Gynaecology CRG (Lancs & South Cumbria)

TUBO-Ovarian Cancer Guidelines

* VALID ON DATE OF PRINTING ONLY – ALL GUIDELINES AVAILABLE ON THE STRATEGIC CLINICAL NETWORK WEBSITE : GMLSC SCN

Date first published	2001	v1.0
Date of last major revision	2009	v2.0
Date of previous revisions	2011 2013	v3.0
Date of revision	22nd July 2015	v4.0
Date of revision	17th February 2017	V4.1
Date of revision	2017	
Date of revision	July 2018	V5.0
Date of revision	August 2020	V6.0
Date of next revision	August 2023	

TUBO-OVARIAN CANCER GUIDELINES

EPIDEMIOLOGY

More than 80% of epithelial ovarian cancers are found in post menopausal women. The peak incidence of this disease occurs at 62 years. Before the age of 45 yrs, these cancers are uncommon. Less than 1 % of epithelial ovarian cancers occur before the age of 21yrs; two thirds of ovarian malignancies in this age group are germ cell tumours. About 30% of ovarian neoplasm in post menopausal women are malignant, whereas only 7% of ovarian epithelial tumours in pre-menopausal patients are malignant.

Familial ovarian cancer accounts for 5% of all cases.

PATHOLOGY

Pathology

All ovarian and Fallopian tube neoplasms should be typed according to the WHO classification and reported using the RCPath dataset(2019)

Assignation of primary site of origin should be performed using the following criterion .

Primary site	Criteria
Fallopian Tube	1. STIC present 2. Invasive mucosal carcinoma present within the fallopian tube, regardless of the presence of STIC, or ovarian or peritoneal disease. 3. Fallopian tube partly or wholly incorporated into a tubo-ovarian mass, regardless of the presence of STIC, or ovarian or peritoneal disease.
Ovary	An ovarian mass or microscopic involvement of the ovary by high-grade serous carcinoma is present, in the absence of STIC or mucosal tubal carcinoma (when examined by a SEE-FIM protocol)
Tubo-ovarian	1. Small biopsy specimen including cytology samples. This should be supported by appropriate immunohistochemistry to exclude the possibility of a uterine serous primary 2. Post-chemotherapy with no residual disease.
Primary Peritoneal	This should only be assigned in primary debulking specimens (i.e. prior to chemotherapy). Peritoneal high-grade serous carcinoma is present in the absence of macroscopic or microscopic involvement of the ovaries (including surface involvement) or tubal mucosa. It is confirmed by appropriate immunohistochemistry to exclude mesothelioma and metastatic carcinoma.

Note each individual criterion is sufficient for assignation of the primary site.

FIGO STAGING FOR OVARIAN MALIGNANCY – 2013 VS 1988

FIGO (2013)	**Stage**	**FIGO (1988)**
Descriptor		*Descriptor*
I: Tumour confined to ovaries or fallopian tube(s)	I	Tumour limited to the ovaries
IA: Tumour limited to 1 ovary (capsule intact) or fallopian tube; no tumour on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings	IA	Tumour limited to one ovary, capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings
IB: Tumour limited to both ovaries (capsules intact) or fallopian tubes; no tumour on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings	IB	Tumour limited to both ovaries, capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings
IC: Tumour limited to 1 or both ovaries or fallopian tubes, with any of the following	IC	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
IC1: Surgical spill	IC1	
IC2: Capsule ruptured before surgery or tumour on ovarian or fallopian tube surface	IC2	
IC3: Malignant cells in the ascites or peritoneal washings	IC3	
II: Tumour involves 1 or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer	II	Tumour involves one or both ovaries with pelvic extension
IIA: Extension and/or implants on uterus and/or fallopian tubes and/ or ovaries	IIA	Extension and/or implants on uterus and/or tube(s); no malignant cells in ascites or peritoneal washings
IIB: Extension to other pelvic intraperitoneal tissues	IIB	Extension to other pelvic tissues; no malignant cells in ascites or peritoneal washings
	IIC	Pelvic extension (IIA or IIB) with malignant cells in ascites or peritoneal washings

III: Tumour involves 1 or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	III	Tumour involves one or both ovaries with microscopically confirmed peritoneal metastases outside the pelvis and/or regional lymph node metastasis
	IIIA	Microscopic peritoneal metastasis beyond pelvis
IIIA1: Positive retroperitoneal lymph nodes only (cytologically or histologically proven)	IIIA1	
IIIA1(i) Metastasis up to 10 mm in greatest dimension	IIIA1(i)	
IIIA1(ii) Metastasis more than 10 mm in greatest dimension	IIIA1(ii)	
IIIA2: Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes	IIIA2	
IIIB: Macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes	IIIB	Macroscopic peritoneal metastasis beyond pelvis, 2 cm or less in greatest dimension.
IIIC: Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retro- peritoneal lymph nodes (includes extension of tumour to capsule of liver and spleen without parenchymal involvement of either organ)	IIIC	Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis
IV: Distant metastasis excluding peritoneal metastases	IV	Distant metastasis (excludes peritoneal metastasis)
IVA: Pleural effusion with positive cytology	IVA	
IVB: Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)	IVB	

DIAGNOSIS OF OVARIAN CANCER / PELVIC MASS.

Any pelvic mass which raises the clinical suspicion of malignant ovarian disease, or which has a high Risk of Malignancy Index, RMI, (see below) should be discussed at the Central Network MDT. Evidence suggests that RMI provides the optimum diagnostic test with both high sensitivity and specificity for predicting malignant status of ovarian masses. (Minimum Standard)

Women presenting with advanced stage disease (large solid, fixed, irregular pelvic mass, ascites, pleural effusion, anorexia etc) should be referred direct to the gynaecological oncology team and discussed at the Network MDT.

RMI scoring will underscore up to 30% of cases of malignant ovarian disease, and these will tend to be early stage cancers (Stage1a). Up to 11% of these cancers will have nodal metastases (pelvic and/or para-aortic) and are at risk of under treatment if staging surgery is omitted, unless a policy of chemotherapy for all these patients is adopted.

It would therefore be prudent if all ovarian masses (unless pure simple cysts) could be discussed at an MDT (local or central) so that RMI and detailed radiological imaging can be discussed, and a pre-operative decision made with regard to surgical extent / lymphadenectomy.

RISK OF MALIGNANCYINDEX(RMI)

R.M.I. = U x M x Ca125, where …

Ca125 is the numeric value (in i.u./L)

M is the menopausal status, Premenopausal = 1, Postmenopausal (no period for 1 year) = 3

(for women with no uterus, if over 50 years the score is 3)

U is an ultrasound based score,

0 for no USS features; 1 for one USS feature, 3 for 2-5 USS features.

