Gynaecology Pathway board

Guidelines for the management of gynaecological cancers

Date Agreed: January 2017
Date for Review: December 2019
INTRODUCTION

One of the principal goals of the pathway board is to improve outcomes in cancer by achieving the evidence-based standards set out in the COG Guidance (NHS Executive). A key objective in reaching this aim is the establishment and maintenance of up-to-date clinical practice guidelines. Such guidelines are intended to raise standards and ensure consistency in the quality of care that patients receive. “Improving Outcomes in Gynaecological Cancer” provides a model framework for multidisciplinary care by expert teams at the Centre and in the Units. The term ‘Centre’ refers to two sites: Central Manchester NHS FT and the Christie NHS FT.

This document has been circulated to and approved by the pathway board. It is envisaged that the contents will be reviewed on an annual basis to ensure that management is current and where possible, evidence-based.

These guidelines are based on the best evidence currently available, and include diagnosis, staging and treatment. There are several fundamental principles on which the guidance is built: accurate pathological diagnosis and staging, multidisciplinary team decision making, appropriate referral to the Centre, and access to clinical nurse specialists.

It is important that eligible women are offered entry into international, national, regional and local cancer trials. Continual improvements in data collection are required in order to comply with NHS standards. Where relevant trials exist for each cancer site, these are described.

The Guidelines are set out by primary tumour site and include investigation and staging, primary treatment, rarer histo-types, follow up and management of recurrent disease. There is also a section on Supportive and Palliative care.

In 2009, guidelines drafted by the Skin Cancer MDT for skin cancer of the external female genitalia were discussed by the then established Gynaecological cancer CSG, as these are generally managed by gynaecological oncologists. The resulting agreed pathway and guidelines for management remain in place and are included under section 5 “Vulval Cancer”. The new 2009 FIGO staging rules are also included as appendices.
Summary of Service Provision by Trusts

There are two gynaecology SMDTs in Greater Manchester and East Cheshire; Central Manchester NHS Foundation Trust and the Christie NHS Foundation Trust. The population has been geographically organised into the following organisational sectors.

Central Manchester NHS Foundation Trust covering the North-East Sector:
- Pennine Acute Hospitals NHS Trust (Bury, North Manchester, Oldham, Rochdale)
- Central Manchester University Hospitals NHS Foundation Trust
- Tameside Acute NHS Foundation Trust

The Christie NHS Foundation Trust covering the North-West/South Sector:
- Wrightington Wigan and Leigh NHS Trust
- Royal Bolton Hospital NHS Foundation Trust
- Salford Royal NHS Foundation Trust
- East Cheshire NHS Trust
- Mid Cheshire NHS Trust
- Stockport Foundation NHS Trust
- University Hospital of South Manchester NHS Foundation Trust
- Christie Hospital NHS Foundation Trust

The named local diagnostic gynaecology teams carry out the diagnostic process for patients from their own catchment, referring patients to the specialist gynaecology cancer teams for specialist care.

Low risk endometrial cancer may be managed by individual surgeons from the diagnostic teams provided that they are named as a member of the diagnostic service, and they attend the specialist MDT as a core member.

The Christie Hospital is the Tertiary Referral Centre for treatment with radiotherapy delivered at The Christie Hospital and the satellite radiotherapy units based at Royal Oldham Hospital and Salford Royal.

Chemotherapy and clinical trials for gynaecology are predominantly delivered at The Christie Hospital. Although chemotherapy for other tumour sites is currently available at a number of local trusts across the area, this pathway is not yet established for gynaecological cancers.
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1.0 CANCER OF THE CERVIX

1.1 Epidemiology
The incidence of cervical cancer has fallen significantly in the UK due to the success of the Cervical Screening Programme. There are now approximately 2700 new cases in the UK and approximately 1,000 deaths per year. Squamous carcinoma and adenocarcinoma carry the same prognosis, which is stage dependent. The increasing cure rate partly reflects down staging achieved through screening and increased health awareness by women.

1.2 Diagnosis and management of micro-invasive disease (FIGO 1A₁ +1A₂)
This is currently defined as disease with stromal invasion measuring no more than 5 mm and a lesion width of no more than 7 mm. Stage 1A₁ is < 3 mm invasion and 1A₂ is 3 - 5 mm invasion. Lymphatic/vascular channel involvement does not influence the stage but may influence the management.

In women who may wish further children, an excisional biopsy (cone / LLETZ / NETZ) with clear margins both ecto-and endo-cervically is adequate treatment for stage 1A₁ disease (Grade C). If the margins are uncertain or involved with CIN or CGIN, further surgery is required to exclude multifocal invasive disease. For women wishing to have further children, a second excisional treatment is preferable as further surgery. Cone biopsy/ LLETZ/ NETZ and lymphadenectomy is sufficient treatment for women with stage 1A₂ disease (disease >3mm and <5mm in depth) (Grade C). In terms of fertility preservation, conservative management of stage 1A₂ is feasible and should be discussed by the specialist MDT. In women for whom fertility is not an issue, hysterectomy with ovarian conservation (if <45 years) may be the preferred option.

It is imperative that all cases of cervical cancer are discussed at the Sector MDT and are available for review by a specialist team, core member histo-pathologist.

1.3 Diagnosis and staging of frankly Invasive Disease (≥FIGO 1B)

1.3.1 Investigations and Staging
Clinical assessment should include a full history and general examination. Bimanual
vaginal and rectal examination will usually reveal whether the tumour is confined to the cervix or not. An examination under general anaesthesia may be performed to stage the disease. Cystoscopy +/- sigmoidoscopy may also be required where bladder or rectal involvement is a possibility. Full blood count and serum biochemistry should be carried out paying particular attention to anaemia and renal function.

Where renal obstructive uro-pathy is present, there should be discussion with the clinical oncologist with consideration given to correction of the Uropathy before transfer of the patient e.g. nephrostomy. Also any significant anaemia (Hb<10.5gm/dL) should be corrected after diagnosis by blood transfusion.

1.4 Radiological Investigations
Radiological investigation of tumours clinically stage 1B or greater and those considered suitable for primary surgical treatment should include CXR, and MRI of the pelvis to assess tumour volume and lymphadenopathy. CT is better than MRI for evaluating extra-pelvic disease and should be extended to include the chest in patients with advanced or metastatic disease or in atypical histological types of cervical cancer, such as small cell or neuroendocrine malignancies. A non-diagnostic CT scan of the pelvis will be performed at The Christie for radiotherapy planning.

MRI scans will be performed after radical radiotherapy to assess response at 3 monthly intervals, until there is complete radiological response. Routine radiological surveillance thereafter in the follow-up of asymptomatic women is not indicated. Patients with signs of recurrent tumour should be imaged using CT or MRI, depending on the potential treatment options. Cases of incomplete response post radical radiotherapy will be discussed at the SMDT and referred for PET CT, EUA and biopsy to consider suitability for exenterative salvage surgery.
1.4.1 Radiological Guidelines

<table>
<thead>
<tr>
<th>FIGO Stage</th>
<th>Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical &lt;1B</td>
<td>Not indicated</td>
</tr>
<tr>
<td>Clinical 1B Patient fit/suitable for surgery</td>
<td>MRI pelvis</td>
</tr>
<tr>
<td>Clinical ≥1B</td>
<td>MRI – tumour and nodes (inc. para-aortics)</td>
</tr>
<tr>
<td>Clinical advanced/metastatic</td>
<td>CT – chest, abdomen, pelvis</td>
</tr>
<tr>
<td>Small cell or other atypical histology</td>
<td>CT – chest, abdomen, pelvis</td>
</tr>
<tr>
<td>Follow-up</td>
<td>MRI post radiotherapy until complete response or residual disease established CT if MR not possible</td>
</tr>
<tr>
<td>Suspected recurrence</td>
<td>CT/MR/PET CT to assess feasibility of further treatment</td>
</tr>
</tbody>
</table>

1.5 Primary Treatment

Women with frankly invasive cervical cancer should be managed in consultation with the MDT and referred to the Centre. MDT management plan needs to take account of patient choice once the patient is informed of the possible clinical management options, taking into account reproductive and psycho-sexual needs.

1.5.1 FIGO 1b1/IIa

Low volume early stage disease (IB1/IIA1) can be managed equally effectively by radical surgery or chemo-radiotherapy and brachytherapy (Grade A). Surgery is generally preferred because of ovarian preservation, length of treatment and avoidance of radiation effects; however, patient preference may influence management. Extensive LVSI may influence the treatment choice, favouring radical chemo-radiation.

Bulky (>4cm) early stage disease is better managed by radical chemo-radiation (Grade A) and to avoid both radical surgery combined with radiotherapy, which may result in increased morbidity. Strong radiological evidence of lymphadenopathy is a contraindication to surgical treatment.

Surgery for cervical cancer should be undertaken by a gynaecological oncologist at the Centre and decisions regarding adjuvant or primary radiotherapy should be made in discussion with the clinical oncologist in the gynaecological team (Grade C). In women
with small volume stage IB1 disease (<4cm diameter) who wish to have further children, 
consideration can be given to radical trachelectomy with lymphadenectomy, which 
should be undertaken by a gynaecological oncologist trained in the procedure (Grade C). 
Patients should be appropriately counselled about the risks of pre-term labour, the need 
for specialist feto-maternal care in subsequent pregnancy and the need for Caesarean 
delivery (Grade B).

Radical surgery, if performed, would normally comprise a Piver-Rutledge type II or III 
procedure dependent on tumour size; full iliac and obturator node dissection to 2cms 
above the bifurcation of the common iliac arteries is required. Para-aortic nodes are 
removed if enlarged or if pelvic nodes are suspicious, but not routinely. Hysterectomy is 
performed with a 2 cm vaginal cuff. Suction drainage to the pelvis may be used 
according to an individual surgeons practice but is not essential (Grade A) and indwelling 
catheterisation for at least five days with a urethral or supra-pubic catheter is usually 
required. Residual urine volume should be <150 ml, before permanent removal of the 
catheter. As with all major pelvic surgery, thrombo-prophylaxis and prophylactic IV 
antibiotics should be administered.

1.5.2 FIGO IB₂/IIB-IV

Primary surgery is not indicated for bulky stage IB disease or above. Those patients 
with bulky IB (>4cms) and locally advanced disease stages IIA2, IIB and III and some 
stage IV should be offered chemo-radiation if fit (Grade A). Patients must have good 
performance status 0 or 1 and have adequate renal function (isotope GFR>50ml/min) 
and adequate marrow reserves if they are to receive concurrent cisplatin weekly during 
their external beam radiotherapy.

External beam pelvic radiotherapy is administered to the pelvis using IMRT (delivered 
with VMAT technique at The Christie), dose of 45Gy in 25 fractions over 5 weeks with 
weekly concomitant cisplatin. The field includes the cervix, uterus, parametrium, upper 
vagina, ovaries and loco-regional nodes including obturator, external, internal and 
common iliac. The superior border is at the level of the aortic bifurcation but may be 
extended superiorly if suspicious nodal disease is identified. It is acknowledged that this 
is associated with higher toxicity.
External beam radiotherapy is followed by intra-cavitary brachytherapy, generally during the 2 weeks following completion of pelvic radiotherapy. Gaps between intra-cavitary and external beam therapy should be kept to a minimum compatible with the patient’s medical condition (RCR document “The Avoidance of Gaps in Radiotherapy”). The overall treatment time should be ≤7-8 weeks. An external beam boost to the cervix tumour may be given over 8-10 fractions in patients where cannulation of the uterus is not possible or medical reasons prohibit a general anaesthetic.

Patients should be given written information and advice about radiotherapy reactions, both early and late. Written consent relating to treatment and morbidity should be recorded by a member of the treating medical team and the patient prior to the start of treatment.

1.5.3 Adjuvant Radiotherapy

Radiotherapy after radical hysterectomy should be considered if central tumour margins are doubtful (i.e. <5mm), if there are positive nodes, if the primary tumour is of poor prognostic type (grade C). Concurrent Cisplatin is offered during external beam radiotherapy provided the patient has adequate renal function and marrow reserve.

The radiotherapy to the pelvis is given as for radical radiotherapy described in section 1.5.2. Brachytherapy may be combined with external beam in these patients if there is any doubt about adequacy of surgical margins in the vagina or if there has been recurrence centrally after primary surgery.
1.6 Management Algorithm

<table>
<thead>
<tr>
<th>FIGO stage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA1</td>
<td>Cone biopsy or “simple” hysterectomy</td>
</tr>
<tr>
<td>Stage IA2</td>
<td>Cone biopsy or “simple” hysterectomy plus pelvic lymphadenectomy</td>
</tr>
<tr>
<td>Stage IB1/IIA1</td>
<td>Radical hysterectomy and lymphadenectomy or radical Radiotherapy. Consider tracheectomy if fertility preservation desired</td>
</tr>
<tr>
<td>Stage IB2 or IIA2(&gt; 4cm)</td>
<td>Radical radiotherapy with concomitant Cisplatin chemotherapy</td>
</tr>
<tr>
<td>Stage IIB, III, IV</td>
<td>Radical radiotherapy with concomitant chemotherapy.</td>
</tr>
</tbody>
</table>

1.7 Rare Histo-types
Squamous carcinoma, adenosquamous carcinoma and adenocarcinoma tend to be managed along the above lines. Rare small cell tumours and neuroendocrine tumours require treatment with chemotherapy, recognising the poor prognosis. Aggressive surgery is probably not indicated initially as the principal risk for these women is blood borne metastases. These women will normally be referred to the lung cancer team for chemotherapy.

1.8 Follow-up
Patients should be followed up at 3-6 monthly intervals for the first 2 years (90% of recurrences will occur by 2 years with 80% of recurrences occurring in the first year after treatment). Thereafter patients will be seen at 6 monthly intervals for 5 years. Follow-up will be to manage any potentially curable recurrence. It is always good practice to discuss continuation or discontinuation of follow-up with individual patients so that their views can be taken into consideration.

Routine vault smears either post radiotherapy or post radical surgery is not indicated, and need not be performed. Cytology following radiotherapy is very unreliable and difficult to interpret.
### Table 1: follow up cytology post cervical cancer treatment (NHSCSP 20, 3rd edition, March 2016, Public Health England)

<table>
<thead>
<tr>
<th>treatment</th>
<th>Cytology on Follow up</th>
<th>Where?</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLETZ / NETZ / Knife cone</td>
<td>Smear 6 and 12 months after treatment then annually for the next 9 years.</td>
<td>Local colposcopy clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NHSCSP recall</td>
</tr>
<tr>
<td>Trachelectomy</td>
<td>Colposcopy + smear</td>
<td>Gynae Oncology surgeon</td>
</tr>
<tr>
<td>Total (simple) hysterectomy Or Radical</td>
<td>If residual CIN</td>
<td>GP</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>• completely excised CIN1/2/3 or CIN 1</td>
<td>Local colposcopy clinic</td>
</tr>
<tr>
<td></td>
<td>• incompletely excised then vaginal vault cytology 6 and 18 months post-surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• incompletely excised CIN 2/3 then vault cytology at 6, 18 and 24 months post-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>surgery and annually for the next 9 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If no CIN, on surgical specimen (cancer only)</td>
<td>n/a</td>
</tr>
<tr>
<td></td>
<td>• No cytology on follow up</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy + / - chemotherapy</td>
<td>No cytology on follow up</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Reference:


Routine follow-up imaging is not indicated out with a trial or in the absence of symptoms or abnormalities detected on clinical examination. For those patients with bulky tumours treated with radiotherapy +/- chemotherapy, MR scans are performed at three months following completion of treatment to check that there has been resolution of disease. Follow-up interval scans may be performed if residual disease is identified at three months when discussed at the multidisciplinary meeting at the cancer centre.

