West Yorkshire & Harrogate Cancer Alliance

Including York Teaching Hospitals NHS Foundation Trust and Hull & East Yorkshire Hospital Trust

Guidelines for the Investigation and Treatment of Testicular Cancers

Version 4.1

Updated June 2017

i Document Control

Title	Guidelines for the Investigation and Treatment of Testicular Cancers
Author(s)	Dan Stark, Leeds Teaching Hospitals NHS Trust
Owner	West Yorkshire & Harrogate Cancer Alliance

Version Control		
Version/ Draft	**Date**	**Revision summary**
0.1	29/07/2009	Initial draft version
0.2	29/07/2009	Amendments made following comments
0.3	07/08/2009	Amendments made following consultation
1	19/08/2009	Final Version
1.1	29/06/2010	Amendments made following comments
1.2	20/08/2010	Guidelines amended into 3 separate documents: 1. Bladder Renal and Prostate 2. Penile 3. Testicular Additional follow-up protocols added
2.0	06/09/2012	Full review of guidelines. Updates to Section 14 Palliative Care, Section 12 Pathology and MDT contacts
3.0	20/05/2015 & October 2016	Review of guidelines.
4.0	April 2017	Review and update
4.1	June 2017	Further amendments made to various sections

Contributors to current version		
Contributor	**Author/Editor**	**Section/Contribution**
C Rock/S Kite		Palliative Care
Dan Stark		Review and Update

ii Information Reader Box

Title	Guidelines for the Investigation and Treatment of Testicular Cancers
Author(s)	Dan Stark, Leeds Teaching Hospitals NHS Trust
Review date	June 2017
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Proposed Target Audience for Consultation / Final Statement	**WY&H, and HC&V Cancer Alliances:** Urology MDT Teams Lead Cancer Nurses Lead Cancer Managers Lead Cancer Commissioners
Proposed Circulation List for Final Statement	All WY&H Cancer Alliance guidelines will be made available electronically on the Wakefield CCG website. No hard copies will be supplied.
Contact details	West Yorkshire & Harrogate Cancer Alliance NHS Wakefield CCG White Rose House West Parade Wakefield WF1 1LT

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iv Document sign-off

Agreement of the Guidelines for the Investigation and Treatment of Testicular Cancers.

Name	Position	Organisation	Date agreed
Mr D Stark	MDT Lead Clinician for the Testicular SMDT	Leeds Teaching Hospitals NHS Trust	11/7/2017
Mr P Koenig	MDT Lead	Airedale NHS Foundation Trust	11/7/2017
Mr R Chahal	MDT Lead	Bradford Teaching Hospitals NHS Foundation Trust	11/7/2017
Mr N Bryan	MDT Lead	Calderdale & Huddersfield NHS Foundation Trust	11/7/2017
Miss A Davies	MDT Lead	Harrogate & District NHS Foundation Trust	11/7/2017
Mr N Smith	MDT Lead	Hull & East Yorkshire Hospitals NHS Trust	11/7/2017
Mr J Cartledge	MDT Lead	Leeds Teaching Hospitals NHS Trust	11/7/2017
Mr M Dooldeniya	MDT Lead	Mid Yorkshire Hospitals NHS Trust	11/7/2017
Mr L Coombs	MDT Lead	North Lincolnshire & Goole Hospitals NHS Foundation Trust	11/7/2017
Mr R Wilson	MDT Lead	York Hospitals NHS Foundation Trust	11/7/2017

1 Introduction

1.1 National Guidance for Urological Cancer

- All patients with urological cancers should be managed by multidisciplinary urological cancer teams. These teams should function in the context of dedicated specialist services, with working arrangements and protocols agreed throughout each cancer network. Patients should be specifically assured of:
    - Streamlined services, designed to minimise delays;
    - Balanced information about management options for their condition;
    - Improved management for progressive and recurrent disease.

1.2 Purpose and Scope of these Guidelines

The purpose of this document is to set out agreed clinical guidelines for the investigation and management of Testicular Cancer which are based on NICE Improving Outcome Guidance for Urological Cancers and subsequent NHS service standards for Urological Cancers.

The document also describes the roles of the local care and specialist teams.

These clinical guidelines were written by members of the Testicular Cancer SMDT and will be reviewed at least every three years or when new guidance is available. These guidelines are influenced by international best practice, most notably the European Urology Association guidelines group.

1.3 Urological Cancer Services

The Yorkshire & Humber Clinical Network (CN) has a resident population of approximately 5.8 million. There are 24 Clinical Commissioning Groups (CCGs) and 14 Acute Hospital Trusts within the Network. The Cancer Centre is based at Leeds Teaching Hospitals NHS Trust.

The Testicular SMDT covers the West Yorkshire & Harrogate Cancer Alliance and the Humber Coast & Vale Cancer Alliance with a population in excess of 3.6 million

Hospital Trust	**Team**
Airedale NHS Foundation Trust	Diagnostic/Local MDT
Bradford Teaching Hospitals NHS Foundation Trust	Diagnostic/Local /Specialist MDT
Calderdale & Huddersfield NHS Foundation Trust	Diagnostic/Local MDT
Harrogate and District NHS Foundation Trust	Diagnostic/Local MDT

Leeds Teaching Hospitals NHS Trust	Diagnostic/Local /Specialist MDT
Mid Yorkshire Hospitals NHS Trust	Diagnostic/Local /Specialist MDT
York Hospitals NHS Foundation Trust	Diagnostic/Local MDT

1.3.1 Local MDT Teams

Hospital Trust	MDT Lead
Airedale NHS Foundation Trust	Mr P Koenig
Calderdale & Huddersfield NHS Foundation Trust	Mr N Bryan
Harrogate and District NHS Foundation Trust	Mr J Gill
York Hospitals NHS Foundation Trust **	Mr R Wilson

****York Hospital is now part of the Humber Coast and Vale Cancer Alliance**

The Germ cell MDT based in Leeds provides review of all cases referred to oncology service in Hull also and includes in the core membership Dr Mohammad Butt, Medical Oncologist, Hull Cancer Centre. His team also supports and operates by these guidelines

1.3.2 Supranetwork Teams

Testicular Cancer — Leeds Teaching Hospitals NHS Trust
Lead Clinician Dr D Stark

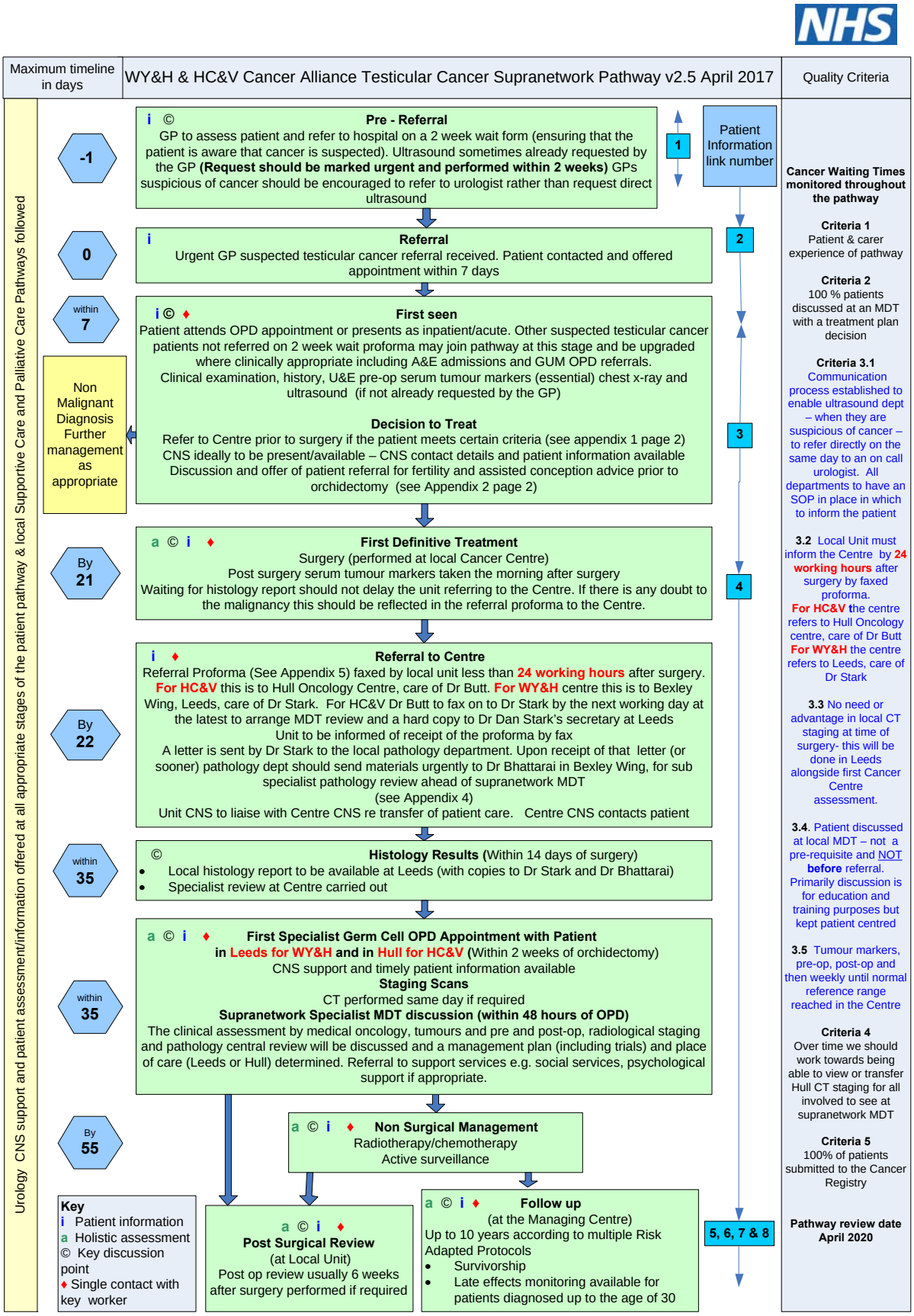
Hospital Trust	Supranetwork Team
Leeds Teaching Hospitals NHS Trust	Leeds Prostate, Kidney and Germ Cell Specialist MDT

1.4 Testicular Cancer Supranetwork Pathway

A West Yorkshire & Harrogate and Humber Coast & Vale Testicular Cancer Supranetwork Pathway has been developed. This pathway covers the West Yorkshire & Harrogate Cancer Alliance and the Humber Coast & Vale Cancer Alliance.

Please find the Testicular Cancer Supranetwork Pathway (v2.5 April 2017) overleaf.

Teenagers and Young Adults
Two Teenage and Young Adults with Cancer - Initial Management Pathways (16-18 years) and (19-24) have been developed.