Ultra-sound features:

Multi-locular cyst

Evidence of solid areas

Evidence of metastasis

Presence of ascites

Bilateral lesions

Interpretation of RMI

RMI ≥250 should be discussed at the specialist MDT and should undergo staging surgery as defined in *Surgical Management* section (NICE CG122). It is reasonable that masses with RMI in the range of 2 5-250 might provoke some debate at the MDT and clinicians may bring these cases at their discretion. It is recognised that a proportion of women will undergo unnecessary staging surgery due to the specificity of the RMI. Recent data would suggest that the specificity of the process in L&SCCN may be as low as 70% (Network Audit 2011) In view of this the L&SCCN network has agreed a policy of utilizing MRI in an

attempt to differentiate indeterminate ovarian masses at the discretion of the specialist MDT radiologists. Furthermore the pathology service at Royal Preston Hospital has offered the facility of frozen pathologic al sections of ovarian masses. Initially this will take the form of a pilot exercise to assess the sensitivity and specificity of frozen section in this circumstance. Cases identified at the specialist MDT will be scheduled for staging laparotomy and frozen section.

Risk	RMI	Women (%)	Risk of Cancer (%)
Low	<25	40	<3
Moderate	25-250	30	20
High	>250	30	75

CONDITIONS THATMAYELEVATECA 125

Malignant Conditions	Non-Malignant conditions-Gynaecological	Non-Malignant conditions-non Gynaecological
Ovarian	Acute PID	Acute pancreatitis
Cervical	Adenomyosis	Chronic liver disease
Colorectal	Benign ovarian neoplasm	Cirrhosis
Fallopian tube	Endometriosis	Colitis
Gastric	Meig's syndrome	Diverticulitis
Mammary	Ovarian hyperstimulation	Mesothelioma
Pancreatic	Uterine fibroids	PeriCarditis
Pulmonary		Renal disease
		Congestive Cardiac Failure
		SLE
		Polyarteritis nodosa

SIMPLE CYSTS IN OLDER WOMEN

In a peri- or post-menopausal woman, an ovarian mass of < 5 cm with negative tumour markers and no sinister ultrasound findings, i.e. simple, unilateral, unilocular, the risk of malignancy is <1 %. 50% of them will resolve within three months. They can therefore be managed conservatively and observed for 4 months. If the lesion is not neoplastic, it should remain the same size or regress. Repeat RMI should be performed at 4 months. If the cyst persists the patient should be re-assessed at 12 months and if still no change then discharged.

Aspiration is NOT recommended. Cytology has low sensitivity (25%) at detecting malignant cells and there is risk of spill.

Laparoscopy

If it is decided to offer surgical removal of small cysts with low RMI; laparoscopic removal of BOTH ovaries & tubes may be considered, in a tissue bag to prevent and cyst spill or contamination.

ASSESSMENT OF WOMEN WITH CONFIRMED, OR AT HIGH RISK OF, OVARIAN MALIGNANCY

CLINICAL MANAGEMENT

Performance status, WHO score (ECOG score should be documented in the case note of all new presentations).

INVESTIGATIONS:

Blood

FBC, LFTs, U&E's, Clotting, X-match

CA 125, CEA in all cases. (Ca19-9 is not required routinely)

AFP, βHCG, LDH in women under 40 years. (i.e. markers for germ cell tumours).

Radiological

CXR, CT scan of pelvis and abdomen.

Imaging should be interpreted by a radiologist with an interest in gynaecological imaging.

Women with symptoms or radiological signs of infiltrative gastro-intestinal involvement should be assessed / discussed with colorectal surgeons prior to surgery. Lower or upper barium studies (or gastroscopy / colonoscopy) may be appropriate, and the guidance of the Radiologists can be sought at the MDT.

Large pleural effusions might need to be drained for symptomatic relief or pre-operative anaesthetic optimisation. Small pleural effusions do not need to be drained for diagnostic purposes if it would not alter the patients treatment as to whether they were considered stage 3 or 4.

Tests of Cardio-Pulmonary Function.

Patients with clinical evidence of cardiac and/or pulmonary limitation should be considered for tests of function. These include:

ECHO cardiography
Spirometry
CPEX testing: LTH criteria include: (see appendix)

1. Major gynaecology oncology surgery
2. Age > 65 years
3. Veterans Specific Activity Questionnaire (VSAQ) ≤ 6
4. Revised Cardiac Risk Index (RCRI) ≥ 2

Biopsy

If primary surgery is going to be the treatment plan, then pre-operative biopsies are not required.
If the disease is considered inoperable, or the patient unfit, and primary chemotherapy is to be the treatment, then radiologically directed biopsy is the preferred diagnostic investigation.
In very occassional cases when biopsy is not possible, positive cytology with high Ca125 is acceptable but this situation is to be avoided as much as possible.

Laparoscopy

In cases where radiological biopsy is not possible laparoscopic biopsy is the final option for a tissue diagnosis. This can be done under careful local anaesthetic in selected patients who are considered too sick for General anaesthesia, although such patients should also be counselled about the role of palliative care as best management.

Metastatic Tumours

A number of women presenting with apparent malignant pelvic or abdominal disease will prove to have secondary disease, with a variety of primary sites including colon, stomach, pancreas, breast, lymphoma etc. A general systemic history and examination which includes consideration of these systems is therefore mandatory.

Pre-treatment biopsy is likely to be helpful in these cases.

TREATMENT - *Epithelial tumours*

MANAGEMENTOF STAGEI DISEASE

In early stage disease when the tumour is confined to one or both ovaries, surgery can be curative, however, it is important that an adequate procedure has been performed to avoid understaging.

Washings, biopsy of any adhesions, careful inspection and palpation of the whole abdominal cavity should be performed. Frozen section of a mass with indeterminate RMI can be used in selected cases.

The NICE clinical guideline CG122 recommends optimal surgical staging for (presumed) stage 1 ovarian cancer; Optimal surgical staging is defined as:

- Midline laparotomy to allow thorough assessment of abdomen and pelvis,
- Removal of ovarian cyst without causing capsular rupture followed by total abdominal hysterectomy and removal of the contralateral tube and ovary.
- Infracolic omentectomy
- Biopsies of suspicious looking peritoneal nodules
- Iliac and peri-aortic lymph node sampling.

Systematic lymphadenectomy (formal dissection of iliac and obturator nodes, as well as para-aortic nodes including those above the IMA and below the renal vessels) is not supported by sufficient evidence and could lead to an unnecessary increased surgical morbidity.

PRESERVATIONOF FERTILITY

In selected patients who desire childbearing and who have grade I tumours, unilateral salpingo-oophorectomy may not be associated with high risk of recurrence. If potential Stage I disea se has not been adequately surgically staged, the multidisciplinary team should consider repeat exploratory laparotomy or adjuvant chemotherapy.

If the tumour is grade III, clear cell, densely adherent, or greater than stage IC, the chance of relapse and subsequent death from ovarian cancer is substantial (up to 20%), although the importance of tumour rupture, if it is the only adverse characteristic, is not clear.

Access to Egg salvage/storage.