Alternate follow-up between the referring surgeon and the oncologist is desirable if this is in accordance to the patient’s wishes. Patients with treatment effects that require surgical intervention may require indefinite and individualised follow-up, as per their
need. It is acknowledged that it is relatively unusual to detect asymptomatic recurrence in a well patient at routine follow-up. It should be emphasized that patient-initiated attendance with symptoms between routine follow-up visits is more important in the detection of recurrence.

1.8.1 Suggested Follow-up intervals

Surgery Only

Year 1: three monthly

Year 2, 3, 4 and 5: six monthly

Radiotherapy (Primary & Adjuvant, though primary may remain solely under the Christie clinical oncologists)

3 months: Christie

6 months: Gynaecologist

9 months: Christie

12 months: Gynaecologist

18 months: Christie

24 months: Gynaecologist

30 months: Christie

36 months: Gynaecologist

42 months: Christie

48 months: Gynaecologist

54 months: Christie

60 months: Gynaecologist

1.9 Recurrent disease

Patients who develop symptoms/signs suspicious of recurrence should be referred to the multi-disciplinary team at the centre. Those patients who have received prior pelvic radiotherapy should be assessed with a view to surgical salvage, which normally means pelvic exenterating.
Exenteration is used in highly selected cases of recurrent pelvic cancer when the aim is to salvage recurrence with curative intent. It is generally employed for central recurrence of cervical cancer when radiotherapy had already been used. Under optimal circumstances it is associated with a 5-year survival rate of 50% (Grade C), so case selection is paramount.

Assessment of women for exenteration and exenterative procedures are the responsibility of a multidisciplinary surgical team comprising a gynaecological oncologist and a urological oncology surgeon and /or a colorectal cancer surgeon, as appropriate. These women require careful assessment. The prognosis is extremely poor in the presence of any sidewall disease, in which case exenteration should not be performed.

Recurrences in radiation naïve women are usually best treated with chemo-radiation; central recurrence carries a far better prognosis than side wall recurrence.

Those patients who are inoperable or who have metastatic disease outside the pelvis should be considered for palliative radiotherapy or chemotherapy.

1.10 Fistulae
Fistulae may arise as a consequence of advanced pelvic disease but are also late problems following pelvic radiotherapy for locally advanced tumour where there is invasion of adjacent bladder and bowel.

In the absence of clinical evidence of active disease, a CT scan should be performed to assess with a view to surgical management.

Those patients with fistulae associated with progressive malignancy should have surgical assessment to consider palliative bowel or urinary diversions.

Uncontrolled loss of small bowel contents leads to skin excoriation. Palliative care measures include a trial of Ocreotide by subcutaneous infusion (300-600mgs/24 hours) and attempts to solidify/bulk the stool using Loperamide and Fybogel. Intensive skin care with use of barrier creams (e.g. Cavilon) is important.
1.11 **Sexual Rehabilitation Clinic**

Women who undergo treatments for any gynaecological cancer may experience physical and/or psychological sexual issues afterwards, which may affect their own sexuality, body image and fertility or their intimate relationships with their partners. Women require information prior to treatment about possible sexual dysfunction afterwards. Assessment of sexual function/dysfunction should be routine follow-up post-surgery, radiotherapy and/or chemotherapy. Following radiotherapy, to the vagina, patients are advised and educated in the use of vaginal dilators in order to prevent/minimise vaginal stenosis. They are also given basic information when appropriate about returning to sexual activity.

If women have sexual dysfunction/sexuality problems beyond the scope of the team providing follow-up they should be referred to the appropriate specialist. The Sexual Rehabilitation Clinic at St. Mary’s Hospital offers a service to any woman post gynaecological cancer treatment, with either physical or psychosexual problems by an appropriately trained nurse specialist, psychosexual therapist and gynaecologist.

1.12 **Patient Information**

Following confirmation of the diagnosis and recommended treatment plan at the MDT the Unit Lead and CNS should relay the information to the patient together with the information booklet ‘cervical cancer’.

The information on the mode of treatment can also be given at this stage.

If the patient is treated at the cancer centre a check should be made to ascertain the patient has received the relevant patient information and if found to be missing, given at this stage. If the mode of the treatment is changed at upon review of the patient then the relevant information given.
2.0 VAGINAL CANCER

2.1 Investigations/Staging
Imaging is not routinely indicated for micro-invasive or clinical stage I tumours. MRI may be helpful for surgical treatment planning in more extensive disease, and to assess the lymph nodes. CT will be required for radiotherapy treatment planning.

2.2 Diagnosis and Treatment
Vaginal cancer is almost always squamous carcinoma and is rare. It should be diagnosed only in the following circumstances:

(i) In the presence of a normal cervix.
(ii) Following documented total hysterectomy.
(iii) More than 10 years following cure of cervical cancer.

The principles of management are similar to cervical cancer. A superficial lesion at the vault (post hysterectomy) or posterior fornix may be resectable and curable by means of vaginectomy. More deeply infiltrative tumours are generally best treated by radiotherapy +/- concurrent Cisplatin chemotherapy, which offers vaginal preservation. All cases of vaginal cancer should be referred to the Centre for management decisions, allowing treatment options and side effects of treatment to be fully explained to the patient so they can be involved in the decision making process.

2.3 Patient Information
Following confirmation of the diagnosis and recommended treatment plan at the MDT the Unit Lead and CNS should relay the information to the patient together with the information booklet regarding radiotherapy which will be the mode of treatment in the majority of cases. If an examination under anaesthetic is required to confirm diagnosis and plan treatment this information leaflet should be given.

When the patient is treated at the cancer centre a check should be made to ascertain the patient has received the relevant patient information and if found to be missing, given at this stage. If the mode of the treatment is changed at upon review of the patient then the relevant information given.
3.0 ENDOMETRIAL CANCER

3.1 Epidemiology

The incidence of this disease is rising in line with increasing life expectancy and levels of obesity such that endometrial cancer is now the commonest gynaecological malignancy. The majority of patients have early disease, survival being 90% in Stage I. The overall 5-year survival rate of 70% reflects the poor prognosis in more advanced disease. A significant minority of women with endometrial cancer have significant (sometimes life-limiting) co-morbidity and/or morbid obesity. There are significantly increased peri-operative requirements for this group of women and an increasing dependence on High Dependency Unit support. Pelvic surgery in women with morbid obesity can be particularly challenging. This, together with the need for a high degree of peri-operative support is likely to lead to an increased trend towards centralisation of even “low risk” cases in the future.

3.2 Prevention and Screening

There is no evidence that screening asymptomatic women in the general population with TVUS or endometrial sampling reduces the mortality from endometrial cancer (level 2+).

Women with Lynch Syndrome and their first degree relatives could be offered annual screening with TVUS and endometrial biopsy from the age of 35 years after counselling about the risks, benefits and limitations of screening. There is no formalised programme in place and provision for these patients varies between institutions (Grade C, level 4, expert evidence).

There is no current evidence upon which to base a recommendation of screening in women with a previous history of breast cancer or with a known BRCA mutation (Grade C – expert opinion, level 4).

Routine screening with TVUS, endometrial biopsy, or both has not been shown to be effective in women who are on tamoxifen therapy. Postmenopausal women taking tamoxifen should be routinely questioned at breast cancer follow up visits about symptoms of vaginal bleeding/discharge and should be made aware of the risks. Symptoms in these women should be investigated with hysteroscopy as well as biopsy and ultrasound. Tamoxifen use should be reassessed if hyperplasia is identified. Pre-treatment screening of postmenopausal women may be beneficial to identify high-risk groups with pre-existing occult abnormalities. Premenopausal women should receive standard gynaecological care (13) (level 2+).

There is no evidence to support a screening programme in PCOS, diabetes or obesity.
3.3 Investigations

Recurrent PMB should be investigated by hysteroscopy and endometrial biopsy (Level 4, Grade D). Trans-vaginal scan (TVS) with measurement of endometrial thickness should be employed as initial investigation for women presenting with PMB (Level 2++, Grade B).

Double layer endometrial thickness measurements on TVS with a cut off of ≥ 4 mm should be investigated. In the absence of any irregularity of the endometrial profile e.g. fluid, no further investigations are required unless there is recurrent PMB (Level 2++ - 4, Grade B).

In patients with a TVS endometrial thickness measurement of ≥ 4 mm, an outpatient endometrial biopsy should be carried out (Level 2++, Grade B).

Hysteroscopy should only be carried out if outpatient endometrial biopsy is not feasible or for women with ultrasound irregularities and at high risk of endometrial cancer (Level 2++, Grade B). Hysteroscopy should be preferably carried out as an outpatient procedure (Level 2++, Grade C).

Hysterectomy may be considered in cases of unexplained recurrent PMB (Level 4, Grade D).

3.3.1 Imaging guidelines in endometrial carcinoma

Imaging of the pelvis should be performed in all women with endometrial cancer (Grade D).

All women with a high risk of potential metastases (high grade histological subtypes) should have a CT of the chest, abdomen and pelvis preoperatively to help plan surgery or potentially avoid upfront surgery if metastatic disease is found. The yield from CT scanning in low risk disease is very small, is very unlikely to alter the ultimate outcome and is not mandatory (Grade D).

MRI of the pelvis is useful to identify lymph node metastases and may be useful to stratify patients into pathways of care (Grade D).

PET is not recommended for routine preoperative staging in the NHS outside a clinical trial (Grade D).

3.4 Surgical Treatment of presumed early disease

Surgery may be limited to hysterectomy and bilateral salpingo-oophorectomy in those patients with grade I or II endometrioid adenocarcinoma which appears confined to the uterus. However, there will be a proportion of women who may require further surgery or adjuvant treatment using this
approach due to underestimation of histological grade on pre-operative biopsy or the presence of other risk factors on final histological examination (Grade D).

Lymphadenectomy in this instance does not improve survival or reduce the risk of disease recurrence (Grade A).

The accuracy of risk assessment may be increased by intra-operative frozen section analysis and radiological investigation (Grade B).

Sentinel lymph node biopsy appears to have good diagnostic performance; however, current evidence is lacking to support its inclusion in routine clinical practice (Grade B).

Surgery should be performed laparoscopically, wherever possible, as it is associated with a lower rate of severe post-operative morbidity and shorter hospital stays compared with laparotomy. It is, therefore, a more cost effective approach (Grade A).

Laparoscopic surgery is not associated with a significant adverse impact on disease recurrence and overall survival (Grade A).

Robotic surgery appears to be non-inferior to laparoscopy for the treatment of endometrial cancer, but has a higher cost association (Grade C).

Robotic hysterectomy is associated with improved operative outcome and a lower complication rate compared with laparoscopic hysterectomy in obese and morbidly obese women (Grade C).

Surgery for presumed low grade, stage I disease can be performed in a cancer unit as this does not appear to affect disease specific survival (Grade D).

Radical hysterectomy is an alternative to simple hysterectomy and adjuvant radiotherapy for patients with stage II disease (Grade B).

Complete surgical staging including pelvic and para-aortic lymphadenectomy and omental biopsy is appropriate for high grade disease and non-endometrioid endometrial cancers. They should be operated on in a cancer centre. All such patients should be considered for recruitment into clinical trials, e.g. ENGOT/EN1 or STATEC (Grade C).
3.5  Surgical management of advanced disease (stage III, IV)

The aim of surgery in the management of advanced stage endometrial cancer should be complete surgical resection of all visible disease as this significantly prolongs survival (Grade C).

Systematic lymphadenectomy should be performed in preference to palpation and removal of clinically enlarged nodes only as the latter is inaccurate (Grade B).

Complete resection of macroscopic nodal disease improves disease specific survival (Grade B).

Patients with advanced disease should be operated on in a cancer centre by gynaecological oncologists as this improves survival (Grade C).

Surgery may be used to treat localised recurrent disease and can be curative (Grade C).

Surgery may be appropriate for patients with advanced disease at presentation who have responded to neoadjuvant chemotherapy or radiotherapy (Grade D).

The use of neoadjuvant chemotherapy in the context of treating advanced endometrial cancer has not been formally assessed in randomised controlled trials. However, it would seem reasonable, based upon available data from the management of epithelial ovarian tumours, to offer neoadjuvant chemotherapy to women with advanced disease where complete resection is unlikely to be achievable at primary surgery. Such cases should be discussed at the MDT and surgery could then be offered to those women who have responded to initial chemotherapy.

Debulking palliative surgery has a role in providing symptomatic relief (Grade C).

3.6  Management of patients considered unfit for definitive surgical management or wishing to preserve fertility

For those women who are unfit for standard treatment for endometrial endometrioid disease i.e. Hysterectomy and bilateral salpingo-oophorectomy under general anaesthesia either due to morbid obesity or inter-current medical conditions may be considered for simple vaginal hysterectomy, definitive pelvic radiotherapy or conservative management with progestogens/aromatase inhibitors. Ideally, patients should be referred to a dedicated clinic to discuss and consider appropriate options including recruitment into relevant clinical trials wherever possible.

Radiotherapy as primary treatment of endometrial cancer is only considered in exceptional cases, recurrence rates of up to 18% have been reported in these patients in a recent retrospective study. (1)
Higher failures with radiotherapy to pelvic cancers have been reported in prostate cancer in obese patients.\(^3\)

Generally, the recommended oral progestogens are Megestrol 160mg daily, Medroxyprogesterone acetate (MPA) 200mg or 400mg daily. However, a much lower dose is likely to be equally effective and in patients with a history of cardiac failure less problematic with respect to fluid retention. Aromatase inhibitors may be an alternative in such patients. The comparative efficacy of progestogens and aromatase inhibitors has never been investigated in a randomised controlled trial.

The FeMMe (ANZGOG) trial is a randomised controlled trial of conservative management in comorbid patients and those desiring fertility, and may provide some answers to manage this challenging clinical scenario.

Vaginal hysterectomy is likely to offer good palliation in women with non endometrioid cancer who are less likely to respond to alternative e.g. progestogens (Grade C evidence).

Current evidence suggests that conservative management of endometrial cancer may be safe in the short term in selected women with low grade endometrial cancer and with superficial myometrial invasion.

Women with endometrial cancer desiring fertility should be counselled carefully about the current known response rates on progestogens and progression risk. MDT should involve specialist Gynaepathology review, imaging, and follow-up with regular endometrial sampling and individualised care in the management of these patients.

3.7 Adjuvant radiotherapy

Radiotherapy may be used as post-operative adjuvant treatment in women at high risk of developing recurrent disease according to the following guidance:

- Post-operative adjuvant radiotherapy improves survival and also reduces the risk of loco-regional recurrence from 15% to 6% in women with stage 1 disease with at least 2 risk factors of grade 3 tumours, >50% myometrial invasion and >60 years of age (Grade A). Women with more aggressive histological sub-types should also be referred for a discussion regarding post-operative adjuvant treatment (PORTEC 1).

- Brachytherapy to the vault has equivalent local control as external beam radiotherapy to the pelvis (<2%) for G1-2, >50% myometrial invasion. Pelvic side wall recurrence is slightly higher
with vault brachytherapy alone (5% vs 2%) however survival is the same as the rate of distant metastases is equivalent. Therefore vault brachytherapy rather than external beam radiotherapy is recommended for this group of patients. Vault brachytherapy may also be used for G3 disease with <50% myometrial invasion as these were also included in a smaller number in the trial (PORTEC 2, Grade A).

- Patients with no or <50% myometrial invasion, G1-2 are at low risk of recurrence and are not given adjuvant radiotherapy (Grade A).
- Pelvic external beam radiotherapy is indicated for stage 2-3 disease. A combination of pelvic external beam radiotherapy plus vault brachytherapy is recommended in stage 2 disease or stage 3 disease with cervical involvement.
- Pelvic radiotherapy may be omitted following negative pelvic lymphadenectomy with total a node count of >6 nodes from each pelvic side wall for stage 1B G3 and stage 2 G1-2.