Maximum timeline in days
WY&H & HC&V Cancer Alliance Testicular Cancer Supranetwork Pathway v2.5 April 2017
Quality Criteria
Urology CNS support and patient assessment/information offered at all appropriate stages of the patient pathway & local Supportive Care and Palliative Care Pathways followed
-1
Pre - Referral
GP to assess patient and refer to hospital on a 2 week wait form (ensuring that the patient is aware that cancer is suspected). Ultrasound sometimes already requested by the GP (Request should be marked urgent and performed within 2 weeks) GPs suspicious of cancer should be encouraged to refer to urologist rather than request direct ultrasound
1
Patient Information link number
0
Referral
Urgent GP suspected testicular cancer referral received. Patient contacted and offered appointment within 7 days
2
within 7
First seen
Patient attends OPD appointment or presents as inpatient/acute. Other suspected testicular cancer patients not referred on 2 week wait proforma may join pathway at this stage and be upgraded where clinically appropriate including A&E admissions and GUM OPD referrals.
Clinical examination, history, U&E pre-op serum tumour markers (essential) chest x-ray and ultrasound (if not already requested by the GP)
Decision to Treat
Refer to Centre prior to surgery if the patient meets certain criteria (see appendix 1 page 2)
CNS ideally to be present/available – CNS contact details and patient information available
Discussion and offer of patient referral for fertility and assisted conception advice prior to orchidectomy (see Appendix 2 page 2)
3
Non Malignant Diagnosis Further management as appropriate
By 21
First Definitive Treatment
Surgery (performed at local Cancer Centre)
Post surgery serum tumour markers taken the morning after surgery
Waiting for histology report should not delay the unit referring to the Centre. If there is any doubt to the malignancy this should be reflected in the referral proforma to the Centre.
4
By 22
Referral to Centre
Referral Proforma (See Appendix 5) faxed by local unit less than 24 working hours after surgery. For HC&V this is to Hull Oncology Centre, care of Dr Butt. For WY&H centre this is to Bexley Wing, Leeds, care of Dr Stark. For HC&V Dr Butt to fax on to Dr Stark by the next working day at the latest to arrange MDT review and a hard copy to Dr Dan Stark's secretary at Leeds
Unit to be informed of receipt of the proforma by fax
A letter is sent by Dr Stark to the local pathology department. Upon receipt of that letter (or sooner) pathology dept should send materials urgently to Dr Bhattarai in Bexley Wing, for sub specialist pathology review ahead of supranetwork MDT
(see Appendix 4)
Unit CNS to liaise with Centre CNS re transfer of patient care. Centre CNS contacts patient
within 35
Histology Results (Within 14 days of surgery)
Local histology report to be available at Leeds (with copies to Dr Stark and Dr Bhattarai)
Specialist review at Centre carried out
within 35
First Specialist Germ Cell OPD Appointment with Patient
in Leeds for WY&H and in Hull for HC&V (Within 2 weeks of orchidectomy)
CNS support and timely patient information available
Staging Scans
CT performed same day if required
Supranetwork Specialist MDT discussion (within 48 hours of OPD)
The clinical assessment by medical oncology, tumours and pre and post-op, radiological staging and pathology central review will be discussed and a management plan (including trials) and place of care (Leeds or Hull) determined. Referral to support services e.g. social services, psychological support if appropriate.
By 55
Non Surgical Management
Radiotherapy/chemotherapy
Active surveillance
Post Surgical Review
(at Local Unit)
Post op review usually 6 weeks after surgery performed if required
Follow up
(at the Managing Centre)
Up to 10 years according to multiple Risk Adapted Protocols
Survivorship
Late effects monitoring available for patients diagnosed up to the age of 30
5, 6, 7 & 8
Key
i Patient information
a Holistic assessment
© Key discussion point
♦ Single contact with key worker
Cancer Waiting Times monitored throughout the pathway
Criteria 1
Patient & carer experience of pathway
Criteria 2
100 % patients discussed at an MDT with a treatment plan decision
Criteria 3.1
Communication process established to enable ultrasound dept – when they are suspicious of cancer – to refer directly on the same day to an on call urologist. All departments to have an SOP in place in which to inform the patient
3.2 Local Unit must inform the Centre by 24 working hours after surgery by faxed proforma.
For HC&V the centre refers to Hull Oncology centre, care of Dr Butt
For WY&H the centre refers to Leeds, care of Dr Stark
3.3 No need or advantage in local CT staging at time of surgery- this will be done in Leeds alongside first Cancer Centre assessment.
3.4. Patient discussed at local MDT – not a pre-requisite and NOT before referral. Primarily discussion is for education and training purposes but kept patient centred
3.5 Tumour markers, pre-op, post-op and then weekly until normal reference range reached in the Centre
Criteria 4
Over time we should work towards being able to view or transfer Hull CT staging for all involved to see at supranetwork MDT
Criteria 5
100% of patients submitted to the Cancer Registry
Pathway review date April 2020

West Yorkshire & Harrogate and Humber Coast & Vale Cancer Alliances

Title	Testicular Pathway
Author & Owner	Dan Stark and members of the former YCN NSSG Urology Group

Version Control		
Version/ Draft	**Date**	**Revision summary**
1.0	July 2009	Original version published
1.1	Feb 2010	Pathway reviewed and updated to include NEYHCA details
2.0	July 2011	Full review and update to Fax Referral Proforma (Appendix 5). Date of Pathway Review changed. Change to hours allowed from orchidectomy to notification at Leeds/Hull, in line with Peer Review requirements (from 36 to 24 working hours)
2.1	March 2012	Review date changed, otherwise no change to pathway
2.2	December 2012	Timelines reviewed and updated. HYCCN changed to NEYHCA
2.3	December 2012	Fax number updated (see page 4)
2.4	February 2015	Specialist histopathology contact updated.
2.5	March 2017	Addenda about U&E and CT location added

Supranetwork Testicular Cancer 'Timed' Pathway Guidelines

The Supranetwork Testicular Cancer pathway incorporates the local Supportive and Palliative Care Pathways. Key discussion points, key information, key worker contacts and holistic assessments are identified by symbols along the Testicular pathway. The Testicular pathway is supported by a tumour specific Patient Information Pathway. The Patient Information Pathway supports the steps in the testicular pathway such as referral, diagnostic procedures and tests, diagnosis, treatments and side effects and support services. Each stage is numbered from 1 to 8 indicating when the information might be offered. Additional national resources to meet assessed or expressed patient/carer information needs may be offered at any stage along the pathway

Appendix 1: Criteria for referral to centre prior to surgery

The indication for discussing this between the managing Urologist and Dr Dan Stark (or deputy) in Leeds should be:

- Metastatic disease visible on chest X-ray
- Abdominal mass clinically evaluable or palpable
- Clinically significant cervical or axillary lymphadenopathy

- Weight loss >10% in the presence of a clinical testicular mass.

A consideration in these patients may well be performing ultrasound abdomen as well as ultrasound testis in the local hospital prior to telephone discussion with Leeds Medical Oncology with the result. Then planning for surgery, chemotherapy and definitive staging can take place simultaneously in Leeds.

Appendix 2: Criteria for discussion and offer of patient referral for fertility and assisted conception advice prior to orchidectomy to include

- Bi-lateral tumours
- Known pre-existing oligo or azoospermia
- A high risk of testicular intertubular neoplasia (manifest by testicular atrophy, volume <12mls in a patient less than 40 years, gross calcification on ultrasound).

If the patient is unwell early telephone or fax referral to Dr Dan Stark in Leeds allows us to co-ordinate staging, fertility advice, chemotherapy and orchidectomy within a single team in Leeds, and is better than splitting the process between a regional centre and Leeds

Appendix 3: Referral to Centre Process

Referral to be made to Medical Oncology at Leeds by faxed pro-forma, followed by a letter with all the information from the pro-forma if that is preferred. The responsibilities for this falls to the operating surgeon performing orchidectomy. It should be completed so that it is received in Leeds/Hull respectively within 24 working hours of orchidectomy. For HC&V the centre refers to the Hull Oncology Centre, care of Dr Butt. For WY&H the centre refers to Leeds, care of Dr Stark. For HC&V Dr Butt to fax on to Dr Stark by the next working day at the latest to arrange MDT review.

Appendix 4: Histology report

Upon receipt of a referral in the Leeds Germ Cell team; using the fax pro-forma a standard histology request letter will be sent by that team to the local Pathology department. By copying this letter to Dr Bhattarai secretary in Urological Pathology at St James' with the full patient details we can provide earlier notice to Pathology that central review is going to be required, making it more likely that the standard is met of local pathology report and slides being available within 16 days of surgery for definitive decision making in the Regional Germ Cell MDT in Leeds.

As soon as the patient is diagnosed with testicular cancer and if age appropriate (16 – 24 years) refer patient to the Teenage and Young Adult Unit (TYAS) at Leeds and follow the WY&H and HC&V Teenage and Young Adult with Cancer pathway.

Appendix 5: Fax referral Pro-Forma Leeds

Please send hard copy of this pro-forma and any letter or other reports to Dr Dan Stark's secretary Oncology Level 4 Bexley Wing St James's Institute of Oncology
Tel: 0113 2068266 **Please fax to: 0113 2067871 FAO Dr Dan Stark**

Patients Name		
GP details GP fax No		
Referring clinician & local hospital reference/case note number		
NHS number		
Date of birth		
Address		
Contact telephone number for patient		
Patient awareness	Has the patient been today cancer is a possible diagnosis for their testicular swelling	Y/N
	Has the patient been informed they will have contact from the Germ Cell Tumour Service in Leeds as a result of this surgery	Y/N
Pre-operative findings		
Approximate length of history (in months)		
Chest x-ray result		Normal/Abnormal
Testicular ultrasound result summary (please include a copy of result with paper referral)		
Laterality of tumour		Left / Right
Inguinal orchidectomy date		
Pre-operative tumour markers sent & results		Y/N date:
(We will arrange the CT in Leeds once pathology is confirmed)		hCG
		AFP
		LDH
		eGFR
Other notes/concerns (the patient will be seen at +/-14 days from orchidectomy unless problems are raised here)		

Fax referral Pro-Forma Hull
Please send hard copy of this pro-forma to Dr Mohammad Butt's secretary in Queen's Centre for Oncology, CHH. Tel: 01482461303
Please fax to: 01482607739, FAO: Dr Mohammad Butt

Patients Name		
GP details GP fax No		
Referring clinician & local hospital reference/case note number		
NHS number		
Date of birth		
Address		
Contact telephone number for patient		
Patient awareness	Has the patient been today cancer is a possible diagnosis for their testicular swelling	Y/N
	Has the patient been informed they will have contact from the Germ Cell Tumour Service in Hull as a result of this surgery	Y/N
Pre-operative findings		
Approximate length of history (in months)		
Chest x-ray result		Normal/Abnormal
Testicular ultrasound result (please include a copy of result with paper referral)		
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Pre-operative tumour markers sent & results		Y/N date:
(We will arrange the CT in Hull once pathology is confirmed)		hCG
		AFP
		LDH
		eGFR
Other notes/concerns (the patient will be seen at +/-14 days from orchidectomy unless problems are raised here)		

1.5 Patient Information

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

2 Testicular cancer

The initial diagnosis and surgical management of Testicular Germ Cell Tumours is a Cancer Unit activity but the further investigation and management of the patient should be by a Specialised Multidisciplinary Team at the Cancer Centre. Urgent referral for this is paramount for successful outcomes. A successful Germ Cell Tumour Service requires a Multidisciplinary Team ethos and a full range of supportive services such as Specialised Nursing, Pharmacy, Radiology, Social Services, Psychological Support Services, Assisted conception and Fertility Services, and Specialist Surgical Services (abdominal and thoracic). The regional service based in Leeds is involved in clinical trials and studies at local, national and international levels (MRC, EORTC and NCRI) supported by Research Nurses based locally.