Patients who's treatment will require removal of both ovaries, and who would like to consider the option of future fertility, can be referred to an appropriate reproductive medicine facility for a rapid assessment.

Mr Andrew Drakeley, based at the Liverpool Women's Hospital, is able to offer this service and provide practical advice on an individual case basis; he can be contacted at the hospital.. These patients can also be referred to Dr Cheryl Fitzgerald at St Marys, Manchester.

MANAGEMENTOF "ADVANCED" DISEASE

Women presenting with advanced disease need to be discussed at the Network MDT and a decision made regarding Primary Surgery or Neo-Adjuvant chemotherapy and Interval DeBulking surgery. If the MDT feel that primary surgery is unlikely to achieve optimal debulking or that the patient is initially unfit for surgery then primary chemotherapy should be offered.

Primary Surgical DeBulking

Historic evidence suggests that the standard for treatment of ovarian cancer is optimal primary debulking surgery prior to chemotherapy. Maximal surgical effort should be undertaken to achieve complete macroscopic debulking.

Patients who are symptomatic with a pelvic/abdominal mass, or who have bowel obstruction (established or imminent) should be considered for primary surgery (with or without an accompanying colo-rectal surgeon). However, all other factors should be considered in order to individualise each patient's care; for example co-morbidities, general health and nutritional status at presentation.

Neo-Adjuvant Chemotherapy.

Women presenting with advanced disease (not amenable to primary optimal debulking) or significant medical factors suggesting a high peri-operative morbidity should be considered for primary chemotherapy. Histological diagnosis can be achieved by radiological guided biopsy, mini-laparotomy or laparoscopy.

If the patient's medical condition improves after three cycles of chemotherapy then interval debulking surgery should be considered at that point, again with maximal surgical effort to achieve complete macroscopic debulking.

A recent EORTC study, No 55971, suggests that both approaches are equally effective but the primary chemotherapy with IDS approach is less morbid. The UK CHORUS study also supports this.

The EORTC study 55971 also suggests that maximal surgical effort should be adopted for IDS.

Criteria for Interval De-Bulking Surgery (IDS)

All cases must be considered for IDS and reviewed at the Network MDT.
IDS should be planned in advance, to take place between the 3rd and 4th cycles of chemotherapy.
A CT scan, Ca125 and clinical assessment (including performance status) should be made after the 3rd cycle of chemotherapy; this forms the basis for a decision about the appropriateness of IDS.
IDS should only be embarked upon where the condition for avoiding primary surgery has clearly changed. This usually means that features of inoperability on the CT no longer exist and/or that the patients' performance status has improved to the satisfaction of the MDT consensus.
Where tumour response to chemotherapy has been poor, and surgery is therefore declined, or surgery proceeds but fails to achieve optimal debulking, then a change in chemotherapy should be considered.

Post -surgery

Patients should be booked in the MDT as soon as possible after surgery with histology results so that a plan for appropriate treatment can be made, and then seen in the appropriate clinic to discuss the treatment plan.. A baseline post-operative Ca125 should be arranged with a CT scan if sub-optimal debulking was achieved to measure the response of subsequent chemotherapy.

ADJUVANT CHEMOTHERAPY FOR STAGE IC - IV DISEASE

Adjuvant chemotherapy should be considered for patients with high risk stage 1A/B disease (grade 3 or clear cell) as well as inadequately staged patients, and for all patients with stage 1C-IV disease.

For stage I disease there is no data that combination carboplatin plus paclitaxel is superior to carboplatin single agent and this is what is recommended in the NICE guidelines. It is reasonable to use single agent carboplatin or combination carboplatin / paclitaxel for these patients. It is a lack of data rather than negative data for combination treatment in stage I disease and therefore can be discussed on a case by case basis. (supported by international guidelines ie NCCN and ESMO)

For stage II-IV disease international guidelines recommend combination treatment with carboplatin and paclitaxel in patients fit enough to receive this (NCCN, ESMO). Trials have been contradictory regarding the improvement with combination versus single agent carboplatin. The JGOG 3062 showed benefit of carboplatin with weekly paclitaxel over the standard three weekly regimen although the recently reported MITO7 trial showed no significant improvement in PFS for the weekly regime although it did show increased tolerability. The UK ICON8 trial equally showed no difference in PFS with weekly Rx therefore 3 weekly remains standard.

Patients should be offered entry into the ICON 8B trial if eligible (trial to assess the relative merits of weekly paclitaxel and avastin in the higher risk subgroup).

Patients who are unfit for combination chemotherapy should be offered single agent therapy, or weekly combination chemotherapy initially

Patients with stage III-IV disease who are not having IDS or patients who have suboptimal debulking surgery should be considered for treatment with carboplatin, paclitaxel and Bevacizumab.

All patients with non-mucinous epithelial ovarian cancer should be offered germline BRCA genetic testing. Stage III and IV patients should also be offered somatic testing of tumour if germline negative. Stage III and IV patients with a confirmed BRCA mutation (germline or somatic) who respond to 1st line platinum based chemotherapy should be offered maintenance treatment with olaparib (SOLO2 trial – improved PFS and OS data awaited).

Patients not eligible for olaparib and not on maintenance bevacizumab with stage III and IV disease and response to 1st line platinum chemotherapy can be considered for maintenance treatment within a clinical trial setting (ie ATHENA trial).

NEOADJUVANT CHEMOTHERAPY

Regimens are as for adjuvant chemotherapy. Two trials have now shown bevacizumab to be safe in selected patients in the neoadjuvant setting as long as this is stopped 6 weeks prior to surgery.

If IDS takes place, chemotherapy should continue with a further three cycles of the same chemotherapy. If a patient has been treated initially with single agent carboplatin and histology after surgery shows a poor response then consider adding paclitaxel for the remaining cycles if the patient is fit enough.

Following surgery, if there is residual disease of >1cm then adding in Bevacizumab to carboplatin and paclitaxel should be considered. Discussion of the amount of residual disease following surgery should be clearly documented at the MDT to support this decision. Both GOG 0218 and ICON 7 have shown improved PFS for this approach and ICON 7 has shown an improvement in OS for the subgro up of high risk stage III/IV patients defined as those with >1cm of residual disease following surgery.

FOLLOW-UP

Follow up should be at the local hospital and consist of a clinical history and examination. The schedule and nature of follow up should be determined for each individual as defined in the L&SCCN Gynaecology NSSG Follow up Guidelines. If symptoms or signs suggest possible recurrence, Ca125 should be measured and a CT scan requested.

Patients with evidence of recurrence are generally managed by the oncology team. Chemotherapy will be the initial treatment but if patients fit the DESKTOP III criteria they should be considered for second debulking surgery as below. All such patients should be discussed at the Network MDT.

The results of the OVO5 study indicate no advantage to early treatment based on rising Ca125 levels. Routine measurement of Ca125 as part of follow-up should be decided on an individual basis with clinician and patient.