Vaginal vault brachytherapy is given with pulsed dose rate or high dose rate iridium. External beam radiotherapy is delivered using VMAT, 45Gy in 25 fractions over 5 weeks.

### 3.8 Primary Radiotherapy
Where a woman is considered unfit for surgery, radiotherapy may be used as primary treatment although this is not as effective as surgery (Grade B). The patient should be scanned to assess extent of disease, preferably with MR. Intra-cavitary brachytherapy may be considered although generally the reasons that exclude the patient from surgery also do so for brachytherapy as it involves a short GA followed by a period of immobility (at least 3-4 hours) and lying flat. External beam radiotherapy may be given over 10-25 fractions.

### 3.9 Adjuvant chemotherapy
The benefit of adjuvant chemotherapy in endometrial cancer is not fully defined. There have been four randomized phase III trials that have attempted to address this question. The largest (GOG 122) reported a significant 12% improvement in 5-year survival in patients with optimally debulked stage III/IV disease treated with chemotherapy as opposed to whole abdominal irradiation. This result was not reproduced in an Italian study although only 22% of patients in this study had IIIC disease (pre-2009 staging). The use of an abbreviated (and sub-optimal) chemotherapy regimen was also no more effective than pelvic irradiation in a Japanese trial predominantly in patients with stage I tumours although a subset of patients with deep myometrium invasion and grade 3 tumours appeared to gain significant benefit from chemotherapy. All three studies indicated that the
incidence of distant metastases was reduced in patients receiving chemotherapy suggesting that combining adjuvant chemotherapy and pelvic irradiation may be the most effective adjuvant regimen.

The recently presented EORTC 55591 study, added four cycles of chemotherapy to pelvic irradiation and reported statistically significant improvements in both disease recurrence and cancer specific survival (10%) in patients with high risk, early stage disease receiving chemotherapy.

Enrolment into the PORTEC3 trial that addressed the role of adjuvant and concurrent chemotherapy in addition to pelvic radiotherapy has recently completed. A recent Cochrane review (Galaal et al 2014) of all available evidence, estimates a clinically significant improvement in OS with adjuvant chemotherapy (HR 0.75 compared to radiotherapy alone) for patients with stage III and IV disease and the Network recommendations given below are consistent with this and current European Society of Medical Oncology guidelines (Colombo et al 2013)

Chemotherapy is considered in the adjuvant setting in women with:

- advanced disease (stage IIIA and above)
- high risk, early stage disease (>50% myoinvasion / grade 3)
- stage II with deep myometrial invasion
- myoinvasive serous or clear cell carcinoma
- myoinvasive carcino-sarcoma

There is evidence that chemotherapy does not prevent pelvic recurrence so most patients receiving adjuvant systemic therapy should receive adjuvant pelvic radiotherapy in addition. In most cases, this should follow completion of chemotherapy. However, in patients at very high risk of local pelvic relapse e.g. involved para-cervical or parametrical resection margins or where wound-healing complications will delay chemotherapy administration, it may be appropriate to deliver pelvic irradiation first.

3.10 Adjuvant progestogen Treatment

Progestogens offer no survival benefit in the adjuvant setting and should not be prescribed for this purpose (Grade A)
3.11 Treatment Algorithm for Endometrial Cancer

Histo-pathologically confirmed Endometrial Cancer

CXR, MR scan - to confirm suitability for local surgery & CT T/A/P for high grade histologies

High risk

- >50% myometrial involvement and/or
  - G3
  and/or
  - Suspected cervical involvement
  and/or
  - Susicion of nodal mets on MR/CT
  - Serous/clear cell type or other non-endometrioid type

Refer to gynaecological oncologist at Cancer Centre

Total hysterectomy/BSO
Peritoneal washings
Lymphadenectomy (only where nodes are enlarged or non-endometrioid histology or Grade 3)
Omental biopsy (serous carcinoma)

Refer for adjuvant therapy if G3 or higher stage

Refer for discussion re: radiotherapy if aged >/= 60 years and either <50% myoinvasion/G3 or >50% invasion -G1/2 disease.

Chemotherapy should be considered for non-endometrioid

Low risk

-G1, G2
<50% myometrial involvement

Can be managed by Unit Lead Clinician

Total hysterectomy/BSO
Peritoneal washing

If higher risk features are unexpectedly found on final histopathology, consider adjuvant treatment in conjunction with clinical oncologist (requires case to be discussed at MDT) (see guidelines in left hand box)

1A, G1/2 – radiotherapy not required
3.12 Uterine sarcoma (see also “6. Gynaecological sarcomas”)

3.12.1 Leiomyosarcoma

Recommendations (all Grade C)-

- The cornerstone of management of early LMS is total hysterectomy
- Salpingo-oophorectomy in young women is not mandatory
- Routine pelvic lymphadenectomy is not recommended
- Morcellation of fibroids should be avoided in postmenopausal women
- There is no data on the benefit of adjuvant chemotherapy or radiotherapy

Patients with advanced or recurrent LMS are usually challenged with chemotherapy unless complete surgical resection is possible

Management of patients with primary or recurrent Leiomyo-sarcoma requires a multidisciplinary team approach preferably with the participation of the regional sarcoma team.

3.12.2 Early stage endometrial stromal sarcoma

Surgical treatment with total abdominal hysterectomy and bilateral salpingo-oophorectomy is the cornerstone of the treatment, even in pre-menopausal women (Grade C).

3.12.3 Advanced or recurrent endometrial stromal sarcoma

Surgical resection can be considered in resectable cases.

3.12.4 Early stage undifferentiated endometrial sarcoma

Total abdominal hysterectomy with bilateral salpingo-oophorectomy remains the standard treatment for patients with undifferentiated endometrial sarcoma confined to the uterus.

3.12.5 Advanced or recurrent undifferentiated endometrial sarcoma

The role of debulking of extra-uterine disease is unclear. Retrospective studies showed that optimal cyto-reduction can be associated with better survival when compared with suboptimal debulking.
Patients with advanced disease should be considered for Ifosfamide-based palliative chemotherapy.

3.13 Follow-up

The role of routine follow-up for women with completely resected early stage endometrial carcinoma is not well evidenced. Trials addressing the value (or otherwise) of routine follow-up are needed. A suggested follow-up schedule is given below although timing of follow-up visits may be modified according to individual patient circumstances.

For patients who have only received adjuvant chemotherapy, follow-up should be conducted at the surgical centre so that direct inspection of the vaginal vault can take place if required.

Patients’ views need to be taken into account and it is good practice to discuss discontinuation or continuation of follow-up with individual patients where appropriate. It is acknowledged that it is relatively unusual to detect asymptomatic recurrence in a well patient at routine follow-up. It should be emphasized that patient-initiated attendance with symptoms between routine follow-up visits is more important in the detection of recurrence.

3.13.1 Suggested Follow-up intervals

**Surgery Only**

Year 1: 3 – 4 monthly  
Year 2, 3, 4, and 5: 6 - 12 monthly

**Radiotherapy (Primary & Adjuvant)**

3 months: Christie  
6 months: Gynaecologist  
9 months: Christie  
12 months: Gynaecologist  
18 months: Christie  
24 months: Gynaecologist
30 months: Christie
36 months: Gynaecologist
42 months: Christie
48 months: Gynaecologist
54 months: Christie
60 months: Gynaecologist

3.14 Treatment of Recurrent Endometrial Carcinoma

For patients who develop pelvic recurrence following surgery, radiotherapy may be given with curative intent. Imaging of the chest, abdomen and pelvis should be carried out to assess disease extent. The prognosis is far more favourable for central mucosal disease. Patients are offered pelvic radiotherapy followed by vault brachytherapy.

Extra-pelvic recurrence or recurrence following adjuvant radiotherapy should be considered for chemotherapy which will usually be carboplatin/paclitaxel or single agent carboplatin. Response rates of 50% have been reported with paclitaxel-containing chemotherapy with a modest survival benefit noted on addition of paclitaxel to platinum-based chemotherapy in a phase III trial.

Hormonal treatment, usually with high dose progestogens (Medroxyprogesterone acetate or Megestrol acetate) can be used for women with recurrence. Responses are seen more frequently in women whose index tumour expressed oestrogen and progesterone receptors (usually G1/2 tumours). G3 tumours and non-endometrioid tumours often lack hormone receptors and these tumours are less likely to respond. Although some women have prolonged responses, median length of response is usually reported as 10 months.

3.15 Genetic counselling/testing

Hereditary endometrial cancer accounts for <5% of all endometrial cancers. Endometrial cancer is the index cancer in approximately 50% of women with hereditary non-polyposis colon cancer syndrome (HNPCC), also known as Lynch syndrome.
Women with HNPCC have a 40-60% lifetime risk of developing endometrial cancer and are likely to develop another Lynch syndrome-associated cancer within 11 years of their index cancer. Currently prophylactic hysterectomy is the only proven method of preventing endometrial cancer in affected women.

Recognition of women with HNPCC is important as it enables them and their families to undergo genetic counselling and to receive appropriate screening for bowel cancers. The following women are more likely to have HNPCC and should be referred to the Clinical Genetics team for further discussion/ counselling and testing for HNPCC if appropriate:

1. Any woman with an endometrial cancer diagnosed at the age of 5 or less.
2. A patient with endometrial cancer under the age of 60 and the following family history:
   - A further case of endometrial cancer in a 1st or 2nd relative under the age of 65.
   - A 1st relative with bowel cancer under the age of 50.
   - Two close relatives with bowel cancer under 60 on the same side of the family.
   - Two close relatives on the same side of the family with ovarian or bowel cancer where the bowel cancer is under 60.

3.16 Patient Information

Following confirmation of the diagnosis and recommended treatment plan at the MDT the Unit Lead and CNS should relay the information to the patient together with the information booklet ‘endometrial cancer’.

The information on the mode of treatment can also be given at this stage.

If the patient is treated at the cancer centre a check should be made to ascertain the patient has received the relevant patient information and if found to be missing, given at this stage. If the mode of the treatment is changed upon review of the patient, then the relevant information must be given.
4.0 OVARIAN CANCER

The term ovarian cancer represents a heterogeneous set of diseases of diverse cellular and molecular origin. To date, most clinical trials have included a wide spectrum of subtypes and therefore evidence is often generic. This is likely to change as knowledge of the individual subtypes increases and allows greater stratification of treatment.

High Grade serous cancer of the ovary, fallopian tube and peritoneum are essentially variants of the same disease and appear to share the same progenitor lesion\(^{(1)}\). They are characterised by p53 mutation\(^{(2)}\), genomic instability and high copy number change. They are however, relatively chemo sensitive, particularly in the primary setting and management of the three conditions is similar.

In contrast, low grade serous cancer appears to arise on a background of borderline disease and is almost certainly a true ovarian cancer. Progression from low grade to high grade serous cancer appears to be extremely rare. Low grade serous cancer is chemo resistant (approx. 4% response to chemo in the primary setting) and therefore warrants a different surgical approach in comparison to high grade serous cancer.

Endometrioid cancer is uncommon and current thinking suggests that it usually arises on a background of endometriosis\(^{(3)}\). There is a clear association with clear cell cancer.

Mucinous cancer of the ovary is rarer than previously thought and is often secondary to a bowel or appendiceal primary. Non epithelial tumours have a very different biology, behaviour and therefore treatment. Their management is discussed separately below.

4.1 Epidemiology

Overall survival from ovarian cancer has changed little over the last three decades with a 5-year overall survival of 41%, although median survival has increased significantly.
suggesting that treatment regimens have improved \cite{4,5}. It is the second commonest gynaecological cancer after uterine cancer and the fifth commonest cancer in women.

It usually presents at an advanced stage when cure is uncommon. It is a chemo responsive tumour and the best prospects for survival occur with a protocol of maximal surgical cyto-reduction to a zero residue followed by optimal chemotherapy. This requires expert multidisciplinary teams working to protocol obtain optimal survival.

4.2 Diagnosis and prevention

4.2.1 Screening

No survival benefit from whole population screening has as yet been demonstrated. \cite{6} The UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) trial randomised 200,000 women to observation alone, testing with an algorithm based on serial values of CA125 and multimodal testing or serial ultrasound, showed no reduction in ovarian cancer mortality at primary analysis but a possible reduction in mortality after exclusion of prevalent cases after 7 years of follow-up. Long-term data and cost-effectiveness data are still awaited. Until then, screening cannot be recommended for women deemed to be at low risk of ovarian cancer.

Screening may have a role for women who carry germ line mutations of BRCA1 or BRCA2 and who wish to delay risk reducing surgery \cite{7} but requires careful adherence to screening protocols and should be managed within dedicated clinics.

4.2.2 Symptom awareness and initial testing in primary care

The NICE document “The recognition and initial management of ovarian cancer” issued in April 2011 recommends that General Practitioners become more aware of symptoms and signs in women (especially over the age of 50) \cite{8}. GPs should carry out appropriate tests should any of the following symptoms persist or happen more than 12 times a month.

- Persistent abdominal distension
- Feeling full( early satiety) and/or loss of appetite
- Increased urinary urgency and/or frequency
Initial investigations initiated in primary care should be CA125. An abnormal result should trigger referral for trans-vaginal ultrasound.

No guidance currently exists on the management of an elevated CA125 in the presence of a normal ultrasound scan other than other causes of an elevated CA125 should be sought. It has been estimated that the rate of false positives to true positive elevated CA125 will be in the order of 200:1 [9] and therefore these cases should not be referred to a central MDT for discussion, rather GPs should be encouraged to repeat CA125 at no less than 3 month intervals and only re refer if the CA125 has significantly increased.

4.3 Investigation and Staging

Women with a pelvic mass should have a reasonable effort made to try to establish a pre-operative diagnosis. In addition to the mandatory CA125, CA19-9, CEA (also AFP, beta HCG, LDH in those <40 years) could be measured and an ultrasound examination performed.

Measurement of tumour markers associated with other malignancies (e.g. Ca15-3) may be of occasional benefit but is not advocated as routine practice.

NICE recommends that a risk of malignancy index (see appendix) should be calculated based on the patients’ menopausal status, ultrasound characteristics of the ovarian mass and serum CA-125 level. This can be used to guide the need for central referral (Grade B). All cases in which the RMI score is calculated at 250 or more should be referred to a specialist multidisciplinary team.

Where ovarian malignancy is likely, a gynaecological oncologist should undertake the operation (Grade B). If bowel symptoms exist, efforts should be made to exclude bowel cancer so that the patient can be directed to an appropriate surgeon. It is recognised that a number of ovarian tumours thought likely not to be malignant will be operated on by unit leads.
It is undesirable for specialist teams to operate on benign pelvic masses unless for strong clinical reasons. Pre-operative Investigations should include CXR, full blood count, liver function tests, urea and electrolytes and CA125.

If a complex ovarian mass is thought to represent a borderline ovarian tumour or a possible ovarian malignancy then a CT scan of the abdomen and pelvis should be arranged to exclude upper abdominal disease and help planning any operation. Chest imaging is not mandatory in those patients where the mass is thought to represent a borderline ovarian tumour or early stage ovarian malignancy. CT of the abdomen and pelvis can help with surgical planning if there are clinical signs of complicating factors such as bowel involvement. CT may also be helpful to assess areas that may be inaccessible to effective debulking e.g. coeliac axis / mesentery (see section 4.5.3)

If primary chemotherapy is considered, NICE recommends that a diagnosis of ovarian cancer with should be confirmed by histological evaluation of a core tumour biopsy in all but exceptional cases prior to treatment with cytotoxic chemotherapy. This should be further supported by an appropriate immune profile to determine the histological subtype. Further guidance on this can be found in the Pathology guidelines available here on the Manchester Cancer website. https://manchestercancer.files.wordpress.com/2014/09/2016-pathology-guidelines-for-gynae-cancers-final.pdf

CT abdomen and pelvis are required to document the extent of disease prior to chemotherapy.