Guidelines on the diagnosis and treatment of testicular cancer already exist at the national and international level, in particular the Royal College of Radiologists, Clinical Oncology Information Network (COIN) in association with the Scottish Intercollegiate Guidelines Network (SIGN) Guidelines) on the Management of Adult Testicular Germ Cell tumours, and the European Consensus Guidelines have already been adopted by the testicular tumour service in Yorkshire and should for the most part be followed.

2.1.1 Screening

There is no good evidence that screening programmes for men are indicated in this disease which is rare and the detection rate is likely to be small.

3 Presentation and early diagnosis

Testicular cancer has high growth rates and early detection and diagnosis is important. Delaying presentation is a greater problem than delaying referral and education programmes aimed at young men to inform them about the disease and its curability should be supported. General Practitioners will see only infrequent cases of testicular cancer and need to have a low threshold for referral to specialist services for men presenting with scrotal masses. Between 80% and 90% present with an enlarged testicle or a lump on the testicle; pain is not usually a feature although the patient may complain of a dragging sensation in the groin or scrotum. The presence of pain should not prevent referral. Some patients may present with a decrease of size of the affected testis and rarely patients can present with a hydrocele, gynecomastia or backache as the presenting non-specific symptom. Patients need careful clinical assessment of the testis to distinguish between masses arising from the body of the testis and other intra-scrotal swellings. Urgent direct referral from the GP to the local

Urologist may achieve a quicker distinction between testicular and epididymal masses, easier access to testicular ultrasonography, and any patient suspected of having a testicular malignancy with a lump in the testis, or suspected epididymo-orchitis or orchitis not resolving within two weeks of management, should be referred urgently for urological assessment and the patient should be seen urgently (within 1 week of referral). Any ultrasound request should be urgent and performed within two weeks. If this investigation is requested by a GP and is positive there should be a direct route for referral from the Radiology Department to the local Urologist (same or next working day).

4 Primary investigation and treatment

Having been referred to a Urological Surgeon in the local cancer unit the patient should receive the following assessments:

Clinical history and examination are important, particularly detecting backache, weight loss and lymph nodes in the neck.

Investigations must include:

1. Ultrasound of both testes (if not already performed). This investigation is highly specific for the diagnosis of intra-testicular masses. Ultrasonography of the abdomen is also advisable in the presence of testicular lump for the detection of possible enlarged abdominal lymph nodes.
2. Chest x-ray will often determine whether the patient has pulmonary metastases or not.
3. The serum tumour markers

Alpha Feta Protein (AFP) and Human Chorionic Gonadatrophin (HCG) and the non-specific serum enzyme lactate dehydrogenase (LDH) are central for staging, determining prognosis, treatment and follow-up of testicular germ cell tumours. One or more of these is raised in 75% of cases of non-seminoma and 35% of cases of seminoma. Pre-operative and post-op tumour marker assay and review of these investigations is of paramount importance. Then further assays should be repeated at least once post- operatively alongside the referral of the patient to the cancer centre. Post-operative tumour markers on day 1 after orchidectomy are sufficient. Patient recall to Urology for post-operative markers is not necessary if day 1 post-operative markers are performed and the results examined. If markers are stable or have fallen standard referral by fax is sufficient. If day 1 markers have not been performed post-operative markers should be arranged and reviewed as soon as this becomes apparent by the referring cancer unit Urology team. Further staging investigations are best deferred until after the orchidectomy and recovery, and will be performed by the Germ cell team.

Key tumour marker results must be performed according to a single assay method for all patients in the Network. As the manufacturers assays vary across the region, all results should be interpreted with local normal values, and any marker results where moderate changes in the reading might change management must be repeated in LTHT before management is decided. Markers are interpreted from sequential rather than single readings if uncertainty exists, and interpreted in the context of clinical or laboratory features that can result in unreliable or spurious readings.

Patients with high risk features (such as high serum tumour markers and wide-spread metastases at presentation) should be referred immediately to the regional germ cell clinic for primary chemotherapy prior to orchidectomy, which can be delayed until potentially life-saving chemotherapy has been delivered at the cancer centre. The indication for discussing referral to the cancer centre prior to surgery with Dr Dan Stark (or deputy) in Leeds should be one or more of:

- Metastatic disease visible on chest X-ray
- Abdominal mass clinically evaluable, palpable on ultrasound
- Clinically significant cervical or axillary lymphadenopathy
- Weight loss >10% in the presence of a clinical testicular mass

Any one of these is sufficient for pre-operative discussion.

If the markers have increased between pre and post-op, this patient is at high risk, and **telephone referral** to the Germ Cell Services in the cancer centre is advised.

5 Primary Surgical Management

An orchidectomy should be performed through an inguinal incision with division of the cord at the internal ring. Prior to this the testis having been delivered through the wound and the cord occluded using non-crushing clamps the testis is inspected and if the mass is cancerous the operation is completed. On the rare occasion when the diagnosis is in doubt, representative biopsies may be sent for frozen section and if malignancy is not confirmed then the testis can be reconstituted and replaced and the patient placed on close follow up. Scrotal exploration should usually be avoided with testicular masses, but if performed for what was thought to be an inflammatory non-malignant condition, then an orchidectomy is performed with the division of the cord as high as possible.

There are three things which need to be considered prior to orchidectomy in cases of testicular lump/swelling.

First, the patient's fertility should be a consideration . If he has been having difficulty in fathering a child, has a history of infertility, or has pathology suspected or confirmed in the contralateral testis, referral for potential sperm banking prior to the orchidectomy is recommended, since only the diseased testis may be capable of active spermatogenesis. Referral for sperm banking before orchidectomy should only be offered to patients where the contralateral testis function is in doubt. This would normally delay the operation of orchidectomy by only a few days, and so is unlikely to adversely affect eventual outcome. For patients where contralateral testis function is normal, consideration of cryopreservation of sperm prior to orchidectomy is costly and unnecessary. If further treatments later place fertility at risk, then this issue will be addressed then.

Second, patients may suffer an alteration of body image having undergone an orchidectomy and consideration should be given to the placement of a prosthesis either at the time of the orchidectomy or in the future and patients should be advised about this possibility and the factors in the choice between early and delayed prosthesis.

Third, consideration should be given to biopsying the contralateral testis in patients at high risk of having carcinoma in situ (intratubular germ cell neoplasia, ITGCN) in their other testis. ITGCN occurs in approximately 5% of men with testicular cancer in the opposite testis and is thought to progress to invasive germ cell tumour in almost 100% of cases within a ten year time frame. Patients at risk are of younger age (less than 30 years of age), have a small contralateral testis (less than 16ml), a history of maldescent of the testis or a previous history of subfertility/low sperm count. If a biopsy is considered this should be performed as a separate procedure to the orchidectomy (regowning and regloving, separate instruments) the specimens should be separate to the orchidectomy specimen and consideration given to referral for central pathology review. Patients with intratubular germ cell neoplasia will be offered a course of radiotherapy to that testis after consideration of fertility issues (see later).

5.1 Pathology of the Primary Specimen

There should be a local protocol followed for the handling and preservation of the testis. Valuable information may be lost to the Pathologist through over-energetic disruption by the operating surgeon. The specimen should be bi-valved through the testis and epididymis either in theatre or as soon as it arrives in the Pathology Department to allow for proper fixation in an adequate volume of formaldehyde fixative. Multiple blocks should be taken and in addition to a description of the macroscopic and microscopic size and appearances of the

specimen (using the classification of the British Testicular Tumour Panel and Registry and the World Health Organisation) the Pathologists should comment upon:

- the presence or absence of invasion of blood vessels or lymphatic vessels by tumour
- extension of the tumour into the rete testis, epididymis tunica vaginalis and spermatic cord and
- whether there is involvement of the cut end of the cord or not.

Central review of the pathology by the cancer centre and multidisciplinary team pathologist is mandatory. This process of review should be commenced by the cancer unit pathologist at the point they become aware of the germ cell tumour is either the diagnosis or within their pathological differential diagnosis. The processing and reporting on testicular specimens at the local level should be undertaken as high priority and ideally a histology report be issued within one week of the operation and forwarded to the germ cell MDT pathologist.

6 Referral to the Cancer Centre

As well as the assaying of serum tumour markers post–operatively, referral to the cancer centre multidisciplinary team should be a matter of priority. The agreed referral pro-forma should be completed by the surgeon performing the orchidectomy within 24 hours after the completion of the operation and referred to Dr Stark by Fax using the agreed Pathway. This ensures the patient can be seen at the centre within two weeks of the orchidectomy. Fax from theatre is an effective way to achieve this, immediately after the case has been completed .

It is not acceptable for an orchidectomy to be performed and an outpatient appointment made for the patient, typically one month ahead, and for the referral to be made at that stage. Nor is it acceptable for orchidectomy specimens to be booked to local MDT meetings with referral following that. If there are specific reasons for review of pathology prior to referral, these merit a discussion of the case with the germ cell MDT members to avoid unacceptable patient delays.

There is no need (in fact it is often unhelpful) for further investigations for staging purposes to occur in the cancer unit, since this will be undertaken at the cancer centre and there is good evidence that, where examination such as serum tumour markers and CT scanning are going to be performed on a regular basis, these investigations are best performed according to the same protocol using the same techniques and the same hardware and report by the same laboratory and clinical staff.

The cancer centre also provides a full range of intensive care services, and transplantation facilities for appropriate cases. It has an active cancer of unknown primary service for patients presenting without clinical testicular primary. It has a 24/7 acute oncology service for complications of the cancer and its treatment. It has a full respiratory and haematology service and thoracic surgery for the diagnosis and management of mediastinal masses.