MANAGEMENT OF RECURRENCE

SURGERYFOR RECURRENTDISEASE

Secondary Cytoreductive surgery

Results of the DESKTOP III study have demonstrated an improved PFS and longer time to 1st subsequent therapy (TFST) in patients randomised to secondary cytoreductive surgery at 1st recurrence. The PFS advantage was only seen in patients in whom complete resection was achieved and therefore patients must be appropriately selected for this approach. A futility analysis of GOG213 failed to demonstrate an improved PFS or OS, but patients weren't selected in the same way and the complete resection rate was much lower.

Predictors for resection were found to be : Platinum free interval >6months, positive AGO score (good PS, complete resection at primary surgery, absence of large volume ascites, absence of irresectable looking lesions on imaging, and absence of contraindications to surgery ie comorbidities). If patients fullfill the above then consideration should be made for secondary cytoreductive surgery followed by platinum based chemotherapy. All patients in whom this approach is considered must be discussed at the Network MDT, and decisions made on a case by case basis.

Palliative secondary surgery

An operation performed in patients with symptoms and signs of progressive disease (eg gastro-intestinal obstruction).

In general, surgery should be kept to a minimum. Correction of intestinal obstruction should be reserved for patients who appear most likely to benefit, for example indolent tumour growth, tumours that have been chemosensitive, and minimal carcinomatosis at prior laparotomy or large bowel obstruction only. One would anticipate that patients who undergo such procedures would live for several months or longer.

This surgery should be performed in the centre.

CHEMOTHERAPYFOR RECURRENTDISEASE

Patients with recurrent disease and particularly platinum resistant recurrence should be considered for clinical trials if any exist.

Platinum sensitive disease.

Patients who have had a good response to last platinum based chemotherapy are likely to have a further response. The cut off period of 6 months until progression is no longer used to define platinum sensitivity.

These patients can be re-challenged with Carboplatin, or (depending on performance status and patient preference) offered combination Carboplatin/Taxol. Combination chemotherapy in these circumstances has been shown to have higher response rates and progression free survival

Patients who do not wish to loose their hair can be offered Carboplatin/Caelyx (shown to be equivalent to carboplatin and paclitaxel in the CALYPSO trial but with lower rates of toxicity)

Combination of carboplatin and gemcitabine is another alternative which will not cause alopecia but does tend to be quite myelosuppressive. For patients who have not received 1st line treatment with Bevacizumab this could be considered in combination with carboplatin and gemcitabine for platinum sensitive relapse. (OCEANS trial which shows improved PFS compared to the chemotherapy alone, but no OS improvement although there was considerable cross over in the trial). However the use of avastin as second line treatment has currently been removed from CDF funding and is therefore not funded within the NHS

Patients with or without a BRCA mutation are eligible for the PARP inhibitors Niraparib or Rucaparib as maintenance Rx following response to 2nd line platinum chemotherapy. Patients without BRCA mutation are also eligible for Niraparib or Rucaparib maintenance Rx after response to 3rd line & beyond platinum cheomotherapy if they have not previously had a PARP inhibitor and they show a good response. The NOVA trial shows a prolongation in PFS and a delay until the next line of chemotherapy with Niraparib maintenance therapy.

Patients that respond to 3rd line platinum based chemotherapy and that are known to have a BRCA mutation should be considered for olaparib maintenance therapy following the 3rd line chemotherapy (as long as they have not received a previous PARP inhibitor).

Platinum resistant disease.

Patients who fail to respond well to Platinum or who relapse within 6 months of completing treatment are considered to be Platinum resistant and prognosis for these patients is poor. Single agents showing activity in this setting are:

Paclitaxel (3 weekly or weekly)

Gemcitabine

Caelyx

Topotecan

Etopside

The response rates of each of these agents are around 15% with median PFS around 3-4 months. There is no evidence in this setting that combination chemotherapy offers benefits over single agent (but does increase toxicity). Consideration should be given to PS and quality of life with the choice of the above generally driven by previous treatment and toxicity profiles. These patients should all be referred to the palliative care services if they haven't already.

The current ESMO guielines bring into refute the definition of platinum resistance as defined by the 6 month cut off from previous platinum therapy to relapse. In this situation the benefit of platinum combinations is still 15-25% dependent on previous lines of treatment and therefore platinum treatment may

still be the best option. Patients who gain response from non-platinum chemotherapy can also be considered for further lines of platinum chemotherapy following that if further treatment remains appropriate.

Bevacizumab can be considered with non-platinum chemotherapies in the platinum resistant setting. The AURELIA trial showed an improved PFS with the addition of bevacizumab to weekly paclitaxel, PLD or topotecan. Bevacizumab in this setting is currently not funded through the CDF.

Patients with Platinum resistant disease who are fit should be considered for clinical trials where available

GERM CELL TUMOURS

SEX-CHORD STROMAL TUMOURS

These account for 7% of all malignant ovarian tumours. 70% are Granulosa cell tumours, are most commonly in the sixth decade of life, and usually secrete oestrogen, although some will secrete androgen. Presentation might be due to the effects of endogenous oestrogen, such as proliferative endometrium, or hyperplasia, in a thin, post-menopausal woman.
Most present at an early stage and the prognosis is good.
Often the tumours are small and solid and might be difficult to detect by ultra-sound imaging.
Surgery forms the mainstay of treatment and involves pelvic clearance and infra-colic omentectomy; lymphadenectomy is not required as nodal metastasis is unusual.
Platinum based chemotherapy is used for advanced or recurrent disease.

MALIGNANTGERMCELL TUMOURS

These tumours usually occur in girls under the age of 25 years, although germ cell tumour markers should be measured in any woman with suspected malignant disease under the age of 40 years.
They usually present with abdominal pain.
60% are confined to one ovary at presentation and this, coupled with the usual age of the patient, means that fertility sparing surgery should almost always be the preferred approach.
These cases should be registered with Drs Alison Birtle and/or Dr Weibke Appel.
Dysgerminomas are highly radiosensitive, but as this will lead to premature ovarian failure, chemotherapy is employed where adjuvant or systemic treatment is required.
Non-dysgerminomas can be treated with bleomycin, etopiside and cisplatin.

PREGNANCY

OVARIAN CYSTS IN PREGNANCY

In the assessment of ovarian cysts during pregnancy, Ca125 levels are raised physiologically from 4 - 14 weeks, and are therefore not useful. That said, levels are usually only elevated up to 200 iu/L.

Cancer Antigen (CA) 125 (serum)

Units	Nonpregnant Adult	First Trimester	Second Trimester	Third Trimester
U/ml	< 35	0 - 51.5	0 - 30.8	0 - 56.3

References:

1. .Touitou Y , et. al. Tumour marker antigens during menses and pregnancy. Br J Cancer. 1989;60:419 -20. PMID:2789952
2. Tan MCB, Goedegebuure PS, Eberlein, TJ : Tumor Biology and Tumor Markers In: Townsen d CM Jr, ed. Sabiston Textbook of surgery 18th ed WB Saunders, Philadelphia, 2007 . p762
3. Wallach, J. Interpretation of Diagnostic Tests, Eighth ed. Lippincott Williams & Wilkins, 2007

MANAGEMENTOF OVARIANMASSESIN PREGNANCY- RCOG

If the mass is thought to be benign and unlikely to cause complications, expectant management and follow - up scans are recommended.