Histological diagnosis can be obtained by either an ultrasound or CT scan guided percutaneous biopsy. Alternatively, a laparoscopically guided biopsy can be considered. If a pleural effusion is detected radiologically, consideration should be given to obtaining a sample for cytological analysis as confirmation of stage IVa disease will allow the use of Bevacizumab as part of that individual’s systemic treatment.
4.4 Imaging

**Diagnosis**

- US for initial assessment
- CXR
- MRI if US/clinical diagnosis uncertain

**Staging**

**Clinical / US Stage I**

- RMI calculated on basis of USS features, Ca125 and menopausal status.
- Refer to centre if RMI > 250*

**Clinical Stage >1**

- **Suspected bowel involvement**
  - CT abdomen and pelvis
- **Gross intraperitoneal disease**
  - CT abdomen and pelvis: to assess feasibility of optimal debulking
- **Patient not fit for surgery**
  - CT abdomen and pelvis
  - Image guided biopsy to confirm diagnosis
  - Baseline prior to chemotherapy

**Follow-up**

- Post-op Not routinely indicated
- During chemotherapy CT assessment of response may form part of research protocol for chemotherapy
- During neo-adjuvant chemotherapy CT assessment of response after 3 cycles chemotherapy to assess suitability for interval debulking surgery
- After completion of chemotherapy CT abdomen and pelvis
- Recurrence CT chest, abdomen and pelvis

*NB: where imaging highly suggestive of malignant mass, referral to centre should be made even if RMI <250.
4.5 Primary Treatment of suspected or proven epithelial ovarian cancer

4.5.1 Surgical Treatment

4.5.1.1 Surgical treatment of patients with apparent low stage disease

Laparotomy is the accepted standard primary management, with the purpose of establishing the diagnosis, staging the disease and undertaking complete resection of the disease.

Although there are several small series advocating the use of laparoscopy for the management of presumed early stage disease \citep{10-12} there are no randomised controlled trials and a recent Cochrane review therefore concludes there is insufficient evidence to support the use of laparoscopy in this setting \citep{13}. However, a laparoscopic approach may be appropriate in carefully selected patients.

Laparotomy should be carried out through a vertical incision to enable whatever surgery may be required.

In early stage disease when the tumour is confined to one or both ovaries, surgery can be curative. It is important however that an adequate procedure has been performed to avoid under staging. Washings, biopsy of any adhesions, careful inspection and palpation of the whole abdominal cavity, and omental biopsy/ omentectomy should be performed. Biopsy of the pelvic and abdominal peritoneum should be done with a retroperitoneal lymph node assessment which consists of palpation of the pelvic and para-aortic areas with sampling of any enlarged lymph nodes or random sampling if the nodes are not enlarged\cite{8}.

Frozen section can be of use in the diagnosis of malignancy peri-operatively. Whilst this can be of help to the surgeon, there must be sufficient throughput to ensure that the reporting pathologist has sufficient experience and exposure to cases to ensure a robust service and any such service must be subject to regular audit \citep{14}. A robust protocol for its use should also be agreed with clinical users before commencing.

In women who wish for further children and where the tumour appears to be confined to one ovary, then an individual management plan needs to be drawn up in conjunction with the patient explaining the benefits and risk of removing the one ovary and possible
biopsy of the contralateral ovary. Oophorectomy together with optimal staging may suffice.

A normal looking contralateral ovary need not be biopsied. Several retrospective cohort studies have been published reporting experience of fertility-sparing surgery in a total of 210 patients (grade B). These have confirmed the safety of this approach in stage I disease with an overall relapse rate of 11% (9% in the contralateral ovary).

### 4.5.1.2 Management of patients with advanced disease

Laparotomy is the accepted standard primary management, with the purpose of undertaking maximal debulking. The sites and volume of residual disease at the end of surgery should be clearly documented as these will impact on both prognosis and selection of adjuvant systemic therapy. A final assessment of cyto-reduction status should be given;

- complete macroscopic cyto-reduction (no visible residual disease)
- optimal cyto-reduction (visible residual disease <1cm diameter)
- suboptimal cyto-reduction (visible residual disease >1cm diameter)

Greatest survival benefit is associated with resection of all visible disease, although in the primary surgery setting there is also a smaller survival advantage associated with resection to less than 1cm. No survival advantage has ever been demonstrated to be associated with suboptimal cyto-reduction. The aim of primary surgery should therefore be to leave no visible residual tumour, if this is feasible or residual disease less than 1cm if complete cyto-reduction is not possible (Grade B).

Primary debulking surgery is the standard of care where complete or optimal cytoreduction seems achievable in patients with good performance status. Where this is not achievable 2 randomized trials have showed non inferiority of the neoadjuvant chemotherapy approach followed by interval debulking surgery. Both trials demonstrated reduction in morbidity with neoadjuvant chemotherapy and equal quality of life in both arms (Level I Grade A). There is currently no validated algorithm to predict outcome of surgery and therefore to guide decision making regarding primary or delayed primary surgery [18, 19].
4.5.1.3 Fertility preserving surgery

Any patient wishing to preserve her fertility in the context of possible invasive epithelial ovarian cancer should be discussed within the gynaecological MDT. Initial surgery should comprise of a unilateral salpingo-ophorectomy + peritoneal washings +/- omental biopsy, aiming to keep the ovarian capsule intact and obtain definitive histopathological diagnosis. Further surgery in the form of an omentectomy, pelvic and para-aortic lymph node sampling and peritoneal biopsies + biopsy of any suspicious lesions would then be performed as completion staging surgery. Fertility-sparing surgery can be considered in young patients with stages IA–C and grades I–II EOCs who desire to preserve their fertility.

4.5.2 Chemotherapy

Following histo-pathological confirmation of ovarian cancer, the patient’s management should be discussed with and led by a medical oncologist with an interest in ovarian cancer. All cases should be discussed at a specialist multi-disciplinary team meeting.

For women with optimally staged low-risk disease, adjuvant chemotherapy should not be offered. All optimally staged patients with high risk disease (stage I grade 3 or stage Ib/1c grade 2) should be considered for adjuvant chemotherapy with 6 cycles of carboplatin.

Women who have had incomplete surgery for apparent stage I disease should be considered for restaging or seen by a medical oncologist to discuss the possible benefits and side effects of adjuvant chemotherapy.

Baseline investigations should include FBC, U/E, LFTs, CA125, GFR, CXR and nutritional status. CT of the abdomen and pelvis should be undertaken 4-6 weeks after surgery.

4.5.3 Neoadjuvant Chemotherapy

Primary debulking surgery is the standard-of-care for patients of good performance status when complete or optimal cyto-reduction seems achievable.

However, the EORTC 55791\textsuperscript{[17]} and CHORUS\textsuperscript{[20]} Trials comparing primary surgery and neo-adjuvant chemotherapy in advanced staged disease reported equivalent overall survival in both treatment arms. There was however an improvement in the quality of life for those women randomised to neo-adjuvant chemotherapy.
Therefore, in women with significant medical co-morbidity or whose performance status is poor, consideration should be given at the MDT to recommending initial chemotherapy in place of primary surgery.

Neoadjuvant chemotherapy may also be considered if the prospects for optimal debulking at laparotomy are remote. Patients undergoing NACT should be tracked by the CNS team to allow timely discussion at the MDT and listing for surgery. Surgery should be considered after 3 cycles of chemotherapy and a discussion at the MDT meeting should be arranged for this purpose.

The default position should be to offer surgery after 3 cycles of chemotherapy though each case should be considered on an individual basis. Women who fail to respond adequately to chemotherapy or are considered to have irressectable disease may benefit from continuing chemotherapy.

Deferral of cytoreductive surgery until after 6 cycles of chemotherapy should only occur in exceptional circumstances, generally when reversible patient-related factors prevent surgery being performed in an interval fashion.

Important factors to consider that may preclude debulking are, bulky extra-abdominal disease sites, extensive mesenteric involvement and coeliac axis disease. It should be noted however, that CT appearances have not proven to be a reliable predictor of the feasibility of optimal debulking in several prospective studies (Grade B).

For patients who do not have primary or delayed primary surgery there are no data to support a role for surgery after completion of chemotherapy and this situation should be avoided wherever possible.

There are no absolute indications for neo-adjuvant chemotherapy but this may be considered where:

1. The patient considered medically unfit for surgery (NB: pleural effusion does not in isolation necessarily render a patient unfit for surgery and can be drained preoperatively if large/symptomatic).
2. There is extensive mesenteric involvement.
3. Disease at coeliac axis.
4. Fixed, bulky extra-abdominal disease (NB: omental caking may be operable/amenable to debulking).

It should be emphasised that primary debulking surgery remains the management strategy of choice for the majority of women with suspected ovarian/primary peritoneal cancer.

4.5.4 Adjuvant Treatment for Stage I disease

ICON 1\(^{[21]}\) showed a 9% improvement in 10-year survival in patients with early ovarian cancer who are treated with platinum-based chemotherapy (Grade A). A retrospective subset analysis of data from the ICON-1 trial has indicated that patients with intermediate risk stage I disease (IA moderately differentiated, IB well and moderately differentiated, IC well differentiated) do not benefit substantially from adjuvant chemotherapy and NICE guidelines do not recommend adjuvant chemotherapy in this group.

In the ACTION trial\(^{[21]}\), adjuvant chemotherapy was beneficial in women with stage 1 disease who had not undergone full surgical staging but in those who had been adequately staged (including full lymph node sampling), this effect was lost. This subset analysis however was based on small numbers of patients and should therefore not prevent a discussion on adjuvant chemotherapy with individuals who have high risk stage I disease.

4.5.5 Adjuvant treatment for stage II-IV disease

Patients with more advanced disease (Stage II-IV) will normally all receive post-operative chemotherapy. Currently optimal first-line chemotherapy is platinum based and patients should be offered the choice of single of a combination of carboplatin and paclitaxel (international standard-of-care)\(^{[22]}\) or single agent carboplatin (Grade A).

For patients with high-risk advanced disease (stage III with sub-optimally debulked disease at primary surgery (>1cm diameter residual disease) or stage IV), the ICON7 trial demonstrated 5.5 month and 7.8 month improvements in progression-free survival and overall survival respectively with the addition of the anti-angiogenic monoclonal antibody, Bevacizumab to carboplatin-paclitaxel chemotherapy. Bevacizumab is
administered as concurrent and maintenance therapy and is currently funded in this indication through the Cancer Drugs Fund for a total duration of twelve months therapy.

All patients should be offered the opportunity to participate in clinical trials if they meet the eligibility criteria.

4.6 Management Algorithm

Laparotomy (if fit and if optimal debulking feasible)

Staging and cyto-reduction

If possible, hysterectomy and bilateral salpingo-oophorectomy, omentectomy, resection of other sites of disease to achieve complete cyto-reduction if feasible, relevant biopsies/washings

If high risk stage 1 (G3 or G2 stage Ib/Ic) chemotherapy with carboplatin

If stage II or higher carboplatin ± paclitaxel, consider addition of Bevacizumab to carboplatin-paclitaxel post-operatively for Stage III (sub-optimally debulked) or IV disease

Low or intermediate risk stage I (stage la or G1 stage Ib/Ic) does not require adjuvant chemotherapy. If the patient is not fit for primary surgery and/or if tumour appears unsuitable for debulking after discussion at MDT, for neoadjuvant chemotherapy and consider surgery following 3 cycles.
4.7 Follow-up

At the completion of chemotherapy, a full re-staging evaluation is required. This will take account of performance status, current symptoms, findings on physical examination and the results of full blood count, serum biochemical profile, CA125 level and abdomen and pelvic CT scan.

On the basis of this, remission status (complete remission, partial remission, stable disease, progressive disease) should be assigned. Inpatients with residual there is no benefit from additional chemotherapy at this time (Grade A).

Patients should be followed up off treatment. Visits should occur every three months years 1 and 2, six monthly in years 3-5 (Grade C). No benefit in survival has been demonstrated by the use of regular CA125 in follow up (Grade A) \(^{23}\). However, CA15 monitoring may allow the early identification of surgically resectable recurrence in a minority of patients and trigger imaging that will allow decision making regarding the timing of chemotherapy treatment for many others. It is therefore considered an appropriate component of patient follow-up. It should be emphasized that patient-initiated attendance with symptoms between routine follow-up visits is important in the detection of recurrence.
For patients with complete remission at the end of first-line treatment, telephone FU using a structured symptom-based questionnaire in conjunction with a serum CA125 is an alternative to OP attendance.

4.7.1 Suggested Follow-up intervals

**Surgery Only**
- Years 1 & 2: 3 monthly
- Years 3, 4 & 5: 6 monthly
- Years 6 to 10: annually

**Oncology (Primary & Adjuvant)**
- 3 months: Christie
- 6 months: Gynaecologist
- 9 months: Christie
- 12 months: Gynaecologist
- 15 months: Christie
- 18 months: Gynaecologist
- 24 months: Christie
- 30 months: Gynaecologist
- 36 months: Christie
- 42 months: Gynaecologist
- 48 months: Christie
- 54 months: Gynaecologist
- 60 months: Christie

4.8 Management of recurrence

Although recurrent ovarian cancer is incurable improvements in median survival can be made with the judicious use of second line and subsequent treatments. A priority of management in the recurrent setting is to maintain quality of life.

Patients with signs of recurrent tumour should be imaged by CT of the chest, abdomen and pelvis.
For patients who previously underwent complete cyto-reduction at initial surgery consideration should be given to the MDT discussion at the time of first relapse in order to evaluate the role of surgery, if the criteria listed below are met.

Surgery should be considered if the recurrence occurs

- more than 6 months after completion of primary treatment
- appears confined to less than 2 sites on CT assessment
- in the absence of significant ascites,
- and previous surgery resulted in complete cyto-reduction
- or if it is thought necessary to relieve symptoms

Chemotherapy is the mainstay of treatment for recurrent ovarian cancer. The choice of regimen is dependent on the treatment free interval. When cancer recurs more than six months after completion of first-line therapy, carboplatin forms the basis of treatment regimens. Two phase III studies (grade A) have demonstrated a survival advantage for combination chemotherapy (carboplatin-paclitaxel OR carboplatin-gemcitabine) over single agent carboplatin in this group of patients. Carboplatin-Caelyx® also has proven phase III efficacy in this setting and a platinum-doublet should be considered as standard in platinum-sensitive disease recurrence.

When cancer recurs less than six months after platinum-based chemotherapy, response rates to carboplatin are low and non-cross resistant chemotherapy regimens should be used. NICE has approved Pegylated liposomal doxorubicin (Caelyx®) for the treatment of platinum-resistant recurrent ovarian cancer (grade A) both weekly paclitaxel and gemcitabine are alternative treatment options in this setting. These should be administered under the supervision of a specialist ovarian cancer medical oncologist. In selected cases, the use of dose-intense platinum-based regimens may be considered as these have demonstrated higher response rates, albeit at the expense of greater toxicity in the phase II setting (grade B).

The suitability for clinical trials should be considered in all patients with recurrent ovarian cancer through discussion with the trial coordinator.
The choice of treatment regimen should be made in conjunction with the patient and take into account co-morbid factors, prior chemotherapy side-effects and the patient’s wishes. It should be noted that patients will often derive benefit from receiving multiple lines of chemotherapy after disease relapse.