6.1 Investigation and staging

There is good documentary evidence that the treatment of testicular cancer in the specialised centre leads to improved results. At the point of clinical suspicion of germ cell tumour, prior to final pathological confirmation, patients should be referred to the cancer centre lead clinician and MDT. The patient would normally be seen on the Wednesday morning germ cell clinic within two weeks of surgery if the referral pro-forma is faxed within 24 hours of orchidectomy including the required details.

With timely referral patients will also be contacted by the germ cell support nurse by telephone ahead of that appointment. Therefore it is crucial the patient is made aware of the potential cancer diagnosis explicitly before discharge after orchidectomy. It is of note that if pathology and tumour marker results are not available at the time of referral these reports will be sought by the cancer centre. If the level of pre and operative serum tumour marker results and histology are available, including them with the accompanying fax is very helpful, but not essential. But it is essential they have been seen by the operating surgeon, which means they must have been sent for testing.

At the patients first attendance of the Germ Cell Tumour Clinic

1. the relevant clinical history will be confirmed and further details regarding:

- the duration of symptoms

- post-operative progress,
- history of maldescent and inguinal hernia repair in infancy or childhood,
- family history of testicular cancer,
- history of infertility,
- paternity and wishes about the possibility of further paternity will be obtained
- relevant previous medical history and clinical examination.

2. Clinical examination will include
- orchidectomy scar examination
- examination of the remaining testis for lumps, size and nature.
- examination for masses in the abdomen or in regional or distant lymph nodes.
    - Examination for features of sex hormone deficiency or of gynaecomastia

The patient has the diagnosis confirmed to them based upon local pathology report and is made aware of the possible therapeutic options and likely percentage chances of cure, although final definition of the latter will have to wait until staging examinations are completed and reviewed. Patients should be encouraged to bring their partner/parents or other relative/significant other person to be present at the consultation. At the initial attendance the patient will have a further estimation of serum tumour markers, full blood count and routine biochemistry performed. If the referral from unit to centre is timely staging CT scan of chest, abdomen and pelvis will be performed on the day of initial clinic attendance in the centre, always within one week of that appointment and the result is available for the next week's clinic to enable RMH staging. The CT scan should be performed according to a defined protocol and should be reviewed by a Radiologist experienced in the interpretation of germ cell tumour patient's investigations. Any previous radiology should also be reviewed by this Radiologist. At this consultation the patient is allocated and meets their key worker. Translators are available at 24 hours notice. A Holistic Needs Assessment is confirmed or completed. The patient is given a written summary of their consultation, and offered a copy of the GP letter. That written summary is faxed to the GP from clinic.

The overall clinical scenario with the outcome of the initial germ cell clinic attendance, central specialist review of staging investigations and tumour pathology will take place at the regional MDT meeting, within 48 hours of new patient assessment if referral and transfer of materials has been timely, always within two weeks of the first germ cell clinic visit. Patients all have easy access to the Specialist Nurses present in that clinic, to be able to revisit areas of concern or in need of clarification. At that first attendance there should be the facility for referral either then or at a later date to Specialist Social Work Support and Psychological Support (initially through a Clinical Nurse Specialist)

Sperm banking (at the Assisted Conception Unit Leeds Teaching Hospitals NHS Trust), including written and verbal information about that service, is offered to all patients in whom it is envisaged that the patient may require chemotherapy or radiotherapy that may affect fertility.

Other considerations at the primary consultation at the germ cell tumour clinic will include involvement of Specialist Nurses/Social Workers from the Teenage and Young Adult Regional Principal Treatment Centre at Leeds Teaching Hospitals Trust who regularly attend the clinic for those patients in their teenage years/early twenty's, consideration of support for those in education/higher education with regard to course work/examinations etc, financial and other considerations arising as a result of the diagnosis and its possible treatment, and an enquiry made as to whether the patient has critical illness insurance cover on which a claim may be made.
The serum tumour markers, (LDH, AFP and hCG) having been performed prior to orchidectomy, day 1 post-operatively, and then at the new patient review in germ cell clinic

two weeks later, they will be repeated weekly if elevated in radiological stage 1 disease, until they have fallen within the normal reference range, before starting any adjuvant treatment for stage I disease.

Patients will be staged according to the anatomical staging system (see Chapter 10) devised at the Royal Marsden Hospital (RMH) based upon the clinical examination and the CT scan. Magnetic resonance imaging may be equivalent to CT scanning for the detection of pelvic or abdominal lymph nodes and involves no ionising radiation but is of little value in the evaluation of the chest. This modality of imaging may become more important for follow-up in the near future. Patients with evidence of metastases will also be assessed according to the International Germ Cell Cancer Collaborative Group Prognostic Grouping (see Chapter 11) that divides patients into good, intermediate and prognostic groupings according to the pathological tumour type, site of the primary tumour, the levels of serum tumour markers and the presence or absence of non-pulmonary visceral metastases. This classification is of clinical value in advising patients of their relative prognosis and in determining the therapeutic approach.

Thus the majority of patients should be made aware within three weeks of referral to the germ cell tumour clinic, 3 weeks and 1 day from surgery, of the management approach to be adopted in their particular case. In particular the patient should be aware of the nature, extent and likely success of the treatment proposed. There may be some medical delay in those patients with serum tumour markers which are still falling post-orchidectomy but according to the natural half life of the particular marker until normalisation to distinguish stage 1 disease from stage 1M.

7 Management of disease by type, stage, and other risk stratification systems

7.1 Testicular Intratubular germ cell neoplasia (carcinoma in situ – CIS).

ITGCN occurs in approximately 5% of men with testicular cancer in the opposite testis. Patients identified as having intratubular germ cell neoplasia (ITCGN) are at great risk of developing a second invasive cancer in the remaining testis. Patients at risk are

- of younger age (less than 30 years of age), have a small contralateral testis (less than 16ml),
- a history of maldescent of the testis or a previous history of subfertility/low sperm count.

It is thought to progress to invasive germ cell tumour in almost 100% of cases within a ten year time frame. This risk increases over time; 50% at 5 years, 70% at 7 years. These patients often have low sperm count or azoospermia, and poor endocrine/Leydig cell function, with elevation of luteinising hormone (LH), and a reduction in testosterone levels. In the first instance endocrine and fertility function may be monitored for some months in many patients to allow recovery from the surgical and non-surgical managements' impact upon endocrine and fertility function.

Patients need to be warned early of the markedly increased risk of subsequent malignancy if treatment is not given. Management plans are made in the light of

- Patients who wish to father children
- The nature of the necessary treatment for the primary malignancy.

Management options include:

Radiotherapy: The germinal epithelium can be ablated with radiation and patients will be offered a two week course of radiation to the remaining testis (a dose of between 16 and 20 Gys in 10 Fractions over 2 weeks) to prevent progression to invasive disease whilst at the same time trying to preserve the hormonal function of the supportive stroma of the testis and thus hormone production. These patients also need to be made aware of the possibility of testicular failure and the potential need for hormone replacement therapy in the future. It is also recommended that a further testicular biopsy approximately six to nine months following radiation is considered, to ensure that the germinal epithelium has been ablated

Orchidectomy: Considered for patients who have completed their wish for family and already have or accept the need for endocrine replacement.

Systemic chemotherapy is not adequate treatment for intratubular germ cell neoplasia as late relapse has been described.

7.2 Management of Stage 1 disease

Patients with Stage 1 disease have no clinical, radiological or serological evidence of persistent disease following orchidectomy. Patients with negative CT scans and clinical examination but still have raised tumour markers which do not fall to normal levels post orchidectomy are staged as Stage 1M (RMH staging) and are treated as for metastatic disease (see below).

7.2.1 Stage 1 Seminoma

Patients with Stage 1 Seminoma have between a 9 and 32% chance of harbouring metastatic disease in the para-aortic lymph nodes or elsewhere. The MRC study TE19 has reported initial and follow up results indicating equivalence in terms of efficacy of one course of Carboplatin (AUC7) chemotherapy when compared to para-aortic radiotherapy in the management of Stage I seminoma. There was lower short-term morbidity and greater patient convenience in the Carboplatin arm and a consistent observation of a smaller number of contralateral new primary tumours in the group treated with Carboplatin. Therefore patients may chose between chemotherapy given as per this trial and radiotherapy. The cancer specific survival of either management plan, or surveillance, approaches 98%.

Adjuvant radiotherapy for Stage I seminoma is given as 20 Gys in 10 daily fractions over two weeks. 10% of seminoma patients require a “dog-leg” shaped radiation field to cover the inguino-pelvic lymph nodes as well as the para-aortic nodes because of previous inguino-scrotal surgery or a scrotal orchidectomy causing disruption of lymphatic drainage of the testis.

Patients make an informed choice between adjuvant chemotherapy with Carboplatin, adjuvant radiotherapy and surveillance. The clinicians are broadly guided, considering the range of data, by two longstanding pathological prognostic factors in providing a recommendation to patients who wish; tumour size >4cm, and the presence of invasion of the rete testis. Although the relevance of rete invasion is currently more uncertain, this can be considered.

Surveillance is an effective management strategy of stage 1 seminoma. In electing for surveillance clinicians should consider:

- whether the patient has a reliable serum tumour marker,
- whether follow up with regular CT scanning represent a satisfactory practical plan
- which the patient will comply with, and
- whether the radiation from CT scanning required is acceptable to the patient.
- the patient understanding that will receive three cycles of BEP chemotherapy if they
- relapse. In less fit patients this is intensive treatment.
- the small but relevant risk of reduced fertility with any chemotherapy treatment

Relapses may occur more than 5 years after orchidectomy so follow up often needs to be prolonged. The frequency of examinations and comparison between CT and MRI is currently subject to an MRC randomised controlled trial led internationally by Dr Jonathon Joffe.

7.2.2 Stage 1 Teratoma Low Risk patients

Patients with combined seminoma/teratoma of the testis should be treated as though they had teratoma. Patients with stage 1 malignant teratoma (other than malignant teratoma differentiated) have a 30-50% risk of recurrence with surveillance alone.

The presence of lymphovascular invasion in the primary tumour histologically identifies a higher relapse risk group. The relapse rate for low-risk stage 1 teratoma patients is approximately 25 to 30%.

Consideration when selecting a patient for surveillance, as in seminoma, include:

- whether the patients tumour is known to make serum markers,
- the acceptability for surveillance regimen in terms of compliance and radiation.
- the patient understanding that will receive three cycles of BEP chemotherapy if they
- relapse. In less fit patients this is intensive treatment.
- the small but relevant risk of reduced fertility with any chemotherapy treatment

The follow up schedule is intensive in terms of visits for serological and plain X-ray surveillance. The patient is required to undergo surveillance monthly for the first year, bi-monthly for the second year, quarterly for the third year, six monthly until five years have elapsed postorchidectomy and then annually to the tenth year, although the patient can always seek an earlier appointment should he suspect a recurrence is occurring. Serum tumour markers have to be performed at every attendance and CT scanning is undertaken twice according to the outcome of the MRC TE08 study. The patient undergoes routine clinical assessment at every attendance and also undergoes further investigations should he develop significant symptoms. There is a system of community shared surveillance undergoing implementation in 2015 with evaluation to follow.