There is little evidence to support the routine laparoscopic excision of presumed benign ovarian tumours.

Surgery after 15 weeks of gestation is indicated for large (greater than 5 -10 cm in diameter) and/or symptomatic tumours and those that appear highly suspicious for malignancy (solid or mixed solid and cystic) on ultrasound.

The extent of surgery is decided by the intraoperative findings showing whether the tumour is benign/malignant:

Conservative surgery is indicated for benign masses/borderline ovarian tumours.

More extensive surgery (including staging biopsies) for confirmed higher-grade malignancies.

Rarely, chemotherapy may be given after delivery or at least after 20 weeks in order to minimise the potential fetal toxicity. The short- to medium-term fetal outcome appears to be relatively good."

LAPAROSCOPICMANAGEMENT OF ADNEXAL MASSES IN PREGNANCY - RCOG

A Cochrane review of Laparoscopic surgery for presumed benign ovarian tumor during pregnancy (Bunyavejchevin) found no randomized controlled trials, and the authors concluded that

"The available case series studies of laparoscopic surgery for benign ovarian tumour during pregnancy provide limited insight into the potential benefits and harms associated with this new surgical technique in pregnancy."

Three case series of laparoscopic management published after the Cochrane review were identified:

In a retrospective study, the medical records of 88 patients who underwent laparoscopic surgery for adnexal masses during pregnancy between 2000 and 2009 were reviewed. (Koo) Two spontaneous abortions occurred, both after emergency surgery. The frequency of obstetric complications, such as low birth weight, preterm delivery, use of tocolytics for preterm labor, low Apgar score, and fetal anomaly, was acceptable.

A retrospective study of all cases of laparoscopy during pregnancy performed in a university hospital over six years included ten adnexal masses (Azuar). No maternal complication was observed, no threatened preterm labour occurred after the perioperative course and no neonate required admission in neonatology unit.

In a retrospective study of eleven patients with singleton pregnancy who underwent laparoscopic operation for complicated benign adnexal mass during their first trimester (Ko), all of the patients had an uneventful recovery. Pregnancy was continued to term in nine patients (81.1%) and ongoing at the time of writing in 2 . (Evidence level III)

A guideline from the Society of American Gastrointestinal and Endoscopic Surgeons published in 2011, makes the following recommendation:

"Laparoscopy is safe and effective treatment in gravid patients with symptomatic ovarian cystic masses. Observation is acceptable for all other cystic lesions provided ultrasound is not concerning for malignancy and tumor markers are normal. Initial observation is warranted for most cystic lesions <6 cm in size (Low quality of evidence; Strong recommendation).

(Evidence level IV)

References:

Azuar AS. Bouillet-Dejou L. Jardon K. Lenglet Y. Canis M. Bolandard F. Storme B. Bonnin M. Pezet D. Buc E. Lemery D. Gallot D. [Laparoscopy during pregnancy: experience of the French university hospital of Clermont-Ferrand]. [French] Obstetrique & Fertilite. 37(7-8):598-603, 2009 Jul-Aug. Abstract

Bunyavejchevin S, Phupong V. Laparoscopic surgery for presumed benign ovarian tumor during pregnancy. Cochrane Database of Systematic Reviews 2006, Issue 4. Art. No.: CD005459. DOI: 10.1002/14651858.CD005459.pub2 Abstract and full text (limited in some countries). Full text is available to Fellows, Members and Trainees here

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GENETICS AND OVARIAN CANCER

Genetic testing

Appropriate family history should be assessed for all patients with ovarian cancer.

It is known that even without a family history, patients with a diagnosis of non-mucinous epithelial ovarian cancer have a risk of having a germiline BRCA mutation of just over 10%. Due to this r isk these patients should all be offered BRCA mutation testing. This can be done either from the oncology or surgical clinic with provision of appropriate patient information and consenting regarding personal and family implications by a health care professional trained to do so, or by referral to the genetics services at St Marys. ~~Currently the samples should be sent to St Marys for patients 60yrs and under at diagnosis, and via AZ for patients aver 60yrs~~. Any patient with a positive BRCA test should then be referred on to the local genetics service for further advice and testing of family members. Consideration should also be made for genetics referral of patients with a strong family history even if the BRCA testing is negative.

Consideration should be given to somatic BRCA testing for patients who do not have a germline BRCA mutation. A somatic mutation would not have any implications for other family members but could mean they will gain benefit from PARP inhibitors at an earlier stage in their treatment pathway. Somatic BRCA testing is currently being funded by AZ and is carried out at St Marys.

BRCA1

The frequency of BRCA1 mutation is estimated at between 1/500 – 1/800.

Families with breast cancer only syndromes are linked to BRCA1 45% of the time; families with both ovarian and breast cancer syndromes are linked 80% of the time.

Women established as BRCA1 positive have a 87% (CI72-95%) risk of breast cancer and 44% (CI 28-56%) risk of ovarian cancer by the age of 70 years.

Men who carry BRCA1 mutation have a three-fold increase risk of prostate cancer, and both sexes have a four-fold increased risk of colon cancer.

BRCA2

BRCA2 mutation confers a similar risk of breast cancer but a lower risk than BRCA1 of ovarian cancer. Furthermore, the lower than usual age of presentation seen with BRCA1 is less pronounced with BRCA2.

Families with male breast cancer are usually BRCA2 linked, and BRCA2 increases the risk of other cancers including a seven fold increase in laryngeal cancer and four fold increase in prostate cancer.

Hereditary Syndromes which predispose to Ovarian cancer

Basal cell naevus syndrome
Gonadal dysgenesis (ie 45 XY females)
Gorlin syndrome
Lynch syndrome – type 2
Osteochondromatosis
Peutz-Jegher syndrome

Management of women at increased risk of ovarian cancer.

For women known to be at risk of familial ovarian cancer the recommended surveillance programme is annual trans-vaginal ultrasound combined with annual CA125 blood test.

Prophylactic salpingo-oophorectomy should be discussed, particularly after completion of a family and/or after the age of 40 years. The Fallopian tubes must be removed as they are subject to increase cancer r isk with these syndromes.

Peritoneal cancer that is histologically similar to carcinoma of the ovary

TUMOURS OR BORDERLINEMALIGNANCY

Tumours of low malignant potential (borderline tumours) account for 15% of all epithelial ovarian cancers. Nearly 75% of these are stage I at the time of diagnosis. These tumours must be recognised, since their prognosis and treatment is clearly different from the frankly malignant invasive carcinomas. A review of 22 series (953 patients) with a mean follow-up of 7 years revealed a survival rate of 92 % for a dv anced stage tumours, if patients with so-called invasive implants were excluded. The cause of death was determined to be benign complications of disease (e.g., small bowel obstruction), complications of therapy, and only rarely (0.7%), malignant transformation.

