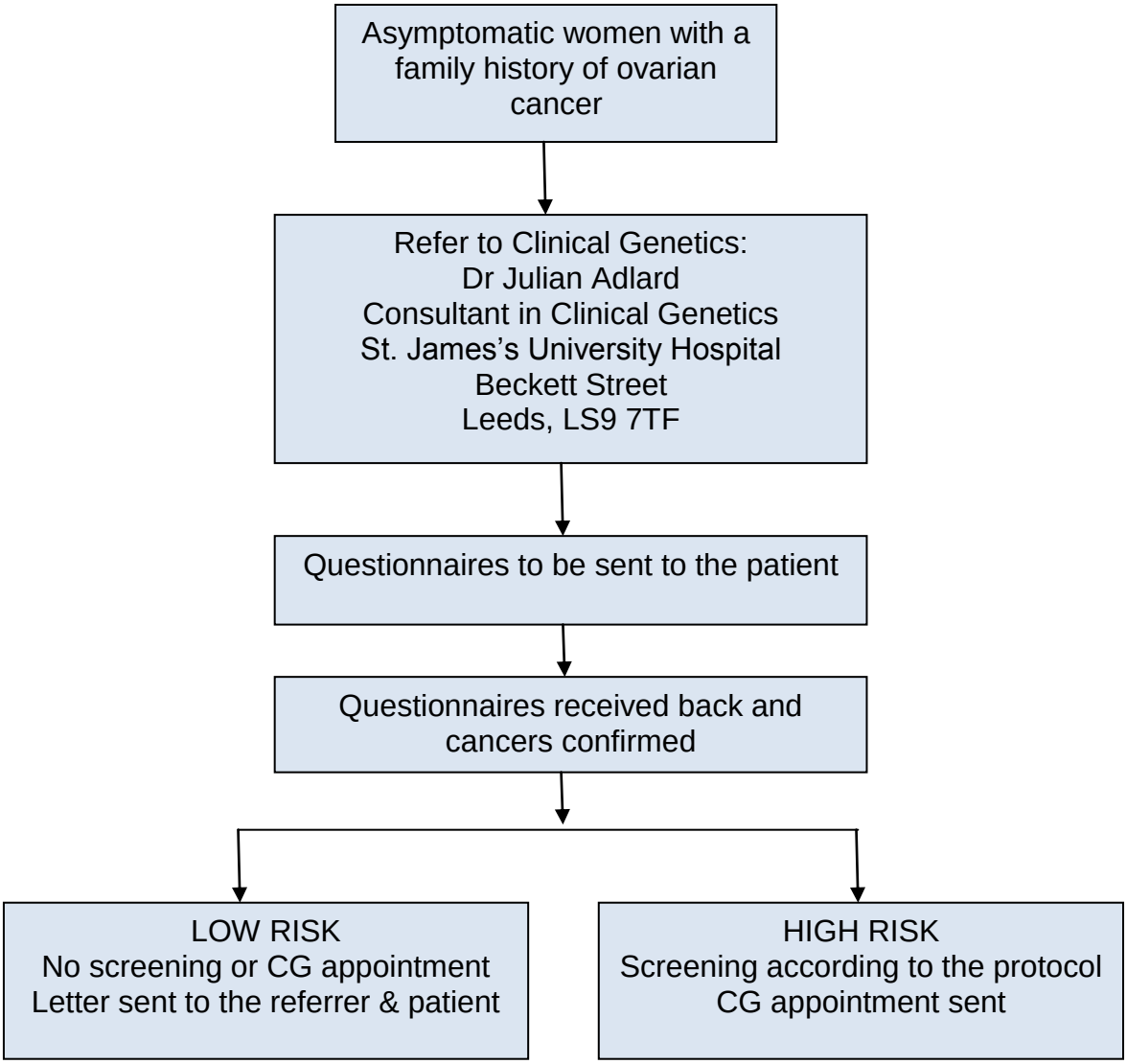
11.3 Screening protocol

Screening should consist of an annual serum CA125 combined with an annual transvaginal and transabdominal ultrasound scan.