If surveillance is judged impractical or unacceptable then consideration should be given to adjuvant chemotherapy with the same regimen as used in high risk Stage I teratoma (see below).

7.2.3 Stage 1 teratoma high-risk patients

Patients with negative post-operative staging investigations but with lymphovascular invasion in the primary tumour pathology have between a 40 and 60% risk of relapse. An MRC protocol administered two cycles of adjuvant BEP chemotherapy (Etoposide 360mg per metre squared per course). This was shown to reduce this risk of relapse to 1 to 2% and this approach is now the standard for this condition. Trial results are awaited for the efficacy of a single course of higher dose BEP.

PET scanning has been examined to provide further risk stratification in Stage I non-seminoma but there is insufficient sensitivity and specificity to be used at present (c.f. MRC study TE22).

For those patients with persistently elevated tumour markers or markers rising ostoperatively (stage 1M) these patients have metastatic disease and should receive chemotherapy as per good prognosis metastatic non seminomatous germ cell tumour (three cycles of ‘Indiana’ BE (500)P).

Stage 1 disease, surveillance and adjuvant chemotherapy and chemotherapy for IGCCC good prognosis advanced disease for patients referred from the HYCCA can be managed in the Hull cancer centre under the guidance of the single regional MDT meeting. All radical or curative radiotherapy treatments are administered in Leeds.

7.2.4 Metastatic Seminoma

More than 80% of seminoma patients present with stage 1 disease; however, approximately 15% fall into the stage 2 category. The majority of those have stage 2A disease, with lymph node involvement less than 2cm in maximum diameter.

Patients with Stage 2A, and Stage 2B disease of less than 3cm are currently managed with a single dose of Carboplatin AUC 7 followed by para-aortic lymph node irradiation giving 30 to 35-36 Gys over 15 to 18 fractions of radiotherapy to a dog-leg field.

Patients with 2B, C or D disease, with a more than 3cm transverse diameter tumour are treated with multi-drug platinum-based chemotherapy (BEP or EP) according to their general health.
Patients with visceral non-pulmonary metastates are treated according to their place in the IGCCCG risk stratification.

Patients with seminoma tend to be older than teratoma patients on the whole. Consequently, the chemotherapy for patients with metastatic seminoma is more often individualised to the patient circumstances/fitness; older patients are more likely to have co-morbid conditions, including impaired renal function, vascular disease, and/or to have a worse smoking history. These are the risk factors for toxicity rather than age of itself. Carboplatin may be used in combinations as alternative to Cisplatin in exceptional circumstances in these patients. For patients with metastatic seminoma stage 3 and 4, there is no good evidence that Bleomycin adds to the efficacy of treatment.

There are other reported regimens for the management of advanced seminoma, such as carboplatin AUC-10, which have specific indications for occaisional use, such as in severe pre-existing neuropathy

7.2.5 Metastatic Non-Seminoma ('Teratoma')

Considerable research effort at national and international levels has led to the development of successful regimes for this condition and emphasis being placed on the greater acceptability and convenience for patients with regimes in recent years without compromising effectiveness.

The IGCCCG classification (Table 2) divides patients in to good, intermediate or poor prognosis depending on the highest assay of their serum tumour markers prior to chemotherapy, the presence of a mediastinal primary, or non-pulmonary visceral metastases.

The internationally standard regime for all patients with metastatic teratoma of the testis is BEP (including 500 mg/m2 per cycle of etoposide and 90IU per cycle of bleomycin). Patients with good prognosis are treated with three cycles of BEP chemotherapy but if four cycles are used then Bleomycin is omitted for the fourth course since the recommended maximum dose of Bleomycin should not normally exceed 270,000 international units (270 mgs). A recently reported joint MRC/EORTC randomised controlled trial (2 x 2 factorial design) has shown that three courses of "American" (Etoposide 500 mg per meter squared per course) BEP is effective as four courses and also that this treatment can be delivered without detriment to survival over three days rather than five days. 5-day administration reduces late neurological toxicity. Thus three cycles of American BEP delivered over a three night stay in hospital is the standard treatment in Yorkshire for good prognosis metastatic non-seminomatous germ cell tumours, including teratoma. There is scope for individualisation of treatment and particularly for those patients with potentially compromised renal or lung function, treatment

can be taken rather more slowly and more than three courses of chemotherapy can be given for patients with anatomically high volume disease.

For intermediate and poor prognosis patients no treatment has been convincingly shown to be superior than four cycles of BEP chemotherapy (Etoposide 500 mgs per metre squared per course) as standard treatment. Studies recently completed examined intensifying BEP using GCSF support ('accelerated BEP'), and an intensive multi-drug regimen within the TE23 national study. Recent international data has suggested advantages in stratification based upon marker decline by day 22, but international consensus falls short of concluding the complex regimen instigated in this GETUG trial is now a standard of care. One of the keystones to successful treatment for metastatic teratoma is the maintenance of the dose-intensity of treatment and the adherence to the treatment schedule. Patients' treatment cannot be delayed due to blocked beds and admissions have to be pre-arranged and if necessary take precedence over other patients having chemotherapy for non-curable conditions. This has been facilitated by the use of ambulatory regimens for BEP. also constructive has been the development of supportive agents such as granulocyte colony stimulating factor (GCSF) and the development of improved anti-emetic regimes (e.g. 5HT3 antagonists). The local indications for GCSF in germ cell tumour management are:

- Dose delay due purely to neutropenia, not restricted by recovery of oral mucositis or
- low platelets.
- Acute support for life threatening septic shock with end organ failure
- Support for very unwell patients who are unlikely to tolerate neutropenia with sepsis.

It is easy to forget that this type of treatment in itself is potentially life threatening, and so patients and staff have to be regularly reminded of the potentially fatal consequences of ignoring symptoms of neutropenic sepsis and the need for a very rapid response in such circumstances. Potential neutropenic sepsis is a medical emergency.

The following is the list of acceptable chemotherapy algorithms for the treatment of germ cell tumours, within their specific indications. None should be administered for any germ-cell indication outside the guidance of the germ cell MDT and the full protocols are available by liaison with the clinical lead:

Carboplatin (AUC 7)
Carboplatin (AUC2 sequentially)
Carboplatin (AUC2) plus etoposide
Carboplatin (AUC4) EB
Carboplatin (AUC10)

Indiana BE(500) P 5 day
5 day E (500)P
Adjuvant 3-day BE (360)P
Adjuvant 5-day BE (360)P
VelP
POMB/ACE

Cisplatin, Paclitaxel and Belomycin
VIP
T (250)IP
Gemcitabine and Paclitaxel
Etoposide oral
High-Dose Methotrexate single agent

Bleomycin single-agent
Cyclophosphamide (Priming)
CarboPEC
High dose Carboplatin and Etoposide

Cisplatin may be administered as an in-patient on a chemotherapy competent ward or in an ambulatory care unit. Ifosfamide is administered as an in-patient. Methotrexate at doses requiring urinary alkalinisation and folinic acid rescue is administered as an in-patient

There is some concern that mediastinal resection of residual masses almost inevitably exposures patients to high flow oxygen. We have implemented the use of Etoposide, Ifosfamide and Cisplatin (VeIP) for 4 cycles as an option to be actively considered for mediastinal primary germ cell tumours where post-chemotherapy resection is considered likely.

8 Post Chemotherapy masses

8.1 Seminoma

Resection for post chemotherapy residual masses in seminoma is not routinely indicated, as the complete remission rate for seminoma is extremely high, viable tumour is rarely found in resected specimens and resection of seminoma residua is highly morbid, due to lack of clear tissue planes.

Radiological assessment of residual masses is advised, and recent work has examined the role of carefully timed PET scans, with the possibility of post-chemotherapy/radiotherapy at a later stage for persistent masses which are increasing in size. However, the routine use of radiotherapy for residual masses is not recommended.

8.2 Teratoma

Residual masses may remain after chemotherapy and marker normalisation in teratoma patients. About 20% of these masses will contain viable tumour and of the remaining 80%, half will contain mature teratoma differentiated (TD) and half scar & fibrous tissue. Any masses greater than 9mm in diameter should be removed surgically to resect TD and identify residual viable tumour, within 4-6 weeks of completion of chemotherapy, if recovery from chemotherapy allows. If resection is not possible should be kept under very close follow up radiologically.

Retroperitoneal lymph node dissections should use a template, not be resection simply of radiologically or macroscopically involved nodes. The attempts at surgical intervention must be radical e.g. it may be necessary to sacrifice a kidney or resect an inferior vena cava etc, and this work should be undertaken by a limited number of surgeons. Such work is undertaken by two Urological Surgeons and one Thoracic Surgeon in Leeds at the present time. The pathology of the resected specimen should be undertaken or reviewed by a specialist pathologist working in the germ cell Multidisciplinary Team.

Where viable germ cell cancer is found in the resected specimens further chemotherapy should be considered.

8.3 Treatment of relapsed disease

Following treatment, patients are kept under review (see section on follow up) and following adequate treatment less than 10% of patients with good prognosis disease will relapse. This is rather higher in patients with intermediate and poor prognosis disease. The timing of relapse is important.

- Patients who progress on or relapse shortly after primary treatment are likely to have ‘primary platinum resistant’ disease and need an aggressive approach, as their prognosis is poor. In these circumstances alternative chemotherapy regimes may be used but if the disease is apparently localised to one anatomical site then a “desperation” operation may be performed urgently with potential curative results.
- Fortunately the majority of relapses recur after many months or possibly years after primary treatment and, again depending on the anatomical extent of the disease, the primary approach may well be surgical plus chemotherapy.

- One concern for physicians at the diagnosis of relapse is that growing disease sites may consist of growing teratoma differentiated, for which further chemotherapy will be ineffective. The radiological and tumour marker profile as well as the previous histology may help to judge the probability of growing teratoma differentiated syndrome in an individual patient. Growing TD can involve many retroperitoneal structures and although not metastatic local invasion can be life-limiting. Moreover residual unresected TD can undergo malignant transformation to undifferentiated germ cell tumour, carcinoma, sarcoma or mixed tumours.