Radiotherapy should be considered for localised deposits of disease that are painful, ulcerating or bleeding. Psychological support is particularly important at this stage and the palliative care team should be involved earlier rather than later. Appropriate nursing care and other facilities can be arranged at home and if necessary, referral to a local hospice can be made.

4.8.1 Maintenance therapy post chemotherapy for recurrent disease

There is no evidence to support the use of maintenance chemotherapy or endocrine therapy after response to induction treatment.

Although two phase III trials (OCEANS and AURELIA) have shown a clinical benefit for the addition of concurrent and maintenance bevacizumab to chemotherapy in both platinum-sensitive and platinum-resistant settings, NHS funding is currently not available in these indications.

Maintenance olaparib (an oral PARP inhibitor) substantially prolongs progression-free survival after response to platinum-based chemotherapy in patients with BRCA-mutation associated high grade serous ovarian cancer. NICE approval has been granted for the use of olaparib after third-line chemotherapy in this patient group.

Alternative maintenance strategies, in particular broadening the use of PARP inhibitors in high grade serous carcinoma are currently being explored in phase III clinical trials.

A substantial portfolio of clinical trials evaluating novel treatment strategies in relapsed ovarian cancer is available at The Christie. The suitability of patients for clinical trial participation should be actively considered at each disease relapse and relevant trials discussed with the patient if appropriate.
4.9 Bowel Obstruction in Association with Recurrent/Progressing Ovarian Cancer

Bowel obstruction secondary to disseminated intra-peritoneal tumour is a common development in advanced ovarian cancer. Where symptoms are thought to be due to a single anatomical site of obstruction on imaging, review by the surgical team should be requested although only selected patients may be suitable for palliative procedures to relieve or bypass the obstruction.

When surgery is not an option, it is important to achieve optimal control of nausea, colic and other abdominal pain. This is achieved through continuous subcutaneous infusions of anti-emetics, antispasmodics, anti-secretory agents and analgesics in a Graseby MS26 syringe driver.

Commonly used drugs include:

- Cyclizine 150 mg/24 hours + haloperidol 2.5-5 mg/24 hours
- Hyoscine butyl bromide 60-240 mg/24 hours (if colic)
- Octreotide (anti-secretory if high volume output persists)
- Diamorphine as titrated

A transdermal fentanyl patch is a useful option for those who require regular strong opioid analgesia provided that analgesia requirements are stable.

All stimulant laxatives should be avoided; softeners (docusate) may be given by mouth if tolerated. Pro-kinetic anti-emetics (eg. Metoclopramide) should be used with caution and discontinued if they exacerbate pain.

Note: It is possible to manage bowel obstruction in the terminal phase without IV fluids and nasogastric drainage for many patients. However, high small bowel obstruction will cause more frequent vomits. A trial of Hyoscine butylbromide (start at 60mg/24hours and increase in 60mg increments every 24 hours if symptoms still poorly controlled) or Octreotide (300–600gs/24 hours) may reduce these to a tolerable level.

If not, a nasogastric tube should be offered and consideration of a venting gastrostomy to manage the problem if anticipated survival is still some weeks. Chemotherapy may be considered in patients who develop bowel obstruction during their initial presentation.
and assessment as there is a reasonable chance of inducing sufficient tumour shrinkage to relieve obstruction.

When bowel obstruction occurs in the context of relapsed disease, the role of chemotherapy is unclear. The role of parenteral feeding in patients with bowel obstruction is contentious. It may be initiated alongside chemotherapy when this is a treatment option; individual patients may ask to continue supported feeding even if active treatment is discontinued. The use of TPN may sometimes be appropriate in careful assessed individuals of good performance status whose symptoms are well-controlled and who have no ascites or other disease-related problems.

4.10 Genetic Counselling/Testing

NICE recommend testing for germ line BRCA1 and BRCA2 gene mutations in patients where the risk of carrying a mutation is >10%. Knowledge of BRCA mutation status is of key importance for counselling of close relatives but also impacts on management of the affected patient. It will inform decisions regarding risk-reducing mastectomy but also may enable the patient to access PARP inhibitors as part of their management if their ovarian cancer recurs. The following patients groups should be referred for testing:

High Grade serous carcinoma

- All patients diagnosed under the age of 60 years old, irrespective of family history.
- All patients with a personal history of breast cancer.
- All patients diagnosed >60yo with 1 other first or second degree relative with ovarian, pancreatic or breast cancer or early onset prostate cancer

Other histological subtypes of ovarian cancer

- All high grade endometrioid/ clear cell ovary diagnosed <60yo with 1 other first or second degree relative with ovarian or breast cancer
- All other ovarian cancers need a classical high risk family history. ie.
  1. Two or more first or second degree relatives diagnosed with ovarian cancer at any age.
  2. One first or second degree relative with ovarian cancer and one first degree or
second degree relative with breast cancer, at least one of whom was diagnosed under the age of fifty.

3. One first or second degree relative with ovarian cancer and two first or second degree relatives with bowel and endometrial cancer (on the same side of the family), at least one diagnosed under the age of fifty.

4. One first degree relative with breast and ovarian cancer as primaries, at least one diagnosed under the age of sixty.

4.11 Non-epithelial Ovarian Tumours

4.11.1 Sex-cord Stromal Tumours

These tumours vary in their degree of malignancy from relatively benign with a low risk of recurrence after removal to highly malignant with a high risk of recurrence

- Laparotomy and surgery as for epithelial tumours
- Consider chemotherapy (Platinum/Adriamycin/Cyclophosphamide) for any residual or recurrent disease.
- Consider Inhibin as a tumour marker

4.11.2 Germ Cell Tumours

Germ cell tumours are remarkably chemo-sensitive. These tumours often occur in younger women and the most important consideration is often preservation of reproductive function. These cases require expert care.

- Tumour markers are CA125, AFP, beta HCG, LDH
- Diagnostic laparotomy EXCEPT in paediatric cases who should be referred to Paediatric oncology for radiological guided biopsy
- In selected cases with bilateral ovarian involvement consider unilateral salpingo-oophorectomy (fertility sparing surgery)
- Post-operative chemotherapy: Platinum, Etoposide, Bleomycin for 4 cycles or until tumour marker negative

They should be discussed at the MDT for an individualised management decision.

Following any surgical treatment provided patients with germ cell tumours should be referred to the germ cell team (Drs Welch/ Leahy) at the Christie Hospital for treatment/ follow-up.
Girls under 16 years are treated by Dr Bernadette Brennan, Consultant Paediatric Oncologist at Manchester Children’s Hospital.

4.12 **Borderline ovarian tumours**

Borderline ovarian tumours (BOTs) are a heterogeneous group of tumours ranging from tumours with a benign natural history to premalignant lesions capable of malignant transformation.

These tumours account for up to 15% of all epithelial ovarian tumours. They generally present at a younger age than carcinomas and nearly 75% are stage I at presentation. Adequate surgical staging, tumour sampling and expert histo-pathological review are crucial in making the diagnosis.

If the diagnosis of BOT is made as an incidental finding following surgery then the case (but not the patient) should be referred to the centre MDT for histological review and discussion. Referral should include the operation note in addition to the histology. MDT review and discussion should include a discussion of the role of further surgery dependent upon the histology, fertility desires and completeness of the primary surgery. If the patient is to be considered for further surgery then this should be carried out at the centre.

Patients should be followed up for 5 years. This should include the use of ultrasound where the contralateral ovary remains in situ, and consideration of tumour markers where these were raised at primary diagnosis [25]. The diagnosis of recurrent disease should always include histological confirmation.

In young patients with stage I disease, fertility-sparing surgery can be considered. In mucinous borderline tumours, particularly those associated with mucinous ascites (pseudomyxoma peritonei) or extension outside of the ovary, appendectomy should be performed.

If true PMP is diagnosed, further management should be discussed with the PMP multidisciplinary team at the Christie. 5-year disease-specific survival for true stage I
borderline disease is close to 100%. As with all gynaecological cancers the value of routine follow-up is not known.

Relapsed disease should be managed surgically and the low risk of malignant transformation excluded at histo-pathological review. In the absence of malignant change, the role of chemotherapy is unclear and there is little evidence to suggest that it alters the course of advanced recurrent disease in any beneficial way.

4.13 Management of emergency admissions with ovarian cancer
A significant number of women with undiagnosed ovarian cancer can present to general surgeons as an emergency with bowel obstruction requiring surgery. Where ovarian cancer is suspected either following clinical assessment or at emergency laparotomy a gynaecological opinion should be sought. Each unit or centre should have an agreed plan for responding to this situation and this should be agreed locally. In the cancer unit or centre, the lead gynaecological cancer clinician or a gynaecological oncologist respectively, should be involved as soon as is practicable.

4.14 Patient Information
Following confirmation of the diagnosis of an ovarian mass and recommended treatment plan for surgery at the MDT the Unit Lead and CNS should relay the information to the patient together with the information booklet.

If a diagnosis of ovarian cancer has been made by histopathological or cytological review and the patient is to receive systemic anti-cancer treatment or neo-adjuvant chemotherapy then the Unit Lead and CNS should supply the ‘chemotherapy’ booklet.

If the patient is treated at the cancer centre a check should be made to ascertain the patient has received the relevant patient information and if found to be missing, given at this stage. If the mode of the treatment is changed, at review of the patient then the relevant information given. Information regarding specific types of chemotherapy should be given by the medical oncologist and CNS at the Christie.
If a diagnosis of borderline ovarian tumour is made the clinician and CNS who informs the patient of the diagnosis should offer the information leaflet at this point.
5.0 VULVAL CANCER

5.1 Epidemiology
Vulval cancer is rare and accounts for approximately 3-5% of all gynaecological malignancies. Each year approximately 1000 new cases of vulval cancer are diagnosed in the UK with around 380 deaths per year. Vulval cancer tends to occur in older women and is particularly rare in those under 25 although an increasing number of invasive tumours are being found in younger women, especially those who are immuno-compromised.

Vulval maturation disorders e.g. lichen sclerosis, and Vulval Intraepithelial peoplasia (VIN) are known to predispose to vulval cancer. Lichen sclerosis mainly affects older women. An increasing number of younger women are presenting with HPV-related VIN. Other rare conditions that pre-dispose to vulval cancer are Paget’s disease of the vulva and vulval melanoma in situ.

5.2 Diagnosis
A suspicion of vulval cancer should be raised by vulval ulceration, vulval lump or non-resolving vulval irritation or discomfort. Vulval warts are uncommon in elderly women and should be viewed with suspicion.

Diagnosis is based upon a representative biopsy of the tumour that should include the area of epithelium where there is a transition of normal to malignant tissue. These can generally be obtained with local anaesthetic as an out-patient. Diagnostic biopsies should be of a sufficient size (greater than 1-mm depth) to allow measurement of depth of invasion and orientated to allow quality pathological interpretation.

In general marginal biopsy (wedge/punch) on small tumours will suffice. For small suspicious lesions, women should be referred to the gynaecological cancer centre, either after a small biopsy that leaves the lesion identifiable or no biopsy at all.

The site and size of the lesion are important variables in treatment planning and these should be assessable at the centre. Careful examination of the lesion is mandatory and appropriate documentation of the size and location is important. Suspected spread to
adjacent structures (e.g. urethra, anus, bone) should be noted. Both groins should be examined.

Excision biopsies prior to referral should be avoided as these are usually insufficient as treatment and may compromise definitive surgery. It is therefore preferable to refer suspicious lesions directly to the Gynaecological Cancer Centre without a biopsy.

Ideally, consideration should be given to obtaining photographic representation of all lesions, if possible. Referral should include sending all relevant histo-pathological material to the specialist gynaecological pathologist in the gynaecological cancer centre. All new cases of vulval cancer should be discussed at the cancer centre gynaecological multidisciplinary team meeting. [Grade B/C]

Vulval cancer is associated with high cure rates when the disease remains localised to the vulva. Rates of recurrence increase markedly when groin nodes become involved, especially if bilateral. Surgery is the mainstay of treatment and less mutilating surgery is now employed.

Surgery for vulval cancer should be performed by a gynaecological oncologist. Therefore all patients with vulval cancer should be referred to the Cancer Centre.

5.3 Further investigations and staging

As the majority of patients with vulval cancer are in the older age group, the list of investigations required will vary considerably to reflect the nature of any concurrent illness or performance status.

Minimum investigations include: Chest X-ray, FBC, U+E, LFTs.

Staging is surgico-pathological. Imaging is not routinely indicated. In patients with locally advanced disease, MRI may be helpful to assess extent of disease and identify inguinal and pelvic lymph node metastases. CT is an alternative modality for the assessment of groin nodes.
Where locally advanced disease is suspected or where there is doubt about the resectability of the tumour, examination under general anaesthesia (EUA) may be required in order to plan further management. EUA may be required in order to obtain a diagnostic biopsy in a woman who is very symptomatic with pain. Consideration should be given to performing a joint EUA where necessary, involving other relevant team members such as plastic/colorectal surgeons or a clinical oncologist. This should be arranged and carried out by the centre clinician. [Grade B/C]

Endoscopic evaluation of the bladder or rectum is very rarely required although these should be considered together with endoscopic biopsy where there is suspected bladder or rectal involvement and if the findings would influence management [Grade C].

Clinically suspicious nodes can be sampled in the outpatient setting using fine needle aspiration (FNA) or trucut biopsy.

### 5.3.1 Imaging guidelines in Vaginal / vulval carcinoma

<table>
<thead>
<tr>
<th>Imaging</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Not indicated</td>
</tr>
<tr>
<td><strong>Staging</strong></td>
<td>Not routinely indicated in vulval Ca though may be performed to assess local extent of disease MRI for staging vaginal cancer CT if MRI contra-indicated</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Not routinely indicated</td>
</tr>
<tr>
<td><strong>Suspected recurrence</strong></td>
<td>CT / MR to assess feasibility of radiotherapy</td>
</tr>
</tbody>
</table>
5.4 Surgical Treatment

Surgery is the standard treatment of vulval cancer and less mutilating surgery is now employed. Management should be concentrated in the hands of gynaecological oncologists if optimal results are to be achieved [Grade B/C].

For small tumours of < 2 cms and < 1 mm depth of invasion (DOI), excision with a 1 cm clear surgical margin is sufficient.

Adequate disease free margins are important as these are associated with risk of recurrence and disease free survival. The risk of recurrence increases as the disease free histological margins decrease (> 8.0 mm: 0%; 8.0-4.8 mm: 8%; < 4.8 mm: 54%).

The disease free margin is the measured histological margin on the fixed specimen; hence it is inevitably less than the intra-operative surgical margin. It is therefore essential to aim for an intra-operative margin of at least 10-20 mm on the fresh surgical specimen.

Radical treatment should not be undertaken without prior biopsy confirmation of malignancy [Grade C].

5.4.1 Stage IA disease (<1 mm DOI)

Wide local excision, observing the above margins is sufficient. Inguino-femoral lymphadenectomy should not be performed as the risk of nodal metastasis is very low (< 3%) and the associated morbidity of lymphadenectomy is high [Grade B].

Groin dissection should also be omitted cases of verrucous tumours of the vulva, basal cell carcinoma and malignant melanoma [Grade B].

5.4.2 Stage 1B disease

Where depth of invasion exceeds 1mm or the lesion is measured at >2cm in size, inguino-femoral lymphadenectomy is required to exclude nodal metastases. Pelvic node dissection should not be performed.
Both superficial inguinal and deep femoral nodes should be removed. Superficial groin node dissection alone should not be performed as it is associated with a higher risk of groin recurrence [Grade B].

Preservation of the long saphenous vein may reduce both groin wound and subsequent lower limb problems [Grade C].