- A normal CA125 and a normal scan - repeat the tests in one year.
- An elevated CA125 or a doubling of the level within the normal range :
    - If the scan is normal - repeat the tests in six weeks.
    - If the scan is abnormal - refer to the lead gynaecologist in the appropriate cancer unit.
- Simple cysts <5 cm in diameter with a normal CA125 - repeat the scan and CA125 in six weeks :-
    - If no changes - repeat in a further four months.

    - If there is a doubling of the CA125 level, or if the cyst increases in size - refer to the lead gynaecologist at the local cancer unit.
- All ‘positive’ scans - these patients should be referred regardless of CA125 level. (The criteria for diagnosing a ‘positive scan’ is described in section 11.5).
- Where there is doubt as to whether a patient has ovarian malignancy and whether they require urgent management, it may be helpful to calculate their RMI (section 11.7).

11.4 Referral pathway for women with a family history of ovarian cancer



11.5 Criteria for diagnosing a positive scan

11.5.1 Premenopausal women

Ovaries

- Scan during the first 10 days of a cycle; both transabdominal and transvaginal scans are recommended.
- Simple ovarian cysts <2.5cm in diameter are regarded as normal.
- Any cyst >2.5cm in diameter requires a repeat scan in 6-8 weeks.
- A persistent cyst >2.5cm in diameter requires a morphological score and Doppler studies.
- A score ≥3 should be considered a "positive scan"[21]. Expert radiological review is required to help exclude diagnoses such as endometriosis or dermoid cysts.

Other findings

- The presence of pleural effusions, ascites, an omental cake and hydronephrosis should be actively looked for on the screening scan. If present, the scan is positive regardless of the appearance of the ovaries.

11.5.2 Postmenopausal women

Ovaries

- Transabdominal and transvaginal scans are required.
- Simple ovarian cysts <5 cm in diameter can be observed with a repeat scan in 6 weeks. Cysts of this nature are often stable for long periods of time and, provided they do not enlarge, can be managed conservatively.
- Simple cysts >5cm in diameter, or cysts that show progressive enlargement, indicate a "positive scan".
- Any cyst showing complexity (e.g. a thick wall and septae or nodular projections) indicates a "positive scan". Doppler can help refine this group. Resistance Indices of 0.5 or less obtained from central vessels within the lesion increase the likelihood of malignancy.
- Ovarian volume: - If a woman is not on HRT, an ovarian volume of over 9mls is abnormal and requires a repeat scan.

Other findings

- The endometrial thickness should be routinely measured; if <4mm endometrial cancer is unlikely; if ≥8mm a biposy should be considered (HRT and Tamoxifen notwithstanding)
- The presence of a pleural effusion, ascites, an omental cake and hydronephrosis should be checked for as part of the routine screen.

Caveat

- If an operation is being done to remove a persistent cyst, an ultrasound scan is advised the day prior to surgery to ensure the cyst is still present.

[21] J.P.Lerner et al. Transvaginal ultrasonographic characterisation of ovarian masses with an improved, weighted scoring system. Am J Obstet Gynecol 1994; 170:81-85.

11.6 Ultrasound scan report for ovarian cancer screening

Age:

Menstrual state:

INITIAL TRANSABDOMINAL SCAN :-				
Uterine morphology/fibroids :-				
Ovaries :-	**RIGHT**		**LEFT**	
Size (calculate volume) Describe any anomaly (and sizes) - cystic unilocular multilocular - complex (cystic and solid) - solid				
Kidneys (? obstructed)				
TRANSVAGINAL SCAN :-				
Confirm morphology seen transabdominally :-				
Colour Doppler of Ovaries :-	**RIGHT**		**LEFT**	
Describe colour pattern - central - peripheral rim - mixed - none				
	RIGHT		**LEFT**	
3 measurements of spectral Doppler each ovary :-	**RI**	**PI**	**RI**	**PI**
(calc. RI and PI) 1. 2. 3. Waveform notched? Uterine artery (RI and PI)				
CONCLUSION:				