In early stage disease (stage I/II), no additional treatment is indicated for a completely resected tumour of low malignant potential.

When it is desirable to retain childbearing potential, a unilateral salpingo-oophorectomy is adequate therapy. In the presence of bilateral ovarian cystic neoplasms, or a single ovary, partial oophorectomy can be employed when fertility is desired by the patient.

When childbearing is not a consideration, a total abdominal hysterectomy and bilateral salpingo-oophorectomy is appropriate therapy. The value of complete staging has not been demonstr ated for early stage cases, but the opposite ovary should be carefully evaluated for evidence of bilateral disease.

Although the impact of surgical staging on therapeutic management is not defined, in several studies patients with presumed localized disease were upstaged following complete surgical staging.

Patients with advanced disease should undergo a total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, node sampling, and aggressive cytoreductive surgery. Patients with stage II/III disease with no gross residual tumour have had a 100% survival rate in some series regardless of the follow-up dur ation. The 7-year survival rate of patients with gross residual disease was only 69%

For patients with more advanced stage disease and microscopic or gross residual disease, chemotherapy and/or radiation therapy are not indicated.

There is scant evidence that postoperative chemotherapy or radiation therapy alters the course of this disease in any beneficial way.

PSEUDOMYXOMAPERITONEI AND MUCINOUS TUMOURS

Appendicectomy should be performed even if macroscopically normal, in case primary disease is appendiceal. Pseudomyxoma peritoneii of colorectal origin should de referred to the Christie Hospital for further management.

FOLLOW-UP

Patients who have had complete pelvic clearance for early stage diseasse do not require follow up; they should be offered a single attendance at the Survivorship Clinic (starting 2012) and then returned to the care of their GP.

Patients who have had limited surgery, e.g. fertility sparing, or who have had surgery to remove an adherent and/or ruptured mass should be considered for long term follow up as the risk of recurrence is significant; approx 20%, with a death rate of 7%, over 10 years. *Ref*: http://emedicine.medscape.com/article/1950573-overview#aw2aab6b5

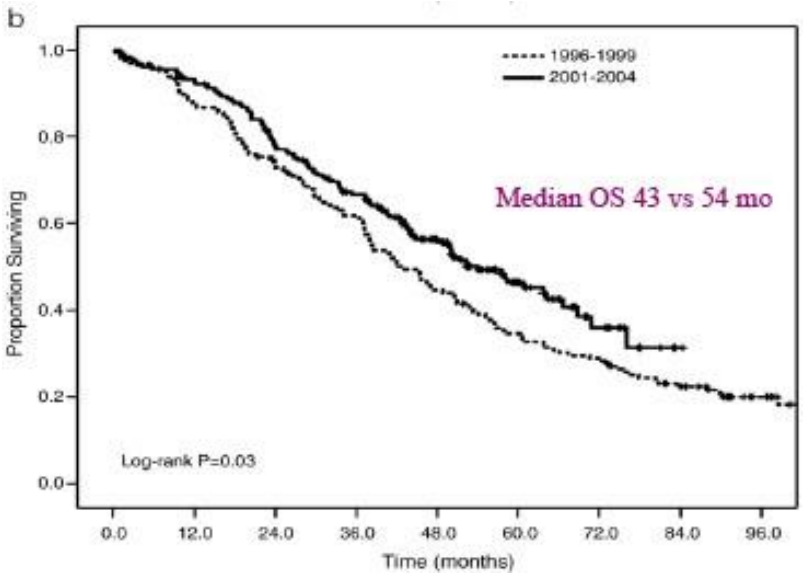
The L&SCCN Gynaecology NSSG and Gynaecology Specialist MDT keep an up to date record of clinical trials open to recruitment on the NCRI research portfolio. A quarterly report is presented to the L&SCCN Gynaecology NSSG on research activity available for gynaecological cancers.

FUTURE CONSIDERATIONS

SUPRA-RADICAL SURGERY

Increasingly, centres around the UK, and indeed around the world, are adopting a more aggressive surgical approach to the removal of ovarian cancer deposits and claiming better results.
NICE interventional procedure guidance 470, "Ultra-radical (extensive) surgery for advanced ovarian cancer", has made a number of recommendations, including…
1.4 Ultra-radical surgery for advanced ovarian cancer should be done by collaboration between surgeons with appropriate expertise (such as specialists in gastrointestinal and hepatobiliary surgery) and/or by specialists in gynaecological cancer surgery with specific training in such extensive surgery.
The procedure should only be done in specialised units with a regular practice in this type of surgery.

Figures from the Memorial Sloan-Kettering centre show improved patient survival since their introduction of "Maximal Surgical Effort"; see the graph.



Ultra-radical (extensive) surgery for advanced ovarian cancer will require additional training, combined operating and resources.
HOWEVER – there is as yet no robust comparison with standard surgery and limited data on the morbidity of such surgery.
Furthermore, the licensing of Bevacizumab for sub-optimally debulked ovarian disease poses another dynamic to the debate around the best treatment modality.

~~*BRCA TESTING*~~

~~Genetic testing is recommended in families who hav a more than 10% risk of carrying a genetic m utation that confers increased cancer risk – High Grade Serous ovarian cancer has a 17% association with BRCA gene fault and these individuals should be counselled regarding referral to cancer genetic services.~~

~~Invite **Charlie Gourley** from Edinburgh to speak on the role of genetic testing, chemosensitivity and I.P chemo-therapy.~~
~~High Grad Serous Ovarian cancer has a high rate (17%) of BRCA gene mutations; some germ line and some somatic; and this influences sensitivity to PARP inhibitors.~~

"BRCAness" Syndrome in Ovarian Cancer: A Case-Control Study Describing the Clinical Features and Outcome of Patients With Epithelial Ovarian Cancer Associated With *BRCA1* and *BRCA2* Mutations

1. **David S.P. Tan, et all (Martin E. Gore) 2008**

Abstract

Purpose We evaluated the clinical impact of germ-line *BRCA1/2* mutations in patients with epithelial ovarian cancer (EOC) on responses to first and subsequent lines of chemotherapy, treatment-free interval (TFI) between each line of therapy, and overall survival (OS).

Patients and Methods Twenty-two EOC patients with germ-line *BRCA1* or *BRCA2* mutations (BRCA-positive) were selected from our database and matched (1:2) with 44 nonhereditary EOC controls (defined by no associated personal history of breast cancer and no family history of breast and ovarian cancer or an uninformative *BRCA* mutation test) for stage, histologic subtype, age, and year of diagnosis. All patients received primary platinum-based chemotherapy. Statistical comparisons included responses after first-, second-, and third-line treatment (χ^2/Fisher's exact test) and median OS (Kaplan-Meier method/log-rank test).