5.4.2.1 Laterised lesions
These are defined as the leading medial tumour edge being at least 1 cm away from the midline.

These are treated with radical wide local excision with adequate margins as above in addition to unilateral inguino-femoral lymphadenectomy. Women undergoing ipsilateral dissection and lymphadenectomy should have clinically negative nodes. If the ipsilateral groin nodes contain metastasis, then the contralateral groin nodes need removal.

5.4.2.2 Midline lesions
With midline lesions, deeper lesions (≥ 5 mm) or where there is significant LVSI, or when clinical groin adenopathy is present, management consists of radical local excision and bilateral inguino-femoral node dissection.

5.4.3 Stage II disease
Standard treatment is radical wide local excision or radical vulvectomy (depending on the site and size of the tumour) and bilateral inguino-femoral lymph node dissection [Grade B].

The use of a “triple” incision technique (separate incisions for the groins) has significantly reduced the surgical morbidity associated with this procedure. Unless required by virtue of the size of the lesion, the radical vulvectomy should be modified to a triple incision procedure [Grade B]. If it is considered that adequate excision will leave too large a defect, and a rotational flap is required, then the procedure should be undertaken with a plastic surgeon.
Reconstructive surgery should be made available to all women where appropriate. This may require plastic surgery input. Vulval reconstruction may help reduce the long term psychological impact for this group of women and may also improve the long term vulval appearance and function. Detailed discussion with a clinical nurse specialist or counsellor specialising in sexual issues is valuable in these circumstances.

Ideally patients being considered for plastic surgery procedures should have a consultation with the plastic surgeon pre-operatively to discuss the proposed procedure and any associated risks. Where primary radical surgery is expected to compromise sexual function, psychosexual counselling should be offered prior to any joint plastic reconstructive procedures [Grade B/C].

5.4.4 Sentinel lymph node dissection
This technique has the potential to reduce the surgical morbidity to the groins and lower limbs in patients with early vulval cancer (stages I and II), the majority of whom (70%) will have negative groin nodes. The negative predictive value of a negative sentinel groin node in vulval cancer has been reported to approach 100%. The GROINSS-V study reported on the safety of performing sentinel groin node dissection in early stage I and II vulval cancers, of less than 4 cm. Groin recurrence rate was low at 2.3%. This compares favourably with patients undergoing a formal inguino-femoral lymphadenectomy.

It is notable however that at least 50% of groin recurrences in the GROINSS-V study occurred in patients with multi-focal disease and where there were protocol violations. There is also a well characterised learning curve for this technique.

Groin recurrence is usually fatal and appropriate initial groin node dissection is the single most important factor in decreasing mortality from vulval cancer.

5.4.5 Advanced, Stage III and IV, Vulval Cancer
Approximately one third of patients with vulval cancer present with stage II and IV disease and are characterised by local extension resulting in serious complex problems. Positive groin nodes are found in more than 50% of these patients and are often
ulcerating and/or fixed to the femoral vessels. Therefore, in many patients, the standard radical surgery may not be enough and either tailored ultra-radical/exenterative surgery or non-surgical treatment should be considered. Many of these women are elderly and treatment plans should be individualized taking into account performance status and morbidity of treatment. The following are required as a minimum: [Grade B/C]

- Formal assessment of co-morbidity, systems function and performance status with the relevant blood and functional tests.
- Assessment of the extent of the disease with Chest X-Ray, Abdo CT and pelvic MR scans.
- Joint EUA involving, the Gynaecological oncologist, clinical oncologist and plastic, colorectal or urology surgeons depending on the extent of disease and involved structures.
- Early involvement of the palliative care team.
- Discussion of the care plan and prognosis with the patient and/or carers to ensure that the treatment plan is based on the individual needs of that patient.

5.4.6 Tumour deemed suitable for primary resection
Radical excision is appropriate and may be in the form of radical vulvectomy, modified radical vulvectomy as a joint procedure including plastic reconstruction, as determined by the extent of tumour. Bilateral groin node dissection or debulking of suspicious enlarged/ulcerating groin nodes is also performed. Adjuvant pelvic and groin irradiation is given if two or more groin nodes are involved. There is no role for pelvic lymphadenectomy.

5.4.7 Disease extending beyond the remit of radical vulvectomy and/or impinging on mid-line structures with the risk of loss of function
There is a lack of a good evidence base to guide treatment in these women and therefore no consensus regarding the best management. Primary chemo-radiotherapy is indicated for women deemed unsuitable for ultra-radical surgery and may allow subsequent sphincter-preserving surgery. Good disease control can be achieved. Surgery may be performed following completion of treatment to remove residual disease.
In cases of large, fixed or ulcerating groin nodes, debulking of groin nodes may be considered prior to radiation treatment if feasible. Alternatively radiotherapy should be considered. There is insufficient evidence to suggest the superiority of one treatment over the other (grade B). There is no consensus as to whether to perform groin dissection after primary radiotherapy treatment where there has been a complete response. Surgery in an irradiated groin is associated with significant morbidity.

### 5.5 Adjuvant radiotherapy

The need for adjuvant radiotherapy is based upon the groin node status and the surgical margins.

There is not enough evidence for routine radiotherapy to the vulva in patients with close but negative margins. Where the closest pathological margin is <8mm consideration should be given to further local excision, although evidence is lacking that this will result in a reduction in local recurrence. Adjuvant radiotherapy may also be considered for tumours larger than 4cm (Grade B).

Adjuvant radiotherapy to the groin(s) is administered if either groin has two or more nodes involved with microscopic metastatic disease, or if there is complete replacement and/or extra-capsular spread in any node. Treatment fields should cover the involved groin and pelvic nodes (Grade B/C). In practice, adjuvant groin radiotherapy is considered with any node positive disease as the incidence and consequence of nodal recurrence is significant.

Decisions regarding radiotherapy should be made with the clinical oncology team at the Christie.

### 5.6 Lymphoedema

In gynaecological cancer, swelling of one or both legs in the absence of hypoalbuminaemia or vein thrombosis is usually due to lymphatic obstruction. This may be a consequence of treatment itself or active pelvic disease. The team has a responsibility to refer such patients to a specialist Lymphoedema service for assessment and management. Proactive treatment can significantly reduce lymphoedema and control swelling even in the presence of progressive disease.
Acute infective episodes may present a florid cellulitis but frequently may be a case of mild erythema and general malaise. These should always be actively treated with Penicillin V 500 mgs q.ds. x 2 weeks (alternatively Erythromycin in those with sensitivity to Penicillin. Severe episodes may require in-patient treatment.

5.7 Recurrent vulval cancer

Both treatment and prognosis depend upon the site and extent of recurrence. Treatment plans should be made within the context of a multi-disciplinary team. Thorough pre-operative assessment is of paramount importance in defining the objective of treatment (curative or palliative) and optimizing the treatment outcome.

Radical excision of localized recurrence gives an approximate 5-year survival rate of 56% when the regional nodes are not involved. In radiation naive patients, radiotherapy should be considered if surgery is likely to impair function. An exenterative procedure may be an option in individual patients. Groin node dissection, unilateral or bilateral, may be considered if not done previously. Indications for post-operative radiotherapy following excision of local recurrence are not clear. Cases require careful consideration by the MDT (Grade B/C).

Groin recurrence carries the worst prognosis and treatment options are often limited. In those who have not received groin irradiation, radiotherapy with or without additional surgery should be considered. If the groins have already been irradiated, palliation (either surgical or systemic treatment) should be considered as early as possible once recurrence is established (Grade B/C).

Systemic chemotherapy after relapse is used depending upon the patient’s general condition and performance status as well as previous response to any chemotherapy regimens. Recruitment to phase II trials is necessary to shed more light on this area of vulval cancer management. To date this has proven difficult due to the rarity of this disease and the morbid patient profile.

5.8 Rare Histology
5.8.1 Malignant melanoma

Malignant melanoma is the second commonest malignant vulval tumour. Treatment is by radical local excision with surgical margins of at least 2cm. In the absence of enlarged nodes, groin node dissection is not indicated. Sentinel node dissection in vulval melanomas has been explored with encouraging results but is currently performed only within the context of clinical trials. CT of chest, abdomen and pelvis are performed to exclude widely metastatic disease. The most useful prognostic indicator for vulval melanoma is Breslow’s thickness. Following surgery or where disease is widely metastatic, women with vulval melanoma should be referred to the melanoma team at Christie Hospital for further management. In the absence of obvious metastases, careful clinical follow-up is usually advised (Grade B).

Histologically confirmed melanoma cases involving the external female genitalia should be discussed at the specialist gynaecological cancer and melanoma MDTs.

<table>
<thead>
<tr>
<th>Breslow’s Depth of Invasion (thickness)</th>
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<tbody>
<tr>
<td>Breslow’s DOI is a measurement of the depth of the lesion measured vertically in mm from the top of the granular layer (or base of superficial ulceration) to the deepest point of tumour involvement. Tumours are classified according to the depth:</td>
</tr>
<tr>
<td>• &lt; or equal to 0.75mm</td>
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<tr>
<td>• 0.76-1.5mm</td>
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<tr>
<td>• 1.51-4mm</td>
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<tr>
<td>• &gt; or equal to 4mm</td>
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The Clark level is another scale that is used. This does not use a measurement but rather indicates the number of structures/layers through which the tumour has penetrated i.e.
Level 1 - Confined to the epidermis
Level 2 - Spread to the upper part of the dermis
Level 3 - Filling of the upper dermis but no extension to lower dermis
Level 4 - Involving the lower part of the dermis
Level 5 - Penetration of fatty tissues

5.8.2 Bartholin’s gland carcinoma
This is a rare form of vulval cancer that tends to be deeply seated and associated with metastatic disease. It is managed in the same way as squamous carcinoma of the vulva. The close proximity to the anal canal may necessitate partial resection and temporary colostomy (Grade B).

5.8.3 Basal cell carcinoma and Verrucous carcinoma
These squamous variants are rarely associated with lymph node metastasis and can be managed by wide local/radical excision. Groin node dissection is not indicated. In basal cell carcinoma, radiotherapy treatment should be considered if surgical resection is thought to compromise sphincter function (Grade B).

Cases of basal cell carcinoma should be discussed at the specialist gynaecological cancer MDT.

5.8.4 Extra-mammary Paget’s disease
Extra-mammary Paget’s disease is a rare intra-epithelial adenocarcinoma arising from apocrine. There is an association with adnexal and internal malignancies especially gastro-intestinal and genito-urinary tract and therefore women should be fully screened to exclude any other underlying malignancy. This should include pelvic and breast examination and imaging with referral for consideration of colonoscopy and cystoscopy.

As there is a significant risk of disease progression, women with Paget’s disease should be managed and followed-up by gynaecological oncologists or in a specialist multi-disciplinary vulval clinic. Surgery is the mainstay of treatment but where surgery is not appropriate, involvement of a dermatologist is advised as non-surgical treatments (e.g. Imiquimod) may be considered.
Women with a diagnosis of vulval Paget’s disease should be discussed at the gynaecological cancer MDT at the cancer centre.

5.9 Follow-up

The vulva is an area that may be difficult for women to self-monitor and the aims of follow-up are to identify recurrence in a timely fashion as well as detect and manage adverse effects of treatment. As with other gynaecological cancers, there is little robust evidence to guide appropriate follow-up intervals. A suggested guide to follow-up intervals is given below.

5.9.1 Suggested Follow-up Protocol

**Surgery Only**
Year 1: 3 monthly
Years 2, 3, 4 and 5: 6 monthly

**Surgery + (chemo) radiotherapy**
3 months: Christie
6 months: Gynaecologist
9 months: Christie
12 months: Gynaecologist
15 months: Christie
18 months: Gynaecologist
24 months: Christie
30 months: Gynaecologist
36 months: Christie
42 months: Gynaecologist
48 months: Christie
54 months: Gynaecologist
60 months: Christie
5.10 Patient Information

Following confirmation of the diagnosis and recommended treatment plan at the MDT the Unit Lead and CNS should relay the information to the patient together with the information booklet ‘vulval cancer’.

The information on the mode of treatment can also be given at this stage. If the patient is treated at the cancer centre a check should be made to ascertain the patient has received the relevant patient information and if found to be missing, given at this stage. If the mode of the treatment is changed at upon review of the patient then the relevant information given.
6.0 GYNAECOLOGICAL SARCOMAS

6.1 Background and specific considerations
Gynaecological sarcomas comprise a number of diverse and rare tumours including specific visceral sarcomas affecting the uterus and ovary and miscellaneous sarcomas of soft tissue that happen to arise within the field of surgical expertise of gynaecological oncologists in the perineum and pelvis. They include the following:

- uterine leiomyo-sarcoma,
- endometrial stromal sarcoma,
- ovarian sarcomas,
- Perineal, vulval and vaginal sarcomas.

*Carcino-sarcomas are epithelial type tumours and not sarcomas and therefore do not come under the remit of the sarcoma guidelines.*

These sarcomas, like other sarcomas, would be ideally managed by teams with sufficient case load to gain specific experience but in practice this may be very difficult to achieve. IOG for Sarcoma specifies that patients with gynaecological sarcoma should have treatment planning supported by joint input from a sarcoma MDT and a gynaecological MDT.

6.2 Patient presentation and referral pathway
Patients with gynaecological sarcomas are likely to present with symptoms and signs indistinguishable from other benign and malignant pelvic tumours i.e. pelvic pain, disturbance of micturition, vaginal bleeding etc. They are likely to present to their GP or through their local DGH Emergency Medicine department and be referred on to local DGH gynaecological services (Cancer Unit).

The Gynaecological Cancer Lead Clinician in the Cancer Unit will refer to one of the network Gynaecological MDTs if a malignant tumour is suspected.

It is recognised that a specific pre-operative diagnosis of sarcoma will not always be apparent although radiological appearances may sometimes suggest sarcoma. Where
sarcoma is suspected, a pre-operative biopsy may be performed in some cases but may be omitted and can be difficult to obtain in many patients. Therefore, the practical solution is that:

- Initial staging and work-up should be carried out by the receiving Gynaecological MDT.
- Notification to the Sarcoma MDT should be made as soon as a sarcoma diagnosis is suspected.
- If a sarcoma diagnosis is made or strongly suspected pre-operatively then the Sarcoma MDT should be involved in pre-operative treatment planning.
- Where the surgical procedure for a suspected sarcoma is a standard gynaecologic operation such as total abdominal hysterectomy or oophorectomy this should be performed by a Gynaecological oncologist from the referring Gynaecological MDT.
- Where the anatomic location or other factors mean that complex pelvic surgery is required, the patient should be referred to the Pelvic MDT at the Christie Hospital; pre-operatively if possible or, if a surgical procedure has already been performed then post-operatively.

6.3 Staging investigations

Where a pre-operative diagnosis of sarcoma is suspected or confirmed it is recommended that pre-operative staging investigations should include CT scan of chest, abdomen and pelvis.

6.4 Surgical treatment

6.4.1 Uterine sarcoma

Where a pre-operative diagnosis of uterine sarcoma is suspected or confirmed it is recommended that the surgical procedure should include the following:

- Total abdominal hysterectomy
- Oophorectomy is not necessary for surgical control if disease is clinically confined to uterus but may be considered if the patient is post-menopausal or (for palliative control) if there is gross tumour involvement of ovaries.
- Lymphadenectomy is not necessary for surgical control if the lymph nodes are not clinically enlarged but nodal excision biopsy is recommended where there is lymphadenopathy.
• Omentectomy is not required for surgical control.