- All cases of suspected or confirmed relapse must be discussed at MDT prior to management decisions unless there is a clinical emergency presentation (eg cerebral haemorrhage)
- We have specific indications for biopsy upon suspicion of recurrent germ cell tumour, whether during stage I surveillance, or after previous non-surgical treatment. These are
    - Categorical indication
        - Over 3 completed years disease-free at first indication of possible relapse
    - Relative indications
        - Unusual anatomical pattern of disease identified at MDT, suggesting a clinically relevant differential diagnosis
        - Recurrence with specific tumour markers normal when those markers were elevated during a previous germ cell tumour episode

Patients with rising markers after first line treatment require urgent restaging, which may need to include the brain and contralateral testis if the site of recurrence is not apparent on initial CT body. Some patients have rising markers with no apparent anatomical recurrence - we recommend surveillance and re-imaging in this situation, while accepting this is psychologically very difficult for most patients. A minority of patients have rising markers after completion of first-line treatment without an apparent relapse site on restaging. These patients are not treated until a site of disease is indicated by clinical or radiological assessment. The process is:

Round 1= first raised marker must be repeated before further actions. If raised, CT high chest and abdomen (+/- pelvis if indicated) is usual 1st time staging (no IV, but with positive oral contrast) if CT is negative - Scrotal US and MRI Brain within 2 weeks.

If negative, observation with weekly markers for 6/52. Then if weekly markers are still concerning restaging round 2; CT head, high chest, abdo and pelvis with IV contrast (and negative oral contrast) on a repeat CT, and if still negative, repeat MRI head and repeat testis USS.

If no cause found and concerns remain based upon 2-3 week-interval marker assays, 3 months from round 2: MRI abdomen, pelvis and head, CXR and Scrotal ultrasound
With any equivocal findings, consider PET (in round 2 or beyond)

Patients relapsing after standard chemotherapy should be considered for clinical trials if possible. American TIP (Taxol, Ifosfamide and Platinum) or VIP (Vinblastine, Ifosfamide and Platinum) are considered in relapsed good/intermediate, and relapsed poor prognosis disease respectively. Both has approximately equivalent efficacy and stem cell harvest is more straightforward after VIP.

However, as with primary management, surgery should be considered as central to the treatment for late relapse and there may be an indication for surgery post chemotherapy.

At second relapse options are limited but include resection, palliative radiotherapy, reinduction chemotherapy followed by high dose treatment with arboplatin/Etoposide/Cyclophosphamide with peripheral blood stem cell rescue, or sequential carboplatin-etoposide autografts.

8.4 Central nervous system metastases

CNS metastases may occur at either initial presentation, as an apparently isolated relapse site or as part of a chemo-resistant systemic relapse. All patients with intermediate or poor prognosis disease should have CT screening for CNS metastasis at initial assessment. Patients presenting with brain metastases at initial presentation or at relapse following adequate treatment for other sites should be treated with curative intent and if possible referred for urgent neurosurgical resection of operable lesions. Radiotherapy has a role in the relapsed patient with CNS disease, either as primary treatment or as an adjuvant to surgical resection. Patient with CNS disease following chemotherapy generally have a poor prognosis.

9 Follow up

The functions of follow-up are:

- to detect relapse at an early stage.
- to monitor and treat treatment-related toxicities.
- to detect contralateral testicular tumours
- to support the patient with regard to other consequences of cancer and its treatment, such as employment, fertility etc.

The follow up of testicular cancer varies somewhat- we have precise protocols, risk stratified, which are followed at Yorkshire Cancer Centre.

Where indicated, rehabilitation referrals are made during or after therapy, according to relevant rehabilitation pathways.

The essential message to the patient about follow up is that the patient can request an early appointment or a further appointment at any time should be suspect that there is a recurrence or the development of a second primary tumour.

We offer shared community surveillance as a standard option to all suitable patients, supported by ongoing self-management advice and written information, and have evidence from our evaluation this is as safe and acceptable as face-to-face clinical review as long as patients can deliver their self-management role.

9.1 Intratubular germ cell neoplasia

While patients being followed for a primary tumour in one testis, care must be taken not to overlook the contralateral or residual testis if it is affected by this premalignant condition.

There is an indication for monitoring this testis with ultrasound scans if radiotherapy treatment is to be delayed for consideration for fertility issues.

Following radiotherapy, a biopsy should be performed between 6 and 12 months after the completion of radiotherapy to prove adequate ablation of the germinal epithelium and the patient should be followed up for a minimum of ten years, usually according to the schedule for the primary contralateral testis tumour.

There are a range of follow-up schedules based upon stage, histological type, risk group, type and outcome of first-line therapy. These include clinical and nurse-led follow up, as well as remote follow-up in implementation.

9.2 Follow-up protocol for Stage I Seminoma after adjuvant radiotherapy

Follow-up protocol for Stage I Seminoma after adjuvant radiotherapy		
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below, in the format Jun-03		
	Jun-09	
Patient name d.o.b Hosp No.		
Interval (mths)	OPA date	Investigations required
3	Sep-09	AFP, hCG, LDH; CXR
6	Dec-09	AFP, hCG, LDH; CXR
9	Mar-10	AFP, hCG, LDH; CXR
12	Jun-10	AFP, hCG, LDH; CT scan
16	Oct-10	AFP, hCG, LDH; CXR
20	Feb-11	AFP, hCG, LDH; CXR
24	Jun-11	AFP, hCG, LDH; CXR
30	Dec-11	AFP, hCG, LDH; CXR
36	Jun-12	AFP, hCG, LDH; CXR
42	Dec-12	AFP, hCG, LDH; CXR
48	Jun-13	AFP, hCG, LDH; CXR
60	Jun-14	AFP, hCG, LDH; CXR

Discharge at 5 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.3 Follow-up protocol for Stage I Seminoma after adjuvant chemotherapy (usually single-dose carboplatin)

Follow-up protocol for Stage I Seminoma after adjuvant chemotherapy (usually single-dose carboplatin)
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below in the format Jun-03

	Jun-09	
Patient name		
d.o.b		
Hosp No.		
Interval (mths)	OPA date	Investigations required
1	Jul-09	AFP, hCG, LDH; FBC
3	Sep-09	AFP, hCG, LDH; CXR
6	Dec-09	AFP, hCG, LDH; CT scan
9	Mar-10	AFP, hCG, LDH; CXR
12	Jun-10	AFP, hCG, LDH; CT scan
16	Oct-10	AFP, hCG, LDH; CXR
20	Feb-11	AFP, hCG, LDH; CXR
24	Jun-11	AFP, hCG, LDH; CT scan
30	Dec-11	AFP, hCG, LDH; CXR
36	Jun-12	AFP, hCG, LDH; CXR
42	Dec-12	AFP, hCG, LDH; CXR
48	Jun-13	AFP, hCG, LDH; CXR
60	Jun-14	AFP, hCG, LDH; CXR

Discharge at 5 years, or to long term follow-up if were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.4 Follow-up protocol for Stage I Seminoma followed up with surveillance only

Follow-up protocol for Stage I Seminoma followed up with surveillance only
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below, in the format Jun-03

	Jun-09	
Patient name		
d.o.b		
Hosp No.		
Interval (mths)	OPA date	Investigations required
3	Sep-09	AFP, hCG, LDH; CXR
6	Dec-09	AFP, hCG, LDH; CT scan
9	Mar-10	AFP, hCG, LDH; CXR
12	Jun-10	AFP, hCG, LDH; CT scan
15	Sep-10	AFP, hCG, LDH; CXR
18	Dec-10	AFP, hCG, LDH; CT scan
21	Mar-11	AFP, hCG, LDH; CXR
24	Jun-11	AFP, hCG, LDH; CT scan
28	Oct-11	AFP, hCG, LDH; CXR
32	Feb-12	AFP, hCG, LDH; CXR
36	Jun-12	AFP, hCG, LDH; CT scan (abdo only)
42	Dec-12	AFP, hCG, LDH; CXR
48	Jun-13	AFP, hCG, LDH; CT scan (abdo only)
54	Dec-13	AFP, hCG, LDH
60	Jun-14	AFP, hCG, LDH; CT scan (abdo only)

Discharge at 5 years, or to long term follow-up if were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.5 Follow-up protocol for high-risk Stage I NSGCT after adjuvant chemotherapy

Follow-up protocol for high-risk Stage I NSGCT after adjuvant chemotherapy		
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below, in the format Jun-03		
	Jan-01	
Patient name		
d.o.b		
Hosp No.		
Interval (months)	OPA date	Investigations required
3	Apr-01	AFP, hCG, LDH
6	Jul-01	AFP, hCG, LDH; CXR
9	Oct-01	AFP, hCG, LDH
12	Jan-02	AFP, hCG, LDH; CT scan
15	Apr-02	AFP, hCG, LDH
18	Jul-02	AFP, hCG, LDH; CXR
21	Oct-02	AFP, hCG, LDH
24	Jan-03	AFP, hCG, LDH; CT scan
28	May-03	AFP, hCG, LDH
32	Sep-03	AFP, hCG, LDH
36	Jan-04	AFP, hCG, LDH; CXR
42	Jul-04	AFP, hCG, LDH
48	Jan-05	AFP, hCG, LDH; CXR
54	Jul-05	AFP, hCG, LDH
60	Jan-06	AFP, hCG, LDH; CXR

9.6 Follow-up protocol for low-risk Stage I NSGCT (intense surveillance programme)

Follow-up protocol for low-risk Stage I NSGCT (intense surveillance programme)		
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below, in the format Jun-03		
	Jan-01	
Patient name d.o.b Hosp No.		
Interval (months)	OPA date	Investigations required
1	Feb-01	AFP, hCG, LDH
2	Mar-01	AFP, hCG, LDH; CXR
3	Apr-01	AFP, hCG, LDH; CT scan
4	May-01	AFP, hCG, LDH; CXR
5	Jun-01	AFP, hCG, LDH
6	Jul-01	AFP, hCG, LDH; CXR
7	Aug-01	AFP, hCG, LDH
8	Sep-01	AFP, hCG, LDH; CXR
9	Oct-01	AFP, hCG, LDH
10	Nov-01	AFP, hCG, LDH; CXR
11	Dec-01	AFP, hCG, LDH
12	Jan-02	AFP, hCG, LDH; CT scan
14	Mar-02	AFP, hCG, LDH
16	May-02	AFP, hCG, LDH; CXR
18	Jul-02	AFP, hCG, LDH
20	Sep-02	AFP, hCG, LDH; CXR
22	Nov-02	AFP, hCG, LDH
24	Jan-03	AFP, hCG, LDH; CXR
27	Apr-03	AFP, hCG, LDH
30	Jul-03	AFP, hCG, LDH; CXR
33	Oct-03	AFP, hCG, LDH
36	Jan-04	AFP, hCG, LDH; CXR
42	Jul-04	AFP, hCG, LDH; CXR
48	Jan-05	AFP, hCG, LDH; CXR
54	Jul-05	AFP, hCG, LDH
60	Jan-06	AFP, hCG, LDH; CXR