Results Compared with controls, *BRCA*-positive patients had higher overall (95.5% *v* 59.1%; $P = .002$) and complete response rates (81.8% *v* 43.2%; $P = .004$) to first-line treatment, higher responses to second- and third-line platinum-based chemotherapy (second line, 91.7% *v* 40.9% [$P = .004$]; third line, 100% *v* 14.3% [$P = .005$]) and longer TFIs. A significant improvement in median OS in *BRCA*-positive patients compared with controls was observed from both time of diagnosis (8.4 *v* 2.9 years; $P < .002$) and time of first relapse (5 *v* 1.6 years; $P < .001$). *BRCA* status, stage, and length of first response were independent prognostic factors from time of first relapse.

Conclusion *BRCA*-positive EOC patients have better outcomes than nonhereditary EOC patients. There exists a clinical syndrome of BRCAness that includes serous histology, high response rates to first- and subsequent lines of platinum-based treatment, longer TFIs between relapses, and improved OS.

IINTRAPERITONEAL CHEMOTHERAPY

IP Chemo Improves Long-Term Survival in Ovarian Cancer

Women with advanced ovarian cancer lived almost a year longer when treated with intraperitoneal (IP) chemotherapy instead of intravenous (IV) therapy, long-term follow-up from two randomized trials showed. The data were presented at the 2013 Annual Meeting of the Society of Gynecologic Oncology (SGO).

IP chemotherapy led to a median overall survival of 62 months compared with 51 months for IV therapy. IP treatment also slowed disease progression by 25% versus IV treatment, study author Devansu Tewari, MD, reported at the SGO meeting.

"Each of these trials demonstrated a significant advantage for intraperitoneal chemotherapy," said Tewari, assistant professor of Obstetrics and Gynecology at the University of California, Irvine. "In this combined analysis, the survival advantage extends to a median follow-up past 10 years."

The data also confirmed the importance of completing IP therapy, as the survival advantage increased with the number of cycles of therapy.

The results came from a combined analysis of the Gynecologic Oncology Group (GOG) 114 and 172 trials. GOG 114 compared IV cisplatin-paclitaxel versus a combination of IV carboplatin, IV paclitaxel, and IP cisplatin (J Clin Oncol. 2001;19:1001-1007). GOG 172 compared IV cisplatin-paclitaxel and a regimen consisting of IV paclitaxel followed by IP cisplatin-paclitaxel.

Both trials had progression-free survival (PFS) as their primary endpoint, and survival was a secondary endpoint. The trials involved a combined total of 876 women with stage III epithelial ovarian carcinoma, optimally resected to ≤1 cm residual tumor.

Tewari reported findings from a median follow-up of 13.8 years in GOG 114 and 9.7 years in GOG 172. The primary results of the individual trials showed a 5.5- to 6-month improvement in media n PFS with IP therapy. In the combined analysis, the data continued to show a 5-month difference in favor of IP therapy (25 vs 20 months). After adjustment, the difference translated into a 16% reduction in the haza rd ratio for progression (P = .03).

The initial reports of survival data showed an 11-month difference in favor of IP therapy in GOG 114 and a 16-month advantage for IP in GOG 172. In an adjusted analysis of the long-term follow-up data from bothtrials, patients receiving IP chemotherapy had a 17% lower mortality risk (P = .048).

Tolerance has been problematic with IP chemotherapy from the first clinical evaluations, an issue reflected in the data from GOG 114 and 172. The 5-year survival rate among patients treated with IP therapy increased from 18% with completion of one or two cycles to 33% with three or four cycles, to 59% for patients who completed five or six cycles of treatment. In GOG 172, only 42% of patients in the IP arm completed the planned six cycles of therapy.

Several ongoing studies are focusing on optimizing IP chemotherapy by evaluating different doses and different drug combinations.

In a discussion following Tewari's presentation, Joan Walker, MD, noted that the consistency of the results from GOG 114, GOG 172, and the earlier GOG 104 trial have been encouraging, but "it can't necessarily be [that] the IP therapy is the only contributing factor [to the survival improvement]."

BEVACIZUMAB & SUB-OPTIMALDEBULKING

NICE TA284

1.1 Bevacizumab in combination with paclitaxel and carboplatin is not recommended for first-line treatment of advanced ovarian cancer (International Federation of Gynaecology and Obstetrics [FIGO] stages IIIB, IIIC and IV epithelial ovarian, fallopian tube or primary peritoneal cancer).

1.2 People currently receiving bevacizumab for first-line treatment of advanced ovarian cancer should be able to continue treatment until they and their clinicians consider it appropriate to stop.

APPENDIX

CPEX Criteria

1. Major Surgery; Any bowel resection, gastrectomy, oesophagectomy, open AAA repair and major gynaecology oncology surgery.

2. Age ≥ 65 years; age is an approximate predictor of reduced physiological reserve, but common sense is required. If the patient runs marathons, for example, then CPEX is not indicated. The "average" 65 year old will require CPEX.

3. Veteran's Specific Activity Questionnaire (VSAQ)

The following is a list of activities which increase in difficulty as you read down the page. Think carefully, then underline the first activity that, if you performed it for a period, would typically cause fatigue, shortness of breath, chest discomfort, or otherwise cause you to want to stop. If you do not normally perform a particular activity, try to imagine what it would be like if you did.

Subject ID #_____Date Completed:_____/_____/_____

1 MET: Bathing, getting dressed, working at a desk

2 METs: Taking a shower, walking down 8 steps

3 METs: Walking slowly on a flat surface for 1-2 blocks, moderate housework (vacuum, sweeping f loors, carrying groceries)

4 METs: Light yard work (raking leaves, weeding, pushing power mower), painting, light carpentry

5 METs: Walking briskly (4 miles in an hour), social dancing, washing a car

6 METs: Playing 9 holes of golf carrying your own clubs, heavy carpentry, mow lawn with push mower

7 METs: Heavy outdoor work (digging, spading soil), playing singles tennis, carry 60 pounds

8 METs: Move heavy furniture, jog slowly, climb stairs quickly, carry 20 pounds upstairs

9 METs: Bicycling at a moderate pace, sawing wood, jumping rope (slowly)

10 METs: Brisk swimming, bicycle up a hill, walking briskly uphill, jog 6 miles per hour

11 METs: Cross country ski, play full court basketball

12 METs: Running briskly, continuously (level grounds, 8 minutes per mile)

4. Revised Cardiac Risk Index (RCRI)

Revised Cardiac Risk Index for Pre-Operative Risk

Estimates risk of cardiac complications after surgery.