6.4.2 Ovarian sarcoma
Where a pre-operative diagnosis of uterine sarcoma is suspected or confirmed it is recommended that the surgical procedure should include the following:

• Unilateral oophorectomy
• Contra-lateral ovarian biopsy
• Omental biopsy
• Hysterectomy is not required for surgical control

6.4.3 Vulval, vaginal and perineal sarcoma
Where a pre-operative diagnosis of vulval, vaginal or perineal sarcoma is suspected or confirmed it is strongly recommended that definitive resection is discussed with the Pelvic Surgical Team at Christie Hospital and with the Sarcoma Team reconstructive surgeons prior to surgery. Sarcoma cases should be discussed at both the specialist gynaecological cancer MDT as well as the sarcoma MDT at the Christie Hospital.

6.5 Post-resection management

6.5.1 Pathology review
• Expert pathological review by a recognised sarcoma pathologist is required to comply with IOG.
• For uterine leiomyosarcoma, ER/PR status should be performed.
• For cases of endometrial stromal sarcoma, CD10 immunohistochemistry should be performed.
• Grade should be reported on the basis of mitotic index and morphology (NB Trojani system is not used)

6.5.2 Post-resection staging investigations
If a CT scan was not performed pre-operatively, this should be done post-operatively to complete staging.
6.5.3 Communication with Sarcoma MDT
The relevant Sarcoma MDT should be informed of the patient’s details including: site, morphology, surgeon, hospital, date of surgery stage and Gynaecological MDT plans regarding adjuvant therapy.

6.5.4 Adjuvant therapy
Network guidelines for the selection of patients with gynaecological sarcoma for adjuvant therapy should be followed (see “3.11, Uterine Sarcoma”). In summary, patients with:
• Completely resected FIGO stage I-IVA uterine leiomyosarcoma (LMS) – no adjuvant therapy.
• Incompletely resected stage III / IV uterine LMS FIGO – consider pelvic radiotherapy (although strictly speaking this is not adjuvant therapy).

6.6 Follow-up
Following definitive treatment follow-up will comply with the standard sarcoma follow-up care plan. Follow-up can be shared between surgical team and treating clinical oncology team or with sarcoma clinical oncology team.
In summary:
Year 1: clinic visits 3 monthly
Year 2: clinic visits 3 monthly
Years 3-5: clinic visits 6 monthly
Years 6-10: annual visits

At each visit a pelvic examination and chest X-ray should be performed. No routine blood tests are required.

6.7 Relapsed or advanced disease
Women with relapsed or advanced disease should be referred to Dr Mike Leahy (Christie hospital) for re-staging and to co-ordinate their multimodal therapy.

• Patients will have re-staging CT scan of chest abdomen and pelvis
• Systemic therapy including hormone therapy (for ESS) will be managed by Dr M Leahy
7. **Clinical Nurse Specialist**

Within the MDT the CNS has a specific role for information, communication and psychological support (Grade C/ IOG).

7.1 **Key Worker**

Cancer Standards require that when the patient comes under the care of that MDT they have the name and contact details for their identified key worker and this should be documented in the patient’s notes (Gynaecology Measures 2014, 14-2E-110). A key worker is a person who, with the patient’s consent and agreement, takes a key role in coordinating the patient’s care and providing continuity. Within many MDTs the CNS is identified as the key worker.

7.2 **Information**

Patients identify the CNS as an important source of information (Grade C). The CNS should provide information relevant to the individual patient at all stages of the patient pathway. Where possible this should be in the form of an Information Prescription (Gynaecology Measures 2014, 14-2E-211). This should include information in different formats as appropriate and should include: disease, treatment options, side-effects of treatment, sources of further information and support including patient support groups.

7.3 **Communication**

To facilitate their role in communicating with patients, carers and the extended MDT the CNS is required to have advanced communication skills. Each MDT is required to have an agreed policy for communicating significant/difficult information (Cancer Standards/Network Guidelines). The CNS plays a pivotal role in the implementation of these standards. This communication role includes appropriate referral to sources of specialist intervention and support, and referral back to primary/local care at the end of an episode of specialist care. Facilitating continuity of care has been identified as an important factor in patient satisfaction (Grade B). Each MDT should have a core member trained to provide level 2 psychological support (Gynaecology Measures 2014, 14-2E-201).
7.4 Support

Support from the CNS has been identified as important in enabling patient participation in decision making (Grade C). The CNS provides an important role in assessing and referring for problems in the areas of: psychological distress (Grade A), sexuality, body image, fertility, menopause, lymphoedema, incontinence, stoma care, complex symptom management, rehabilitation, spirituality, social care and finance. The CNS is responsible for carrying out the Holistic Needs Assessment which should feed into the MDT discussion and treatment plan (Gynaecology Measures 2014: 14-2E-103; 14-2E-108).

7.5 Advanced Nurse Practitioners/Nurse Clinicians

The MDT may include ANP/NC’s who are experienced trained Gynae-oncology nurses who have had additional training in advanced practice. They may see patients pre, peri and post treatment, often in place of a doctor. They undertake aspects of the medical role but combine it with a holistic framework aiming to enhance the patient’s journey. They are a valued member of the MDT.
8.0 SUPPORTIVE AND PALLIATIVE CARE

It is recognised that women and families should have supportive care from diagnosis onwards. This should include:

- Access to information about their disease, aspects of management, available services and how to access them. This may for example include local and national patient support networks.
- Advice on available practical and financial help
- Emotional and spiritual support, with specialist help for those with difficulties in adjustment and coping.
- A meticulous approach to the relief of pain and other symptoms at any stage. This should lead to early referral to specialist services if management of problems should prove difficult.

Pain associated with advanced pelvic tumour can be complex and difficult to control. A thorough assessment is an essential part of management: this will identify different sites and types of pain, e.g. soft tissue, visceral or neuropathic. Each individual pain must be dealt with appropriately.

If it is proving difficult to improve pain relief, or there are problems with side effects of drugs, it is important to seek advice as early as possible (see above in relation to other services). Uncontrolled cancer pain should be viewed as an oncological emergency and warrants admission to hospital or hospice. Neurolytic procedures are helpful for selected patients with sacral, perineal and some visceral pain. Cordotomy may be considered for a few patients with intractable, unilateral pelvic and limb pain. For others with central and bilateral pain, control using an indwelling spinal catheter can be achieved.

Palliative care describes a multidisciplinary approach to the needs of the individual with progressing or advanced cancer and her family, with the aim of maintaining best quality of life and support through the terminal stage and into bereavement. Palliative care is an integral part of the care provided by all primary and hospital teams. Specialist palliative
Care is provided by those with training and who work exclusively within this area across community, hospital and hospice settings.

**Roles and Responsibilities**

**8.1.1 Gynaecological Cancer Specialist Team**

Responsible for regular assessment of the individual and her situation as part of follow up: her main concerns, how she is coping, her expectations and wishes. Effective and time efficient consultations benefit from training in communication skills. All senior oncology staff should have the opportunity to undertake Advanced Communication Skills Training to fulfil the requirements of the Cancer Standards. Good communication between professionals across all services is essential and the specialist team have an important role in ensuring that others are kept up to date about clinical developments and management decisions.

**8.1.2 General Practitioner**

Central to the care of the patient and family and his/her involvement usually precedes the cancer diagnosis and may extend through bereavement and beyond. Often he/she will maintain an overview of the situation and ensure involvement of support services within the community.

**8.2 Specialist Services**

If the individual patient needs exceed the expertise available within the MDT there is a range of specialist services to which the patient can be referred. Referrals may be made through hospital or community teams, but early identification of potential or developing problems, and prompt referral, is essential. Specialist services in relation to gynaecological cancer may include:

- Psychological support, including psycho-sexual counselling
- Genetic counselling
- Lymphoedema management
- Pain Specialists
- Palliative Care
- Complementary therapies
8.2.1 Specialist Psychological Support

This may be indicated for people with difficulties in psychological adjustment, leading to disabling anxiety and depression and much less commonly, psychiatric illness co-existing with cancer. Such problems may also extend to the carers and include complicated grief leading to abnormal bereavement. Each SMDT should have at least one core member of the team with direct clinical contact, who has completed the training necessary to enable them to practice at level 2 for the psychological support of cancer patients and carers, and should receive a minimum of 1 hours clinical supervision by a level 3 or level 4 practitioner per month (Gynaecology Measures 2014, 14-2E-201).

The provision for psycho-oncology services is extremely limited. Referrals if possible should be made to services local to the patient. If patients have been treated at Christies they can be referred to the Psycho-Oncology Team, which is led by Dr Tania Hawthorn, Consultant in Psycho-Oncology, Christie Hospital.

8.2.2 Fertility

Many of the treatments for gynaecological cancer can have an impact on a patient’s fertility. This needs to be considered when discussing treatment options with patients so that they have a full understanding of this to enable them to be involved in the decision making process, discuss options for minimizing impact on fertility (where this is possible) and receiving appropriate support. NICE guidance around fertility preservation in cancer treatment (2004) states:

"Women preparing for medical treatment that is likely to make them infertile should be offered oocyte or embryo cryo-storage as appropriate, if they are well enough to undergo ovarian stimulation and egg collection, provided that this will not worsen their condition and that sufficient time is available...."

And also:

"People preparing for medical treatment that is likely to make them infertile should be offered counselling from someone who is independent of the treatment unit, to help..."
them cope with the stress and the potential physical and psychological implications for
themselves, their partners and any potential children resulting from cryo-storage of
gametes and/or embryos...."

(For more on the guidance:
http://www.nice.org.uk/guidance/index.jsp?action=byID&o=10936)

Following the publication of NICE guidance on fertility a working group in Gr Manchester
piloted and established a fertility pathway for female patients. This is now an established
service provided by the Reproductive Medicine Dept. at St Mary’s led by Dr Cheryl
Fitzgerald. All pre-menopausal female cancer patients who want to discuss fertility
options can be referred by fax (Fax to 0161 224 0957 or phone to discuss 0161 276
6494). Ideally patients should be referred as early as possible in their diagnostic pathway.
Once referred, the Reproductive Medicine Department will contact the patient by
telephone with an appointment date and time. This appointment will be at St Mary’s
Hospital Manchester and staff will aim to see each patient within seven to ten days of
referral.

**8.2.3 Sexual Dysfunction Assessment & Management**

Women who undergo treatment for any gynaecological cancer may experience physical
and/or psychological sexual issues afterwards, which may affect their own sexuality,
body image and fertility or their intimate relationships with their partners. Women
require information prior to treatment about possible sexual dysfunction afterwards.
Assessment of sexual function/dysfunction should be routine follow-up post-surgery,
radiotherapy and/or chemotherapy. Following radiotherapy, to the vagina, patients are
advised and educated in the use of vaginal dilators in order to prevent/minimise vaginal
stenosis as per International Guidelines on Vaginal Dilation after Pelvic Radiotherapy
(Grade C). They are also given basic information when appropriate about returning to
sexual activity & HRT.

If women have sexual dysfunction/sexuality problems beyond the scope of the team
providing follow-up they should be referred to the appropriate specialist. The Sexual
Rehabilitation Clinic at St. Mary’s Hospital offers a service to any woman post
gynaecological cancer treatment, with either physical or psychosexual problems by an
appropriately trained Advanced Nurse Practitioner, psychosexual therapist and
gynaecologist. Service provided at St. Mary’s Hospital (Lead Karen Donnelly, St Marys 0161276-8714). Patients who have been treated at Christie can also be referred to the Christie Psycho-Oncology Team (Lead for Psycho-Sexual Service – Dr Josie Butcher, who also has clinical sessions at St Luke’s Hospice, Winsford). For patients who have had radiotherapy they can be referred back to the Clinical Oncology Nurse Led Clinic (Lead Karen Johnson 0161 446 8101). There will also be psycho-sexual services local to where patients live including generic services such as RELATE.

8.2.4 Genetic Counselling

Provided as a specialist out-patient service at St. Mary’s Hospital and the Christie Hospital (lead: Professor Gareth Evans).

8.2.5 Lymphoedema Management

In gynaecological cancer, swelling of one or both legs in the absence of hypoalbuminaemia or vein thrombosis is usually due to lymphatic obstruction. This may be a consequence of treatment itself or active pelvic disease. The team has a responsibility to refer such patients to a specialist lymphoedema service for assessment and management. Proactive treatment can significantly reduce lymphoedema and control swelling even in the presence of progressive disease. It is important to recognise the need for early referral of patients at high risk of lymphoedema development, as well as those showing early signs of the problem.

Acute infective episodes may present a florid cellulitis but frequently may be a case of mild erythema and general malaise. These should always be actively treated initially with Amoxicillin 500mg 8-hourly and if there is any evidence of Staphaueus (folliculitis, pus, crusting) then Flucloxacillin 500mg 6-hourly should be prescribed in addition or alternative. Patients allergic to Penicillin should be prescribed erythromycin 500mg 6-hourly or clarithromycin 500mg 12 hourly severe episodes may require in-patient treatment. Full guidelines for treating cellulitis in lymphedema can be found in the ‘Consensus Document on the Management of Cellulitis in Lymphoedema produced by the British lymphology society and The Lymphoedema Support Network (http://www.lymphoedema.org/Menu3/Cellulitis%20Consensus.pdf)

Current provision of lymphoedema support in Greater Manchester and Cheshire is patchy. Lymphoedema services are currently available at
- Christie Hospital including service at satellite sites at Oldham and Salford - contact: 0161 446 3795
- St. Ann’s Hospice, Heald Green Little Hulton -contact ), contact 0161 437 8136/: 0161 498 3684
- East Cheshire Hospice, Macclesfield contact01625 610 364
- Dr Kershaw’s Hospice, Oldham contact) 0161 624 2727
- Springhill Hospice, Rochdale , contact 01706 649920
- Neil Cliffe Cancer Care Centre, , Wythenshawe contact 0161 291 2912
- Willow Wood Hospice, Tameside contact 0161 366 2135
- Long Term Condition Unit, Boston House, Wigan contact-01942 525566/01942 482244
- St Luke’s Hospice, Winsford 01606 555683/555682

Beechwood Cancer Care Stockport & Bolton Hospice - provide Key Worker level only and only accept referrals with mild to moderate lymphoedema, affecting one limb only. Referrals can be made centrally via the Christie Service.

8.2.6 Fistulae

Fistulae may arise as a consequence of advanced pelvic disease but are also late problems following pelvic radiotherapy to locally advanced tumour where there is invasion of adjacent bladder and bowel.

In the absence of clinical evidence of active disease, a CT scan should be performed to assess with a view to surgical management.

Those patients with fistulae associated with progressive malignancy should have surgical assessment to consider palliative bowel or urinary diversions.

Uncontrolled loss of small bowel contents leads to skin excoriation. Palliative care measures may include attempts to solidify/bulk the stool using Loperamide and Fybogel.
8.2.7 Complementary Therapies

These may be available to in-patients at some hospitals (contact your local unit for information). Some information about complementary therapies available to out-patients may be accessed through the Cancer Information Services. They are also part of the range of services provided for patients at hospices; both in-patient and day care setting. They may provide a useful introduction to palliative care services.

8.2.8 Pain Specialist Teams

These are hospital based and provide out-patient clinic services. Often pain associated with active, progressing cancer is managed by palliative care specialists as there are often multiple co-existent problems; however pain specialists provide valuable advice and help for those with difficult and intractable pain. Referral to a chronic pain service may be appropriate for those patients who are cured of their cancer but live with difficult pain as a result of treatment or the disease. Often this management requires a multidisciplinary approach in which the focus has moved from the cancer itself to rehabilitation.