11.7 Risk of Malignancy Index (RMI) in ovarian cancer

RMI = U x M x Serum CA125

'U' refers to an ultrasound score :-

- 'U' = 1 if the ultrasound score is 0 or 1.
- 'U' = 3 if the ultrasound score is 2 – 5.

The ultrasound score is calculated by awarding one point for each of the following :-

- a multi-locular lesion.
- solid areas.
- bilateral lesions.
- ascites.
- intra-abdominal metastases.

No points are given when none of these morphological features are present. The maximum score is 5.

'M' refers to a score based on menopausal status :-

- A score of 1 is given for premenopausal patients.
- A score of 3 is given for postmenopausal patients (that is women who have been amenorrhoeic for more than a year, or who are aged over 50 and have had a previous hysterectomy).

An RMI greater than 200 suggests ovarian cancer

12 Appendix 2: Palliative & End of Life Care

12.1 Definitions

Palliative care is part of supportive care. It embraces many elements of supportive care.

Palliative & End of life care is care that helps all those with advanced, progressive, incurable illness to live as well as possible until they die. It enables the supportive and palliative care needs of both patient and family to be identified and met throughout the last year(s) of life and into bereavement. It includes management of pain and other symptoms and provision of psychological, social, spiritual and practical support.

The Department of Health (2008) definition of end of life care states that it includes:

- Adults with advanced, progressive, incurable illness (e.g. advanced cancer, heart failure, COPD, stroke, chronic neurological conditions, dementia);
- Care given in all settings (e.g. home, acute hospital, ambulance, residential/nursing care home, hospice, community hospital, prison);
- Care given in the last year(s) of life
- Patients, carers and family members (including bereavement care).

End of Life Strategy, Department of Health 2008
National Council for Palliative Care Services 2006

12.2 Who Provides Palliative / End of Life Care?

Palliative / end of life care is provided by two distinct categories of health and social care professionals:

- All health care and social care professionals providing the day-to-day care to patients and carers in any care setting
- Those who specialize in palliative care (consultants in palliative medicine and clinical nurse specialists in palliative care, for example) who care for palliative care patients who have complex needs

Those providing day-to-day care should be able to:

- Assess the care needs of each patient and their families across the domains of physical, psychological, social spiritual and information needs
- Meet those needs within the limits of their knowledge, skills, competence in palliative care
- Know when to seek advice from or refer to specialist palliative care services

Training and education in the skills required for palliative / end of life care should be available to and undertaken by all health and social care professionals.

The national strategy *Ambitions for Palliative and End of Life Care 2015-2020* sets out the vision to improve end of life care through partnership and collaborative action between organisations at local level throughout England.

More information can be found at: http://endoflifecareambitions.org.uk/

For more information about local improvements, frameworks, tools to support best practice please contact your local End of Life Care Lead or Specialist Palliative Care Team.
One aspect of care is to discuss with individuals, if they wish, their preferences regarding the type of care they would wish to receive and where they wish to be cared for in case they lose capacity or are unable to express a preference in the future. This is the process of Advance Care Planning (ACP).

An ACP discussion might include:

- the individual's concerns and wishes,
- their important values or personal goals for care,
- their understanding about their illness and prognosis,
- their preferences and wishes for types of care or treatment that may be beneficial in the future and the availability of these.

Such discussions can also inform shared decision-making regarding treatments with palliative intent. Local arrangements for recording this information for each individual patient will differ. Many services are developing/have developed Electronic Palliative Care Co-ordination Systems (EPaCCS) where by this information can be shared across professionals and settings (e.g on SystmOne). Contact your local specialist palliative care team for more information.