Discharge at 5 years, or to long term follow-up if were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.7 Follow-up protocol for Stage I NSGCT where orchidectomy specimen showed only Teratoma Differentiated (Mature Teratoma)

Follow-up protocol for Stage I NSGCT where orchidectomy specimen showed only

Teratoma Differentiated (Mature Teratoma) I.e. limited surveillance policy		
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below, in the format Jun-03		
	Jan-01	
Patient name d.o.b Hosp No.		
Interval (months)	OPA date	Investigations required
2	Mar-01	AFP, hCG, LDH
4	May-01	AFP, hCG, LDH
6	Jul-01	AFP, hCG, LDH; CT scan
8	Sep-01	AFP, hCG, LDH
10	Nov-01	AFP, hCG, LDH
12	Jan-02	AFP, hCG, LDH; CT scan
18	Jul-02	AFP, hCG, LDH
24	Jan-03	AFP, hCG, LDH; CXR
30	Jul-03	AFP, hCG, LDH
36	Jan-04	AFP, hCG, LDH; CXR

Discharge at 3 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.8 Follow-up protocol for Stage II Seminoma after radiotherapy

Follow-up protocol for Stage II Seminoma after radiotherapy
Enter month of completion of most recent treatment (surgery, chemo or RTx) in red box below, in the format Jun-03

	Jan-01	
Patient name		
d.o.b		
Hosp No.		
Interval (months)	OPA date	Investigations required
		AFP, hCG, LDH; CT scan
3	Apr-01	(i.e. book scan immediately after radiotherapy
6	Jul-01	AFP, hCG, LDH; CXR
9	Oct-01	AFP, hCG, LDH; CXR
12	Jan-02	AFP, hCG, LDH; CXR
16	May-02	AFP, hCG, LDH; CXR
20	Sep-02	AFP, hCG, LDH; CXR
24	Jan-03	AFP, hCG, LDH; CXR
30	Jul-03	AFP, hCG, LDH; CXR
36	Jan-04	AFP, hCG, LDH; CXR
42	Jul-04	AFP, hCG, LDH; CXR
48	Jan-05	AFP, hCG, LDH; CXR
60	Jan-06	AFP, hCG, LDH; CXR
6 years	Jan-07	AFP, hCG, LDH; CXR
7 years	Jan-08	AFP, hCG, LDH; CXR
8 years	Jan-09	AFP, hCG, LDH; CXR
9 years	Jan-10	AFP, hCG, LDH; CXR
10 years	Jan-11	AFP, hCG, LDH; CXR

Discharge at 10 years, or to long term follow-up if were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.9 Follow-up protocol for: Stage Im NSGCT after chemo: Good prognosis metastatic tumours treated with chemo - all metastatic seminomas, except intermediate prognosis; Stage II-IV NSGCT with no residual disease on post-chemo CT; and for Stage II-IV NSGCT with residual mass on CT which contains no viable tumour at resection

Follow-up protocol for: Stage Im NSGCT after chemo: good prognosis metastatic tumours treated with chemo - all metastatic seminomas, except intermediate prognosis; Stage II-IV NSGCT with no residual disease on post-chemo CT; and for Stage II-IV NSGCT with residual mass on CT which contains no viable tumour at resection

Enter month of completion of most recent treatment (surgery or chemo) in red box below, in the format Jun-03

Jan-01

Patient name		
d.o.b		
Hosp No.		
Interval (months)	OPA date	Investigations required
3	Apr-01	AFP, hCG, LDH; CXR
6	Jul-01	AFP, hCG, LDH; CT scan
9	Oct-01	AFP, hCG, LDH; CXR
12	Jan-02	AFP, hCG, LDH; CT scan
15	Apr-02	AFP, hCG, LDH; CXR
18	Jul-02	AFP, hCG, LDH; CXR
21	Oct-02	AFP, hCG, LDH; CXR
24	Jan-03	AFP, hCG, LDH; CT scan
30	Jul-03	AFP, hCG, LDH; CXR
36	Jan-04	AFP, hCG, LDH; CXR
42	Jul-04	AFP, hCG, LDH; CXR
48	Jan-05	AFP, hCG, LDH; CXR
54	Jul-05	AFP, hCG, LDH; CXR
60	Jan-06	AFP, hCG, LDH; CXR

Discharge at 5 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise).

9.10 Follow-up protocol for: intermediate prognosis metastatic seminoma following chemo; intermediate and poor prognosis NSGCT treated with chemo and with either no residual disease on post-chemo CT; or with residual disease but no viable tumour at resection

Follow-up protocol for: intermediate prognosis metastatic seminoma following chemo; intermediate and poor prognosis NSGCT treated with chemo and with either no residual

disease on post-chemo CT; or with residual disease but no viable tumour at resection
Enter month of completion of most recent treatment (surgery or chemo) in red box below, in the format Jun-03

	Jan-01	
Patient name d.o.b Hosp No.		
Interval (months)	OPA date	Investigations required
2	Mar-01	AFP, hCG, LDH
4	May-01	AFP, hCG, LDH; CXR
6	Jul-01	AFP, hCG, LDH; CT scan
8	Sep-01	AFP, hCG, LDH; CXR
10	Nov-01	AFP, hCG, LDH
12	Jan-02	AFP, hCG, LDH; CT scan
15	Apr-02	AFP, hCG, LDH; CXR
18	Jul-02	AFP, hCG, LDH; CT scan
21	Oct-02	AFP, hCG, LDH
24	Jan-03	AFP, hCG, LDH; CT scan
27	Apr-03	AFP, hCG, LDH
30	Jul-03	AFP, hCG, LDH; CXR
33	Oct-03	AFP, hCG, LDH
36	Jan-04	AFP, hCG, LDH; CT scan
42	Jul-04	AFP, hCG, LDH; CXR
48	Jan-05	AFP, hCG, LDH; CXR
54	Jul-05	AFP, hCG, LDH; CXR
60	Jan-06	AFP, hCG, LDH; CXR
6 years	Jan-07	AFP, hCG, LDH; CXR
7 years	Jan-08	AFP, hCG, LDH; CXR
8 years	Jan-09	AFP, hCG, LDH; CXR
9 years	Jan-10	AFP, hCG, LDH; CXR
10 years	Jan-11	AFP, hCG, LDH; CXR

Discharge 10 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise).

9.11 Follow-up protocol for: metastatic NSGCT with residual disease on CT scan after chemotherapy, and resection specimen containing viable tumour other than Teratoma Differentiated (Mature Teratoma); and relapsed patients with no evaluable disease on CT scan following 2nd-line chemo

Follow-up protocol for: metastatic NSGCT with residual disease on CT scan after chemotherapy, and resection specimen containing viable tumour other than Teratoma

Differentiated (Mature Teratoma); and relapsed patients with no evaluable disease on CT scan following 2nd-line chemo
Enter month of completion of most recent treatment (surgery or chemo) in red box below, in the format Jun-03

	Jan-01	
Patient name d.o.b Hosp No.		
Interval (months)	OPA date	Investigations required
1	Feb-01	AFP, hCG, LDH
2	Mar-01	AFP, hCG, LDH
3	Apr-01	AFP, hCG, LDH; CXR
4	May-01	AFP, hCG, LDH
5	Jun-01	AFP, hCG, LDH
6	Jul-01	AFP, hCG, LDH; CT scan
7	Aug-01	AFP, hCG, LDH
8	Sep-01	AFP, hCG, LDH
9	Oct-01	AFP, hCG, LDH; CXR
10	Nov-01	AFP, hCG, LDH
11	Dec-01	AFP, hCG, LDH
12	Jan-02	AFP, hCG, LDH; CT scan
14	Mar-02	AFP, hCG, LDH
16	May-02	AFP, hCG, LDH; CXR
18	Jul-02	AFP, hCG, LDH
20	Sep-02	AFP, hCG, LDH; CXR
22	Nov-02	AFP, hCG, LDH
24	Jan-03	AFP, hCG, LDH; CT scan
27	Apr-03	AFP, hCG, LDH
30	Jul-03	AFP, hCG, LDH; CXR
33	Oct-03	AFP, hCG, LDH
36	Jan-04	AFP, hCG, LDH; CT scan
39	Apr-04	AFP, hCG, LDH
42	Jul-04	AFP, hCG, LDH; CXR
45	Oct-04	AFP, hCG, LDH
48	Jan-05	AFP, hCG, LDH; CXR
54	Jul-05	AFP, hCG, LDH; CXR
60	Jan-06	AFP, hCG, LDH; CXR
6 years	Jan-07	AFP, hCG, LDH; CXR
7 years	Jan-08	AFP, hCG, LDH; CXR
8 years	Jan-09	AFP, hCG, LDH; CXR
9 years	Jan-10	AFP, hCG, LDH; CXR
10 years	Jan-11	AFP, hCG, LDH; CXR

Discharge at 10 years, or to long term follow-up if were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.12 Follow-up protocol for sex cord stromal tumours (Sertoli cell and Leydig cell)

Follow-up protocol for sex cord stromal tumours (Sertoli cell and Leydig cell)		
Enter month of completion of most recent treatment (surgery or chemo) in red box below, in the format Jun-03		
	Jan-01	
Patient name d.o.b Hosp No.		
Interval (months)	OPA date	Investigations required
3	Apr-01	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol)
6	Jul-01	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol); CT scan
9	Oct-01	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
12	Jan-02	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol); CT scan
18	Jul-02	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol)
24	Jan-03	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
36	Jan-04	AFP, hCG, LDH, Hormone profile (testosterone, FSH, LH and oestradiol); CXR

Discharge at 3 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.13 Follow-up protocol for metastatic NSGCT with residual disease on CT scan after chemotherapy and resection specimen showing viable Teratoma Differentiated (Mature Teratoma)

Follow-up protocol for metastatic NSGCT with residual disease on CT scan after chemotherapy and resection specimen showing viable Teratoma Differentiated (Mature Teratoma)

Enter month of completion of most recent treatment (surgery or chemo) in red box below, in the format Jun-03