8.2.9 Specialist Palliative Care Teams

These are multidisciplinary and have specialist palliative care nurses and doctors as core members. The palliative care nurse specialists are often referred to “Macmillan nurses” whether working in hospital or community, and often provide support and advice from diagnosis onwards. (It should be noted that other staff, including cancer nurse specialists, physiotherapists and so on may carry the Macmillan title if their posts were pump primed by the cancer charity). In general, specialist palliative care professionals aim to work alongside the oncology or primary care team and would not take over care of the patient except when in an in-patient hospice setting. They network closely with colleagues across hospital, community and hospice settings. They should be seen as a resource, particularly in difficult and distressing situations and those where considerable on-going support to patient and family is required.

Hospices are substantially funded by independently raised monies plus a small contribution from Primary Care Trusts. They provide a range of services which include in-patient care for symptom control, brief (1-2 weeks) respite for families and terminal care. They are unable to make commitments for indefinite intermediate/continuing care, where nursing home may be more appropriate. Hospice services include counselling,
family support, management of breathlessness and lymphoedema. Day care at hospices provides access to a range of multi-professional services including medical assessment, as well as support for those who are socially isolated as a result of their malignant disease.

Palliative care advice to professionals is available through a helpline at St. Ann’s Hospice (0880 970 7970).

**8.2.10 Treatment induced menopause**

Treatment-induced menopause can have a significant impact on quality of life for pre-menopausal women. It is important to discuss this early in the treatment and for decisions to be made by the treating team about appropriateness of HRT. Women can then be supported and informed about their choices in managing their menopause, its symptoms and any potential long-term consequences. As the long-term prescribing of HRT will probably be undertaken by GP’s it is important that at the end of treatment and end of oncology follow-up.
9. **Teenage and Young Adults (TYA)**

Patients under 25yrs with a suspected cancer should also be discussed at the TYA MDT in addition to a Gynae MDT. Patients aged 19-24 years inclusive should be offered choice of referral to a Principal Treatment Centre (Young People) for treatment. The TYA MDT offers holistic expertise in not only treating the cancer, but also in ensuring the young person’s psychosocial and emotional needs are addressed. (Teenage and Young Adults Measures, 2014)

10. **Acute Oncology**

10.1 **Neutropenic Sepsis/Complications of Chemotherapy/Radiotherapy**

24 Hour Hotline is provided by the Christie for any patients who are on or have had recent chemotherapy or radiotherapy. Contact 0161 446 3658

10.2 **Metastatic Spinal Cord Compression (MSCC)**

MSCC can be a complication of metastatic gynaecological malignancy and prompt diagnosis is essential to improving the outcome and quality of life for patients. Clinicians who have a patient they are worried about should contact the MSCC Co-ordinating service urgently, which is based at The Christie on 0161 446 3658.
# FIGO STAGING RULES (UPDATED 2009)

## A. Carcinoma of the cervix

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I</strong></td>
<td>The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)</td>
</tr>
<tr>
<td>IA</td>
<td>Invasive carcinoma which can be diagnosed only by microscopy with deepest invasion $&lt; 5$mm and largest extension $&lt; 7$mm.</td>
</tr>
<tr>
<td>IA1</td>
<td>Measured stromal invasion of $&lt; 3$mm in depth and extension of $&lt; 7$mm.</td>
</tr>
<tr>
<td>IA2</td>
<td>Measured stromal invasion of $&gt; 3$mm and not $&gt; 5$mm with an extension of not $&gt; 7$mm.</td>
</tr>
<tr>
<td>IB</td>
<td>Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA.</td>
</tr>
<tr>
<td>IB1</td>
<td>Clinically visible lesion $&lt; 4$cm in greatest dimension.</td>
</tr>
<tr>
<td>IB2</td>
<td>Clinically visible lesion $&gt; 4$cm in greatest dimension.</td>
</tr>
<tr>
<td><strong>Stage II</strong></td>
<td>Cervical carcinoma invades beyond the uterus but not to the pelvic side wall or to the lower third of the vagina.</td>
</tr>
<tr>
<td>IIA</td>
<td>Without parametrial invasion</td>
</tr>
<tr>
<td>IIA1</td>
<td>Clinically visible lesion $&lt; 4$cm in greatest dimension.</td>
</tr>
<tr>
<td>IIA2</td>
<td>Clinically visible lesion $&gt; 4$cm in greatest dimension.</td>
</tr>
<tr>
<td>IIB</td>
<td>With obvious parametrial invasion</td>
</tr>
<tr>
<td><strong>Stage III</strong></td>
<td>The tumour extends to the pelvic side wall and/or involves lower third of the vagina and/or causes hydronephrosis or non-functioning kidney.</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumour involves lower third of the vagina with no extension to the pelvic side wall.</td>
</tr>
<tr>
<td>IIIB</td>
<td>Extension to the pelvic side wall and/or hydronephrosis or non-functioning kidney.</td>
</tr>
<tr>
<td><strong>Stage IV</strong></td>
<td>The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. Bullous oedema alone does not permit a case to be ascribed to stage IV.</td>
</tr>
<tr>
<td>IVA</td>
<td>Spread of the tumour to adjacent organs.</td>
</tr>
<tr>
<td>IVB</td>
<td>Spread to distant organs.</td>
</tr>
</tbody>
</table>
B. Carcinoma of the vagina

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Intra-epithelial neoplasia grade 3 (VAIN, carcinoma in situ)</td>
</tr>
<tr>
<td>I</td>
<td>Carcinoma limited to vaginal wall</td>
</tr>
<tr>
<td>II</td>
<td>Carcinoma involves sub-vaginal tissue but has not extended to pelvic wall.</td>
</tr>
<tr>
<td>III</td>
<td>Carcinoma extends to pelvic side-wall</td>
</tr>
<tr>
<td>IV</td>
<td>Carcinoma extends beyond the true pelvis or involves (biopsy proven) the mucosa of the bladder or rectum. Bullous oedema alone does not permit a case to be ascribed to stage IV.</td>
</tr>
<tr>
<td>IVA</td>
<td>Carcinoma involves bladder and/or rectal mucosa and/or direct extension beyond the true pelvis.</td>
</tr>
<tr>
<td>IVB</td>
<td>Spread to distant organs.</td>
</tr>
</tbody>
</table>

C. Carcinoma and carcinosarcoma of the endometrium

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumour confined to the corpus uteri</td>
</tr>
<tr>
<td>IA</td>
<td>No or less than 50% myometrial invasion</td>
</tr>
<tr>
<td>IB</td>
<td>Invasion &gt; 50% of myometrial thickness</td>
</tr>
<tr>
<td>II</td>
<td>Tumour invades cervical stroma but does not extend beyond the uterus*</td>
</tr>
<tr>
<td>III</td>
<td>Local and or regional spread of the tumour</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumour invades the serosa of the corpus uteri and/or adnexae**</td>
</tr>
<tr>
<td>IIIB</td>
<td>Vaginal and/or parametrial involvement</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastases to pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td>IIC1</td>
<td>Positive pelvic nodes</td>
</tr>
<tr>
<td>IIC2</td>
<td>Positive para-aortic lymph nodes with or without positive pelvic nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Tumour invades bladder and/or bowel mucosa and/or distant metastases</td>
</tr>
<tr>
<td></td>
<td>Tumour invasion of bladder and/or bowel mucosa</td>
</tr>
<tr>
<td></td>
<td>Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes</td>
</tr>
</tbody>
</table>

*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.
### D. Carcinoma of the ovary

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I</strong></td>
<td>Tumour limited to the ovaries</td>
</tr>
<tr>
<td>IA</td>
<td>Tumour limited to one ovary; capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td>IB</td>
<td>Tumour limited to both ovaries; capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td>IC</td>
<td>Tumour limited to one or both ovaries with any of the following: Capsule ruptured, tumour on ovarian surface, malignant cells in ascites or peritoneal washings.</td>
</tr>
<tr>
<td><strong>Stage II</strong></td>
<td>Tumour involves one or both ovaries with pelvic extension</td>
</tr>
<tr>
<td>IIA</td>
<td>Extension and/or implants on uterus and/or tube(s); no malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td>IIB</td>
<td>Extension to other pelvic tissues; no malignant cells in ascites or peritoneal washings.</td>
</tr>
<tr>
<td>IIC</td>
<td>Pelvic extension (IIA or IIB) with malignant cells in ascites or peritoneal washings</td>
</tr>
<tr>
<td><strong>Stage III</strong></td>
<td>Tumour involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis and/or regional lymph node metastasis</td>
</tr>
<tr>
<td>IIIA</td>
<td>Microscopic peritoneal metastasis beyond pelvis</td>
</tr>
<tr>
<td>IIIB</td>
<td>Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>IIIC</td>
<td>Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis</td>
</tr>
<tr>
<td><strong>Stage IV</strong></td>
<td>Distant metastasis (excludes peritoneal metastasis)</td>
</tr>
</tbody>
</table>

*
### E. Carcinoma of the vulva

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I</strong></td>
<td>Tumour confined to the vulva</td>
</tr>
<tr>
<td>IA</td>
<td>Lesions &lt;2cm in size, confined to the vulva or perineum and with stromal invasion ≤1.0mm, no nodal metastasis</td>
</tr>
<tr>
<td>IB</td>
<td>Lesions &gt;2cm in size or with stromal invasion &gt;1.0mm, confined to the vulva or perineum, with negative nodes</td>
</tr>
<tr>
<td><strong>Stage II</strong></td>
<td>Tumour of any size with extension to adjacent perineal structure (lower 1/3 urethra, lower 1/3 vagina, anus) with negative nodes</td>
</tr>
<tr>
<td><strong>Stage III</strong></td>
<td>Tumour of any size with or without extension to adjacent perineal structures (lower 1/3 urethra, lower 1/3 vagina, anus) with positive inguino-femoral lymph nodes</td>
</tr>
<tr>
<td>IIIA1</td>
<td>With 1 lymph node metastasis (≥5mm), or</td>
</tr>
<tr>
<td>IIIA2</td>
<td>1-2 lymph node metastasis(es) (&lt;5mm)</td>
</tr>
<tr>
<td>IIIB1</td>
<td>With 2 or more lymph node metastases (≥5mm), or</td>
</tr>
<tr>
<td>IIIB2</td>
<td>3 or more lymph node metastases (&lt;5mm)</td>
</tr>
<tr>
<td>IIBC</td>
<td>Positive nodes with extra-capsular spread</td>
</tr>
<tr>
<td><strong>Stage IV</strong></td>
<td>Tumour invades other regional (upper 2/3 urethra, upper 2/3 vagina), or distant structures</td>
</tr>
<tr>
<td>IVA</td>
<td>Tumour 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</td>
</tr>
<tr>
<td>IVB</td>
<td>Any distant metastasis including pelvic lymph nodes</td>
</tr>
</tbody>
</table>
F. Uterine leiomyosarcomas and endometrial stromal sarcomas (ESS)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Tumour limited to uterus</td>
</tr>
<tr>
<td>IA</td>
<td>≤5cm</td>
</tr>
<tr>
<td>IB</td>
<td>&gt;5cm</td>
</tr>
<tr>
<td>II</td>
<td>Tumour extends beyond uterus, within the pelvis</td>
</tr>
<tr>
<td>IIA</td>
<td>Adnexal involvement</td>
</tr>
<tr>
<td>IIB</td>
<td>Involvement of other pelvic tissues</td>
</tr>
<tr>
<td>III</td>
<td>Tumour invades abdominal tissues (not just protruding into the abdomen)</td>
</tr>
<tr>
<td>IIIA</td>
<td>One site</td>
</tr>
<tr>
<td>IIIB</td>
<td>More than one site</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastasis to pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td>IV</td>
<td>Tumour invades bladder and/or rectum</td>
</tr>
<tr>
<td>IVA</td>
<td>Distant metastases</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>

Simultaneous endometrial stromal sarcomas of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumours.
### G. Uterine adenosarcomas

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I</strong></td>
<td><strong>Tumour limited to uterus</strong></td>
</tr>
<tr>
<td>IA</td>
<td>Tumour limited to endometrium/endocervix with no myometrial invasion</td>
</tr>
<tr>
<td>IB</td>
<td>Less than or equal to half myometrial invasion</td>
</tr>
<tr>
<td>IC</td>
<td>More than 50% myometrial invasion</td>
</tr>
<tr>
<td><strong>Stage II</strong></td>
<td><strong>Tumour extends beyond uterus, within the pelvis</strong></td>
</tr>
<tr>
<td>IIA</td>
<td>Adnexal involvement</td>
</tr>
<tr>
<td>IIB</td>
<td>Involvement of other pelvic tissues</td>
</tr>
<tr>
<td><strong>Stage III</strong></td>
<td><strong>Tumour invades abdominal tissues (not just protruding into the abdomen</strong></td>
</tr>
<tr>
<td>IIIA</td>
<td>One site</td>
</tr>
<tr>
<td>IIIIB</td>
<td>More than one site</td>
</tr>
<tr>
<td>IIIC</td>
<td>Metastasis to pelvic and/or para-aortic lymph nodes</td>
</tr>
<tr>
<td><strong>Stage IV</strong></td>
<td><strong>Tumour invades bladder and/or rectum</strong></td>
</tr>
<tr>
<td>IVA</td>
<td>Tumour invades bladder and/or rectum</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastases</td>
</tr>
</tbody>
</table>
APPENDIX II

RISK OF MALIGNANCY INDEX FOR OVARIAN MASSES

The Risk of Malignancy Index scoring system is based on ultrasound findings, menopausal status and serum CA-125 levels. It has been validated in a series of prospective cohort studies. More recent publications have demonstrated its value in routine clinical practice as a tool for triaging patients for cancer centre surgery and also indicated that it behaves comparably to more complex diagnostic models.

RMI scoring system

<table>
<thead>
<tr>
<th>Ultrasound features</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multilocular cyst</td>
<td>0</td>
</tr>
<tr>
<td>Solid areas</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral lesions</td>
<td>3</td>
</tr>
<tr>
<td>Ascites</td>
<td></td>
</tr>
<tr>
<td>Intra-abdominal ascites</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Menopausal status</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-menopausal</td>
<td>1</td>
</tr>
<tr>
<td>Post-menopausal</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CA-125</th>
<th>U/ml</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>=absolute value</td>
</tr>
</tbody>
</table>

RMI score = ultrasound score x menopausal status x CA125

A cut-off score of >250 has been commonly employed, with reported sensitivities of 70-75% and specificities of ≥90%. Positive predictive values of 85-90% have been reported.
APPENDIX III

CARE PATHWAY FOR THE USE OF NEO-ADJUVANT CHEMOTHERAPY IN OVARIAN CANCER

Patient performance status or co-morbid factors preclude upfront surgery OR tightly defined disease characteristics indicate effective debulking unlikely (see section 4.5.3)

Histological confirmation of diagnosis, baseline CT assessment of disease extent, FBC, biochemical profile, GFR

3 cycles of neo-adjuvant carboplatin-based chemotherapy

Reassessment of patient performance status and radiological assessment of disease extent 1-2 weeks after 3rd cycle chemotherapy

Review by gynaecological oncologist 3 weeks after 3rd cycle chemotherapy- to be arranged at commencement of neo-adjuvant treatment. To assess feasibility for surgery

<table>
<thead>
<tr>
<th>Surgery deemed Appropriate</th>
<th>Surgery not appropriate due to potentially reversible patient co-morbidities but response to chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Debulking surgery</td>
<td>Completion of 6 cycles chemotherapy in total</td>
</tr>
<tr>
<td>Completion of 6 cycles chemotherapy in total</td>
<td>Reassess for delayed debulking surgery</td>
</tr>
<tr>
<td></td>
<td>Assess for alternative non-surgical management</td>
</tr>
</tbody>
</table>
References –


8. NICE, Ovarian cancer: the recognition and initial management of ovarian cancer. CG122, 2011.


22. NICE, review of the clinical effectiveness and cost effectiveness of paclitaxel for ovarian cancer. 2003, National Institute for Clinical Excellence