12.3 Specialist Palliative Care

Is provided by specialist multidisciplinary palliative care teams in services or units whose core specialty is palliative care (for example hospices, community or hospital palliative care teams). The specialist teams should include palliative medicine consultants and palliative care nurse specialists together with a range of expertise provided by physiotherapists, occupational therapists, dieticians, pharmacists, social workers and those able to give spiritual and psychological support.

Eligibility for referral to specialist palliative care services is based on patient need not diagnosis. The agreed criteria for referral are as follows:

1. The patient has active, progressive and usually advanced disease for which the prognosis is limited (although it may be several years) and the focus of care is quality of life.

2. The patient has unresolved complex needs that cannot be met by the caring team, for example:
   - Uncontrolled or complicated symptoms (e.g. symptoms not adequately controlled within 48 hours by the referring team, or sooner if causing overwhelming distress).
   - Complex psychological/emotional difficulties.
   - Complex social or family issues.

- Difficult decision making about appropriate future care.

Patients fulfilling these criteria should be referred to and assessed by a member of the specialist palliative care team.

The subsequent care package will be dependent on this assessment and should be made in agreement with the patient, carer(s) and referring team. It is not appropriate for specialist palliative care services to be committed to patients by professionals outside these services. Equally, specialist services should ensure that the assessment process is accessible and responsive to patients in need.

The level of specialist palliative care support required may fluctuate. Shared care of patients between the specialist palliative care professionals and the referring team (for hospital patients) or the primary care team (for patients at home / care home) is usually appropriate. Timely and effective communication is essential in these situations. For these patients advice from specialist palliative care services on a 24 hour basis should be available in all care settings.
Sometimes the specialist palliative care consultant and team may take the lead role in patient care, usually in a specialist in-patient unit (hospice) or designated specialist palliative care beds.

Referral systems for specialist palliative care services vary in different areas. They should be clear to all local referring consultants and primary care teams.

12.4 Further Links and Information

Contact the local Specialist Palliative Care Team for further information

12.5 Directory of West Yorkshire & Harrogate Cancer Alliance Specialist Palliative Care Services

The Directory has been checked and updated in May 2017

Bradford, Airedale, Wharfedale and Craven
Bradford Teaching Hospitals NHS Foundation Trust
Airedale NHS Foundation Trust
NHS Bradford, Airedale, Wharfedale and Craven
Website: www.palliativecare.bradford.nhs.uk

Airedale General Hospital Palliative Care Team	Tel	01535 292184 01535 295016
	Fax	01535 295036
Sue Ryder Care – Manorlands Hospice (Oxenhope)	Tel	01535 642308
	Fax	01535 642902
Bradford Teaching Hospitals Palliative Care Team	Tel	01274 364035
	Fax	01274 366851
Bradford Community Palliative Care Team	Tel	01274 323511
	Fax	01274 215660
Marie Cure Hospice (Bradford)	Tel	01274 337000
	Fax	01274 337095
Out of Hours Advice via on-call Palliative Medicine Consultant via Marie Curie Hospice / Manorlands Hospice	Tel	01274 337000
	Tel	01535 642308

Calderdale and Huddersfield
Calderdale & Huddersfield NHS Foundation Trust
NHS Calderdale
NHS Kirklees
Web: http://www.cht.nhs.uk/services/clinical-services/palliative-and-end-of-life-care/specialist-palliative-care/

Calderdale Royal Hospital & Huddersfield Royal Infirmary Palliative Care Team	Tel	01484 342965
	Fax	none
Calderdale Community Palliative Care Team Left message to confirm fax	Tel	01422 310874
	Fax	01422 378425
Overgate Hospice	Tel	01422 379151
	Fax	01422 384210
Kirkwood Hospice and Community Palliative Care Team	Tel	01484 557906
	Fax	01484 557918
Out of Hours Advice via Hospices	Tel	01422 379151 01484 557900