	Jan-01		
Patient name			
d.o.b			
Hosp No.			
Interval (months)	OPA date		Investigations required
2	Mar-01		AFP, hCG, LDH
4	May-01		AFP, hCG, LDH; CXR
6	Jul-01		AFP, hCG, LDH; CT scan
8	Sep-01		AFP, hCG, LDH; CXR
10	Nov-01		AFP, hCG, LDH
12	Jan-02		AFP, hCG, LDH; CT scan
15	Apr-02		AFP, hCG, LDH
18	Jul-02		AFP, hCG, LDH; CXR
21	Oct-02		AFP, hCG, LDH
24	Jan-03		AFP, hCG, LDH; CT scan
28	May-03		AFP, hCG, LDH
32	Sep-03		AFP, hCG, LDH; CXR
36	Jan-04		AFP, hCG, LDH; CT scan
42	Jul-04		AFP, hCG, LDH; CXR
48	Jan-05		AFP, hCG, LDH; CXR
60	Jan-06		AFP, hCG, LDH; CT scan
6 years	Jan-07		AFP, hCG, LDH; CXR
7 years	Jan-08		AFP, hCG, LDH; CXR
8 years	Jan-09		AFP, hCG, LDH; CXR
9 years	Jan-10		AFP, hCG, LDH; CXR
10 years	Jan-11		AFP, hCG, LDH; CXR

Discharge at 10 years, or to long term follow-up if were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.14 Follow-up protocol following high-dose chemotherapy

Follow-up protocol following high-dose chemotherapy
Enter month of completion of return of stem cells in red box below, in the format Jun-03

	Jan-01	
Patient name		
d.o.b		
Hosp No.		
Interval (months)	OPA date	Investigations required
1	Feb-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
2	Mar-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
3	Apr-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
4	May-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
5	Jun-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
6	Jul-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
7	Aug-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
8	Sep-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
9	Oct-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
10	Nov-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
11	Dec-01	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
12	Jan-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CT scan
14	Mar-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
15	Apr-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
16	May-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
18	Jul-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
20	Sep-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
21	Oct-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
22	Nov-02	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
24	Jan-03	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CT scan
27	Apr-03	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)

28	May-03	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
30	Jul-03	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
32	Sep-03	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
33	Oct-03	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
36	Jan-04	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
39	Apr-04	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
42	Jul-04	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
45	Oct-04	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
48	Jan-05	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
54	Jul-05	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol)
60	Jan-06	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
6 years	Jan-07	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
7 years	Jan-08	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
8 years	Jan-09	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
9 years	Jan-10	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR
10 years	Jan-11	AFP, hCG, LDH, FBC, TFTs, Hormone profile (testosterone, FSH, LH and oestradiol); CXR

Discharge at 10 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise)

9.15 Follow-up protocol for spermatocytic seminoma

Follow-up protocol for spermatocytic seminoma
Enter month of completion of most recent treatment (surgery or chemo) in red box below, in the format Jun-03

	Jan-01		
Patient name			
d.o.b			
Hosp No.			
Interval (months)	OPA date		Investigations required
4	May-01		AFP, hCG, LDH (only CT scan is base-line scan immediately post-orchidectomy)
8	Sep-01		AFP, hCG, LDH
12	Jan-02		AFP, hCG, LDH; CXR
18	Jul-02		AFP, hCG, LDH
24	Jan-03		AFP, hCG, LDH; CXR
30	Jul-03		AFP, hCG, LDH
36	Jan-04		AFP, hCG, LDH

Discharge at 3 years, or to long term follow-up if they were aged up to their 30th birthday at the point of diagnosis (unless in a trial and protocol dictates otherwise).

10 RMH staging

Stage		Definition
I		No evidence of disease outside the testis
IM		As above but with persistently raised post-op tumour markers
II		Infradiaphragmatic nodal involvement
	A	Nodes maximum diameter < 2cm
	B	Nodes maximum diameter 2-5 cm
	C	Nodes maximum diameter 5-10cm
	D	Nodes maximum diameter > 10cm
III		Supra and infradiaphragmatic node involvement
	A	Abdominal nodes < 2cm
	B	Abdominal nodes 2-5cm
	C	Abdominal nodes >5cm
		Neck nodes N +
		Mediastinal nodes M +
IV		Extralymphatic metastases Abdominal nodes A, B, C, as above Mediastinal or neck nodes as for stage 3
	L1	< 3 lung metastases
	L2	Multiple lung metastases < 2 cm maximum diameter
	L3	Multiple lung metastases > 2 cm in diameter
	H+	Liver involvement
		Other sites identified (Br- brain, Bo- bone, Ad-adrenal)

11 IGCCC prognostic grouping

TERATOMA (NSGCT)	SEMINOMA
GOOD PROGNOSIS with all of:	
Testis/retroperitoneal primary No non-pulmonary visceral metastases AFP < 1000 ng/ml HCG < 5000 iu/l LDH < 1.5 upper limit of normal • 56% of teratomas • 5-year survival 92%	Any primary site No non-pulmonary visceral metastases Normal AFP Any HCG Any LDH • 90% of seminomas • 5-year survival 86%
INTERMEDIATE PROGNOSIS with all of	
Testis/retroperitoneal primary No non-pulmonary visceral metastases AFP > 1000 AND < 10000 ng/ml or HCG > 5000 AND < 50000 iu/l or LDH > 1.5 normal < 10 normal • 28% of teratomas • 5-year survival 80%	Any primary site Non-pulmonary visceral metastases Normal AFP Any HCG Any LDH • 10% of seminomas • 5-year survival 73%
POOR PROGNOSIS with any of:	
Mediastinal primary or non-pulmonary Visceral metastases AFP > 10,000 ng/ml or HCG > 50,000 iu/l or LDH > 10 normal • 16% of teratomas • 5-year survival 48%	No patients classified as poor prognosis

12 Pathology

Updated May 2011

12.1 General Principles

It is recommended in the Improving Outcomes in Urological Cancers guidance published in 2002 that all new diagnoses of cancer are reviewed at a multidisciplinary team meeting where pathological features are taken into account in the formulation of the management plan. This will include consideration of the patient's eligibility for entry into trials.

Although pathologists are referred to the Minimum Datasets published by the Royal College of Pathologist, there are features which are not included in these Datasets but are relevant for inclusion into on-going trials. These have been included in the following short guidelines.

12.2 Guidelines for reporting orchidectomy specimens

12.2.1 Classification of the tumour

Tumour type – reference to the WHO classification allows the identification of different tumour components, which can then be grouped into general categories according to the British Classification

12.2.2 Tumour stage

TNM 7 classification

The presence or absence of vascular invasion in teratomas is the sole criterion for immediate chemotherapy rather than surveillance in clinically localised disease. In testicular seminoma, evaluation of tumour size is essential, and the reporting presence or absence or rete testis invasion is a useful parameter to inform post-surgical management.

12.3 Guidelines for reporting retroperitoneal lymph node dissections in patients with germ cell tumours

12.3.1 Characterisation of the specimen

- Presence or absence of recognisable nodal tissue or any other retroperitoneal structures.
- Presence or absence of residual tumour and its type.
- Transformation of differentiated elements into somatic malignancies (carcinomas, sarcomas, leukaemias) should be noted, as it is indicative of poor prognosis.

12.4 Testicular biopsies, orchidectomies and retroperitoneal lymph node dissections

Testicular biopsies: These are performed either in the context of investigations for infertility

or in patients with contralateral testicular tumours, and in both cases, particularly in the testis is atrophic, there is a risk of intratubular germ cell neoplasia. Biopsies are generally examined at 3 levels and spares for immunocytochemistry (PLAP, c-kit) can be useful in the diagnosis of intratubular germ cell neoplasia.

Orchidectomies: The most important aspect of dealing with orchidectomies for tumours is to take sufficient numbers of blocks to ensure that all the different components of the tumours are represented and that the capsule and adjacent testicular parenchyma are sampled for the assessment of vascular invasion, a major determinant of treatment or entry into trials. The size of the primary tumour is essential in seminoma and the presence or absence of invasion of the rete testis is also useful in clinical decision-making in seminoma.

Retroperitoneal lymph node dissections: These are generally performed in patients with testicular germ cell tumours if a mass fails to resolve following chemotherapy. It is important to identify any potential residual tumour because of the implications for the subsequent management and prognosis. It is useful to ink the margins prior to sectioning as the completeness of excision influences outcome, to characterise two main clinical risks, 1. Continual growth of unresected teratoma differentiated becoming inoperable and 2. Malignant transformation of teratoma differentiated to another malignant germ cell tumour, sarcoma or carcinoma which may be chemoresistant in this group of patients.
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13 Radiology

13.1 Imaging of Germ Cell Tumours

Clinical information regarding tumour side and any pre-existing risk factors for pelvic disease is essential for interpretation of equivocal findings and appropriate tailoring of the examination protocol. Histological tumour type is usually not available at the time of the initial staging study. Tumour markers, if known, are helpful.

13.1.1 Diagnostic Staging:

CT remains the mainstay of imaging patients with Testicular and Mediastinal Germ Cell Tumours although trials are underway looking at the use of MRI in surveillance of the abdomen in Testicular Germ Cell Tumour patients who present with early stage disease.

- CT, with oral and intravenous contrast, of the chest, abdomen and pelvis should be performed in all patients.
- This is usually post orchidectomy, performed centrally and arranged by the non-surgical oncology team
- Contrast enhanced CT of the brain is indicated for patients who fall into the poor prognosis category i.e.
    - Liver or bone metastases
    - High tumour markers - AFP >10000, HCG >50000, LDH > 10x normal
    - Primary Mediastinal Germ Cell Tumours

13.1.2 Follow up scans:

- CT of the chest and abdomen alone is sufficient. CT pelvis is not required provided that there has been no pelvic disease on the initial staging study, and there are no risk-factors predictive of pelvic relapse i.e.
    - Bulky abdominal disease (>5cm)
    - Past history of maldescent
    - Orchidopexy or other scrotal surgery
    - Tumour invasion through tunica vaginalis
- No intravenous contrast is required for reassessment of Stage I disease
- When there is nodal disease in the retroperitoneum (Stage II disease), intravenous contrast is only required when the examination is performed to assess suitability for retroperitoneal lymph node dissection (RPLND)
- Intravenous contrast enhancement should be routinely be used for reassessment of patients with liver or intracranial metastatic disease

13.1.3 Patients in Clinical Trials:

Trial protocols generally specify the areas to be imaged and the imaging modality to be used.

14 Palliative & End of Life Care

14.1 Definitions

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

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

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

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

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

14.2 Who Provides Palliative / End of Life Care?

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

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

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

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

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

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

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

For more information about local improvements, frameworks, tools to support best practice please contact your local End of Life Care Lead or Specialist Palliative Care Team.

One aspect of care is to discuss with individuals, if they wish, their preferences regarding the type of care they would wish to receive and where they wish to be cared for in case they lose capacity or are unable to express a preference in the future. This is the process of Advance Care Planning (ACP).

An ACP discussion might include:

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

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

14.3 Specialist Palliative Care

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

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

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

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

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

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

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

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

14.4 Further Links and Information

Contact the local Specialist Palliative Care Team for further information

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

The Directory has been checked and updated in May 2017

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

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

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

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

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

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

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

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

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

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

York
York Hospitals NHS Foundation Trust
NHS North Yorkshire and York

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

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