High-Risk Surgery

- Intraperitoneal
- Intrathoracic
- Suprainguinal vascular

Yes = +1
No = +0

History of ischemic heart disease

- History of MI
- History of positive exercise test
- Current chest pain considered due to myocardial ischemia
- Use of nitrate therapy
- ECG with pathological Q waves

Yes = +1
No = +0

History of congestive heart failure

- Pulmonary edema, bilateral rales or S3 gal op
- Paroxysmal nocturnal dyspnea
- CXR showing pulmonary vascular redistribution

Yes = +1
No = +0

History of cerebrovascular disease

- Prior TIA or stroke

Yes = +1
No = +0

Pre-operative treatment with insulin

Yes = +1
No = +0

RCRI score	Risk of major cardiac event.
0	0.4 %
1	0.9 %
2	6.6 %
3	11 %
4	11 %
5	11 %
6	11 %

"Major cardiac complications" is defined as:

- myocardial infarction
- pulmonary oedema
- ventricular fibrillation or primary cardiac arrest
- complete heart block

End of Life Pathway

The WHO describes palliative care as 'the active, holistic care of patients with advanced, progressive illness'.[1]

The hub of any patients medical health is the GP, they are in an ideal position to provide and coordinate this care for a number of reasons:

- they have long-established relationships with their patients which are so important at this critical time in a patient's life
- they are used to dealing with co-morbidity and uncertainty
- they are trained to treat patients holistically which is central to the palliative care approach.

GPs have to be able to provide high quality, equitable care, and to work together effectively with specialist teams if they are to provide the best primary palliative care for all who require it.

There is an increasing imperative to be able to recognise the needs of all patients nearing the end of their lives, not just those with cancer, and to be able to extend some of the developments in care provided for cancer patients to those with other illnesses, which constitute 75% of all deaths. A large proportion of patients receive news of palliative disease which will lead to end of life from the secondary care and steps need to be put in place to ensure provisions are met, this becomes more relevant when the time frame for commencing end of life provision is approximately one year before death ie at the time of advancing disease.

Proactive end of life care

In order to provide optimal care for any patient nearing the end of their life, i.e. not just in the terminal or dying phase, but in their last year, we need to be able to do three things:

- identify where a patient is on their illness trajectory – do they have years, months, weeks or days to live? This then allows proactive management, calmer planning and less 'fire-fighting' crisis management
- assess their needs, and those of their family/carers, in the light of their advance care plan
- plan (using a management plan) and then provide their care according to the patient's preferences and varying needs, at different times.

A key point is for all hospital and hospice clinicians who recognise that a patient may be in their last year of life to notify the patient's GP and recommend that the patient is added to the palliative care register. The basis for this lies in the End of Life Care Strategy.

End of Life Care Strategy

The strategy was developed over a period of a year by an advisory board led by Professor Mike Richards and six working groups, consulting over 300 stakeholders. It became apparent that a whole systems approach was required. Accordingly the Strategy strongly recommends that a care pathway approach should be followed both for care and the commissioning of end of life care.

Key Steps

Identification of people approaching the end of life, and initiating discussions about preferences for end of life care;

Care planning: assessing needs and preferences, agreeing a care plan to reflect these and reviewing these regularly;

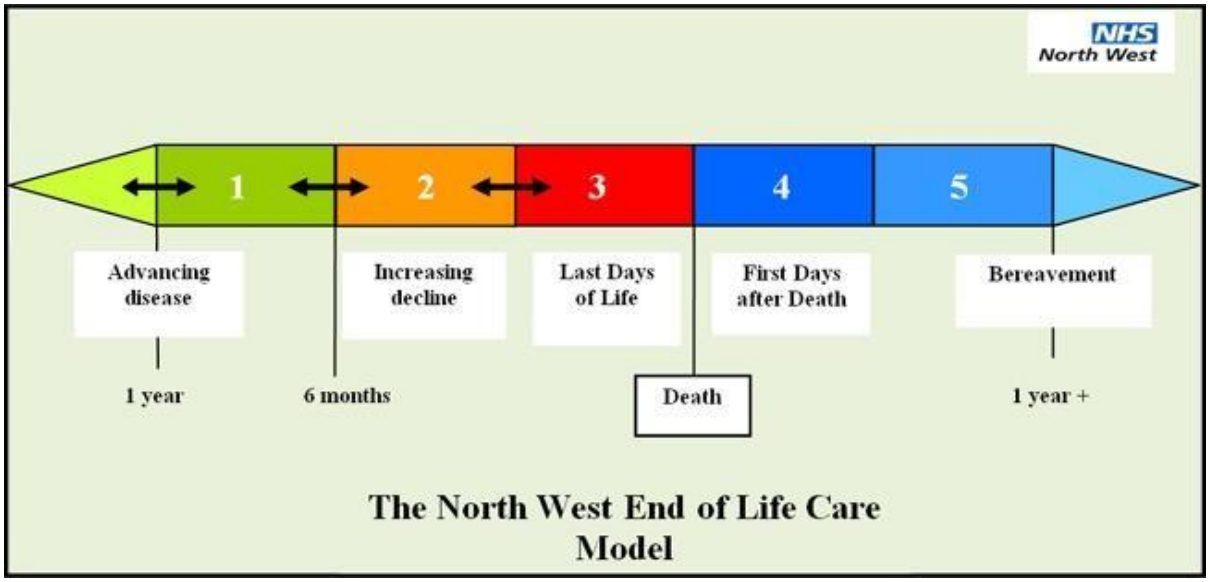
Coordination of care;

Delivery of high quality services in all locations;

Management of the last days of life;

Care after death; and

Support for carers, both during a person's illness and after their death.



The story of a patient's health from diagnosis of a life-limiting illness can be seen with this model. The model comprises five phases as described below with some examples of practice highlighted.

1. Advancing disease – timeframe: 1 year or more.

Example of practice required -the person is placed on a supportive care register in General Practitioner (GP) practice/care home. The person is discussed at monthly multidisciplinary practice/care home meetings.

2. Increasing decline – timeframe: 6 months [approximate].

Example of practice required -DS1500 eligibility review of benefits, Preferred Priorities for Care (PPC) noted, Advance Care Plan (ACP) in place and trigger for continuing healthcare funding assessment

3. Last days of life – timeframe: last few days.

Examples of practice required - primary care team/care home inform community and out of hours services about the person who should be seen by a doctor. End of life drugs prescribed and obtained, and Liverpool Care Pathway (LCP) implemented.

4. First days after death – timeframe: first few days.

Examples of practice required include prompt verification and certification of death, relatives being given information on what to do after a death (including D49 leaflet), how to register the death and how to contact funeral directors

5. Bereavement – timeframe: 1 year or more.

Examples of practice required include access to appropriate support and bereavement services if required.

As health professionals working within gynae oncology, we treat patients who fit all parameters of the end of life scale, what is required of us is to be aware of whereabouts on this scale our patientsfit and advise the GP, District Nurses, Macmillan Nurses accordingly so they can be transferred as appropriate to the primary care end of life register so all their needs can be anticipated and met at the primary level.

References

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