Harrogate and District
Harrogate NHS Foundation Trust
NHS North Yorkshire and York
Website: https:// https://www.hdft.nhs.uk/services/palliative-care/

Harrogate Hospital and Community Palliative Care Team	Tel	01423 553464
	Fax	01423 555763
St Michael's Hospice	Tel	01423 872658
	Fax	01423 815454
Out of Hours Advice via Hospice	Tel	01423 879687

Leeds
Leeds Palliative Care
Website: www.leedspalliativecare.co.uk

Leeds Teaching Hospitals NHS Trust Specialist Palliative Care Team	Tel	0113 2064563
	Fax	0113 2064863
Sue Ryder Care - Wheatfields Hospice and Community Palliative Care Team (West Leeds)	Tel	0113 2787249
	Fax	0113 2302778
St Gemma's Hospice and Community Palliative Care Team (East Leeds)	Tel	0113 2185500
	Fax	0113 2185524
Out of Hours Advice via SJUH Switchboard	Tel	0113 2433144

Mid Yorkshire
Mid Yorkshire Hospitals NHS Trust
NHS Wakefield District
Kirklees PCT
Website: https://www.midyorks.nhs.uk/palliative-care1

Dewsbury Hospital and Community Palliative Care Team	Tel	01924 816052
	Fax	01924 543883
Dewsbury Day Support and Drop-in (Rosewood Centre)	Tel	01924 512039
Mid Yorkshire Hospitals NHS Trust Palliative Care Team	Tel	01924 543801
	Fax	01924 543883
Pontefract Community Palliative Care Team (Prince of Wales Hospice)	Tel	01977 781456
	Fax	01977 796209
Prince of Wales Hospice (Pontefract)	Tel	01977 708 868
	Fax	01977 600097
Wakefield Hospice	Tel	01924 331400
	Fax	01924 362769
Out of Hours Advice via Pinderfields Hospital Switchboard	Tel	01924 541000

York
York Hospitals NHS Foundation Trust
NHS North Yorkshire and York

https://www.yorkhospitals.nhs.uk/our_services/az_of_services/palliative_care/

York Hospital Palliative Care Team both correct	Tel	01904 725835
	Fax	01904 726440
Community Palliative Care Team	Tel	01904 724476
	Fax	01904 777049
St Leonard's Hospice	Tel	01904 708553
	Fax	01904 704337
Out of Hours Advice via Hospice	Tel	01904 708553

13 Appendix 3: FIGO Staging

13.1 FIGO staging of Carcinoma of the Cervix Uteri (2009)

Stage	Definition
Stage I	The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded).
Stage Ia	Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≤5 mm and largest extension ≥7 mm
Stage 1a1	Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm
Stage 1a2	Measured stromal invasion of >3.0 mm and not <5.0 mm with an extension of not <7.0 mm
Stage Ib	Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA*
Stage Ib1	Clinically visible lesion ≤4.0 cm in greatest dimension
Stage Ib2	Clinically visible lesion >4.0 cm in greatest dimension
Stage II	Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina
Stage IIa	Without parametrial invasion
Stage IIa1	Clinically visible lesion ≤4.0 cm in greatest dimension
Stage IIa2	Clinically visible lesion >4 cm in greatest dimension
Stage IIb	With obvious parametrial invasion
Stage III	The tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney**
Stage IIIa	Tumour involves lower-third of the vagina, with no extension to the pelvic wall.
Stage IIIb	Extension to pelvic wall and/or hydronephrosis or non-functioning kidney.
Stage IV	The carcinoma has extended beyond the true pelvis, or has involved (biopsy-proven) the mucosa of the bladder or rectum. A bullous oedema, as such, does not permit a case to be allotted to Stage IV.
Stage IVa	Spread of the growth to adjacent organs
Stage IVb	Spread to distant organs

* All macroscopically visible lesions—even with superficial invasion—are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.00 mm and a horizontal extension of not >7.00 mm. Depth of invasion should not be >5.00mmtaken from the base of the epithelium of the original tissue—superficial or glandular. The depth of invasion

should always be reported in mm, even in those cases with “early (minimal) stromal invasion” (~1 mm). The involvement of vascular/lymphatic spaces should not change the stage allotment.

** On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. All cases with hydronephrosis or non-functioning kidney are included, unless they are known to be due to another cause.

13.2 FIGO Staging of Carcinoma of the Corpus Uteri (2009)

Stage	**Definition**
Stage I*	Tumor confined to the corpus uteri.
Stage IA*	No or less than half myometrial invasion
Stage IB*	Invasion equal to or more than half of the myometrium
Stage II*	Tumor invades cervical stroma, but does not extend beyond the uterus**
Stage III*	Local and/or regional spread of the tumor
Stage IIIA*	Tumor invades the serosa of the corpus uteri and/or adnexae#
Stage IIIB*	Vaginal and/or parametrial involvement#
Stage IIIC*	Metastases to pelvic and/or para-aortic lymph nodes#
Stage IIIC1*	Positive pelvic nodes
Stage IIIC2*	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV*	Tumor invades bladder and/or bowel mucosa, and/or distant metastases
Stage IVA*	Tumour invasion of bladder and/or bowel mucosa.
Stage IVB*	Distant mestastases, including intra-abdominal metastasis and/or inguinal lymph nodes.

* Either G1, G2, or G3.
** Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II.
# Positive cytology has to be reported separately without changing the stage.

13.3 FIGO Staging Carcinoma of the Ovary (2014)

Effective January 1st 2014 (Changes are in italics)

STAGE I: Tumor confined to ovaries				
OLD			NEW	
IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.		IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings.
IB	Tumor involves both ovaries otherwise like IA.		IB	Tumor involves both ovaries otherwise like IA.
IC	Tumor involves 1 or both ovaries with any of the following: capsule rupture, tumor on surface, positive washings/ascites.		*IC Tumor limited to 1 or both ovaries*	
			IC1	*Surgical spill*
			IC2	*Capsule rupture before surgery or tumor on ovarian surface.*
			IC3	*Malignant cells in the ascites or peritoneal washings.*

STAGE II: Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer				
OLD			NEW	
IIA	Extension and/or implant on uterus and/or Fallopian tubes		IIA	Extension and/or implant on uterus and/or Fallopian tubes
IIB	Extension to other pelvic intraperitoneal tissues		IIB	Extension to other pelvic intraperitoneal tissues
IIC	IIA or IIB with positive washings/ascites.			

Old stage IIC has been eliminated

STAGE III: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes				
OLD			NEW	
IIIA	Microscopic metastasis beyond the pelvis.		*IIIA (Positive retroperitoneal lymph nodes and /or microscopic metastasis beyond the pelvis)*	
			IIIA1	*Positive retroperitoneal lymph nodes only*
			IIIA1(i)	*Metastasis ≤ 10 mm*
			IIIA1(ii)	*Metastasis > 10 mm*
			IIIA2	*Microscopic, extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes*
IIIB	Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm in greatest dimension.		IIIB	*Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.*
IIIC	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm in greatest dimension and/or regional lymph node metastasis.		IIIC	*Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.*

STAGE IV: Distant metastasis excluding peritoneal metastasis				
OLD			NEW	
IV	Distant metastasis excluding peritoneal metastasis. Includes hepatic parenchymal metastasis.		*IVA*	*Pleural effusion with positive cytology*
			IVB	Hepatic and/or *splenic parenchymal* metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Other major recommendations are as follows:

- Histologic type including grading should be designated at staging
- Primary site (ovary, Fallopian tube or peritoneum) should be designated where possible
- Tumors that may otherwise qualify for stage I but involved with dense adhesions justify upgrading to stage II if tumor cells are histologically proven to be present in the adhesions

13.4 FIGO Staging of Carcinoma of the Vagina

Stage	Definition
Stage 0	Carcinoma in situ: intraepithelial neoplasia Grade III.
Stage I	The carcinoma is limited to the vaginal wall.
Stage II	The carcinoma has involved the subvaginal tissue but has not extended to the pelvic wall.
Stage III	The carcinoma has extended to the pelvic wall.
Stage IV	The carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum; bullous oedema as such does not permit a case to be allotted to Stage IV.
Stage IVa	Tumour invades bladder and/or rectal mucosa and/or direct extension beyond the true pelvis.
Stage IVb	Spread to distant organs.

13.5 FIGO Staging of Carcinoma of the Vulva (2009)

Stage	Definition
Stage I	Tumor confined to the vulva
Stage Ia	Lesions ≤2 cm in size, confined to the vulva or perineum and with stromal invasion ≤1.0 mm*, no nodal metastasis
Stage Ib	Lesions >2 cm in size or with stromal invasion >1.0 mm*, confined to the vulva or perineum, with negative nodes
Stage II	Tumor of any size with extension to adjacent perineal structures (⅓ lower urethra, ⅓ lower vagina, anus) with negative nodes
Stage III	Tumor of any size with or without extension to adjacent perineal structures (⅓ lower urethra, ⅓ lower vagina, anus) with positive inguino-femoral lymph nodes
Stage IIIa	(i) With 1 lymph node metastasis (≥5 mm), or (ii) 1–2 lymph node metastasis(es) (b5 mm)
Stage IIIb	(i) With 2 or more lymph node metastases (≥5 mm), or (ii) 3 or more lymph node metastases (b5 mm)
Stage IIIc	With positive nodes with extracapsular spread
Stage IV	Tumor invades other regional (⅔ upper urethra, (⅔ upper vagina), or distant structures
Stage IVa	Tumor invades any of the following: (i) upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or (ii) fixed or ulcerated inguino-femoral lymph nodes
Stage IVb	Any distant metastasis including pelvic lymph nodes

* The depth of invasion is defined as the measurement of the tumour from the epithelial-stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.

13.6 FIGO staging for uterine sarcomas

Staging for uterine sarcomas (leiomyosarcomas, endometrial stromal sarcomas, adenosarcomas, and carcinosarcomas).

Leiomyosarcomas and endometrial stromal sarcomas (ESS)*

Stage	**Definition**
Stage I	Tumour limited to uterus
Stage Ia	≤5cm
Stage Ib	>5cm
Stage II	Tumour extends beyond the uterus, within the pelvis
Stage IIa	Adnexal involvement
Stage IIb	Involvement of other pelvic tissues
Stage III	Tumour invades abdominal tissues (not just protruding into the abdomen).
Stage IIIa	One site
Stage IIIb	> one site
Stage IIIc	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IVa	Tumour invades bladder and/or rectum
Stage IVb	Distant metastasis

Adenosarcomas

Stage	**Definition**
Stage I	Tumour limited to uterus
Stage Ia	Tumour limited to endometrium/endocervix with no myometrial invasion
Stage Ib	Less than or equal to half myometrial invasion
Stage Ic	More than half myometrial invasion
Stage II	Tumor extends beyond the uterus, within the pelvis
Stage IIa	IAdnexal involvement
Stage IIb	Involvement of other pelvic tissues
Stage III	Tumour invades abdominal tissues (not just protruding into the abdomen).
Stage IIIa	One site
Stage IIIb	> one site
Stage IIIc	Metastasis to pelvic and/or para-aortic lymph nodes
Stage IVa	Tumour invades bladder and/or rectum
Stage IVb	Distant metastasis

Carcinosarcomas

Carcinosarcomas should be staged as carcinomas of the endometrium.

* Simultaneous endometrial stromal sarcomas of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumors