LONDON CANCER ALLIANCE
West and South

LCA Urological Cancers Clinical Guidelines

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Delivering world class cancer care for London

Contents

Introduction

These guidelines cover the five tumour sites that make up the vast majority of urological cancers, namely the prostate, bladder, kidneys, testicles and penis. The guidance represents the clinical consensus of the members of the London Cancer Alliance (LCA) Urology Pathway Group in their capacity as expert clinical representatives from across LCA providers. It is not intended to be the definitive position on the treatment of patients with a particular cancer type but a best practice guide; this is particularly relevant in prostate cancer and renal cancer where a range of treatment options may be appropriate and the final decision is at the discretion of the treating clinician in consultation with the patient.

In producing these guidelines, the Pathway Group has drawn on multiple sources of best practice guidance, which includes National Institute for Health and Care Excellence (NICE) guidance, Improving Outcomes Guidance (IOG), the National Cancer Action Team (NCAT) *Manual for Cancer Services – Urological Measures* and the guidelines of the European Association of Urology (EAU). The latter are regarded as a gold standard for all European departments and often further afield. They are extensively referenced, including levels of evidence to support key recommendations, and updated annually.

All the LCA guidelines are compliant with the EAU guidelines, and in the case of kidney and bladder we have not attempted to rewrite the guidelines but have merely drawn attention to local policy and areas where practice may differ from the guidelines, and the rationale for any such differences.

The LCA guidelines are designed to be used by all healthcare professionals in Trusts within the LCA who are involved in the care of the urological cancer patient. They have been developed to take into account the wide range of clinical experience of the user and the different clinical settings in which they work. The guidelines are intended to assist in the initial assessment, investigation and management of patients. Adoption of the LCA guidelines will allow widespread implementation of up-to-date and evidence-based management of urological cancer patients, and will assist in the provision of a consistently high standard of care across the LCA.

I hope these guidelines are helpful. Many specialists both within the LCA Urology Pathway Group and the stakeholder group have contributed. There has been extensive opportunity for individuals to review the guidelines, and their comments have been taken into consideration. I would like to thank them for their contributions.

Justin Vale

Chair of the LCA Urology Pathway Group

Executive summary

These guidelines cover the five tumour sites that make up the vast majority of urological cancers, namely the prostate, bladder, kidneys, testicles and penis. The guidance represents the clinical consensus of the members of the LCA Urology Pathway Group in their capacity as expert clinical representatives from across LCA providers.

Chapter 1 provides some guidance which is applicable to all tumour types and covers the following areas: prevention, early diagnosis, multidisciplinary team (MDT) working, survivorship, palliative care, communication and protocols for the treatment of children, teenagers and young adults with urological cancer.

The following sets out where each of the guidelines for the five urological cancer tumour types can be found within this document. Supporting documentation and relevant annexes for each guideline can be found at the end of each chapter.

Chapters 2 and 3 provide the **penile** and **testicular** cancer guidelines respectively. They describe the recommended referral pathway from general practice, through local cancer teams and onwards to the appropriate supra-network centre. They summarise the treatment options available at the centre and also the pathway back to specialist centres for chemo/radiotherapy for selected patient groups and, in the case of testicular cancer, the pathway back to specialist centres for salvage surgery. The principal references for the penile and testicular guidelines are the European Association of Urology (EAU) guidelines (Penile, 2009; Testicular, 2011) with modifications approved by the Urology Pathway Group to reflect the centralisation of specialist services and UK practice.

Chapter 4 provides the **bladder** guidelines. These guidelines are designed as a reference for local urology departments and specialist cancer centres, and to inform purchasers of what to expect from their local service. Suggestions for local audits to continually improve the service and knowledge outcomes are included. The guidelines are closely based on the EAU guideline (2013). They also amalgamate the South and West London cancer network guidelines from the previous cancer networks. Areas of difference from the EAU guidelines are highlighted.

Chapter 5 provides the **renal** cancer guidelines. These guidelines are comprised of three complementary documents. The first is an operational policy which sets out the new arrangements for specialist renal MDTs in the LCA – a reduction in the number of specialist MDTs to improve access to new treatments and trials. The two MDTs are now fully operational. The operational policy has been developed by the Urology Pathway Group which can be found on the LCA website. All new patients will be discussed at the specialist MDT which goes beyond the requirements of the 2002 Improving Outcomes Guidance (IOG). The second LCA renal cancer guidance document is the LCA dataset for pathology reporting of renal cancer to include the requirements of the Royal College of Pathologists, while the third document is a summary of local arrangements for chemotherapy taking into account national guidance and the availability of agents via the Cancer Drugs Fund.

As far as the surgical management of renal cancer is concerned, all the individuals involved in the care of renal cancer patients are signed up to the EAU guidelines on renal cancer available at www.uroweb.org/gls/pdf/10_Renal_Cell_Carcinoma_LR.pdf.

Chapter 6 provides the **prostate** cancer guidelines. These guidelines have been written taking into consideration guidelines from the National Institute for Health and Care Excellence (NICE), the EAU and previously agreed local network tumour working group guidelines. They are designed as a reference for local urology departments, central cancer centres and to inform purchasers what to expect from their local service. The guidelines serve as a basis for audit within the LCA and will be updated over time to account for changes in our understanding and treatment of the disease.

There are a number of appendices attached to these guidelines, including referral forms for referral to palliative care and guidance regarding the referral pathways for the treatment of children, teenagers and young adults with urological cancers.

1 Overview and background

For simplicity, and to avoid repetition in each tumour-specific guideline, this section sets out some general information to cover generic areas of guidance which are applicable to all urological tumour types such as prevention, early diagnosis, multidisciplinary team (MDT) working, survivorship and communication.

1.1 Prevention

The evidence on risk factors for urological cancers suggests that there is substantial scope for prevention. Population-wide initiatives aimed at reducing smoking and improving diet have been highlighted previously as government priorities. These could lead to substantial reductions in the number of people who develop urological cancers.

Half the cases of urinary tract (bladder or kidney) cancer in men and a third of cases in women are likely to be due to smoking. Effective interventions for reducing smoking are described in the document *Improving Outcomes in Lung Cancer: The Manual* (1998); clearly, public health drives to reduce smoking in the community are important if we are to realise our goal of reducing mortality. Urological teams have a duty to encourage patients with newly diagnosed bladder cancer to stop smoking, as this will reduce recurrence rate in the longer term. Such patients should be offered access to local smoking cessation services and support groups.

Prostate cancer is not smoking related, but there is some evidence that dietary modification may reduce risk. Dietary improvements – specifically, increased consumption of vegetables and fish, and decreased consumption of dairy produce and meat – might reduce the prevalence of symptomatic prostate cancer.

Finally, interventions to reduce obesity and hypertension have been suggested as interventions to reduce the prevalence of kidney cancer.

1.2 Early diagnosis

There is no reliable evidence showing that population screening reduces mortality rates from any form of urological cancer. Systematic reviews have concluded that screening for prostate cancer using prostate-specific antigen (PSA) testing cannot be justified on the basis of current evidence.

Guidelines for urgent referral (within 2 weeks) of patients with suspected urological cancer have been published by the Department of Health and are detailed in each tumour-specific guideline:

- macroscopic haematuria in adults
- microscopic haematuria in adults over 50 years
- swellings in the body of the testis
- palpable renal masses
- solid renal masses found on imaging
- elevated age-specific PSA in men with a 10-year life expectancy
- high PSA (>20ng/ml) in any man with a clinically malignant prostate or bone pain
- any suspected penile cancer.

The Urology Pathway Group has produced a list of suggestions for how to improve early diagnosis for each tumour type by public education, primary care access to diagnostics and innovative ideas such as establishment of a portal for urgent upload of digital photographs of suspected penile cancers.

1.3 Multidisciplinary team working in the LCA

1.3.1 The LCA urological cancer network

The following organisations in the LCA integrated cancer system provide at least some services for urological cancer:

- Chelsea and Westminster Hospital NHS Foundation Trust
- Croydon Health Services NHS Trust
- Ealing Hospital NHS Trust
- Epsom and St Helier University Hospitals NHS Trust
- Guy's and St Thomas' NHS Foundation Trust*
- The Hillingdon Hospitals NHS Foundation Trust
- Imperial College Healthcare NHS Trust*
- King's College Hospital NHS Foundation Trust*
- Kingston Hospital NHS Foundation Trust
- Lewisham and Greenwich NHS Trust
- Mount Vernon Cancer Centre (East and North Hertfordshire NHS Trust)*
- The North West London Hospitals NHS Trust
- St George's Healthcare NHS Trust*
- The Royal Marsden NHS Foundation Trust*
- West Middlesex University Hospital NHS Trust

* Denotes the cancer centres within the LCA (not all provide specialist urological cancer services).

All provide local MDT meetings for the discussion of cancer cases. For more complicated cases, patients are referred for discussion at the relevant specialist MDT meeting. There are established guidelines dictating which patients should be discussed at the specialist MDT, published in the *Improving Outcomes Guidance for Urological Cancers* (2002):

- men with early-stage prostate cancer for whom surgery is considered appropriate and who elect to undergo radical prostatectomy
- patients with muscle-invasive bladder cancer
- patients with high-risk superficial bladder tumours; some of these will require referral for management by the specialist team.

Patients with kidney cancer who fall into the following categories:

- those with tumours which have, or may have, invaded major blood vessels

- patients who might benefit from resection of metastases
- patients with bilateral disease or who will require dialysis
- patients with small tumours for whom nephron-sparing surgery may be possible
- patients with von Hippel-Lindau disease or hereditary papillary tumours.

In the case of renal cancer, the LCA Urology Pathway Group has stipulated that all new cases of suspected renal cancer should be discussed at the specialist MDT.

1.3.2 Specialist urological cancer teams

These teams have been established in large hospitals or cancer centres within the LCA under the auspices of the old cancer networks.

For bladder and prostate cancer, the specialist teams are located at Guy's Hospital, The Royal Marsden Hospital, St George's Hospital and Imperial College Healthcare Trust. Each team carries out a cumulative total of at least 100 radical operations for prostate and/or bladder cancer a year and hosts the specialist MDT for that sector.

In the case of renal cancer, the LCA Urology Pathway Group has chosen to consolidate the specialist team into two centres for the purposes of MDT meetings to maximise the availability of trials and highly specialised surgery. These MDT meetings are hosted at Guy's Hospital for the South East sector and The Royal Marsden Hospital (Fulham Road) for the West of London. They have established common clinical policies across the network as a whole, as well as common audits, and each has appointed a lead clinician. Specialist renal cancer surgery takes place at Guy's, King's College Hospital, The Royal Marsden, St George's Hospital and Imperial College Healthcare Trust; all surgeons performing renal cancer surgery in these centres are core members of the specialist team.

1.3.3 Supra-network specialist teams

Patients with testicular or penile cancer are managed by specialist testicular cancer or penile cancer teams working at the supra-network level. There are specialist testicular cancer teams at Guy's, The Royal Marsden, Mount Vernon and Imperial College Healthcare. There is one specialist penile cancer team serving the LCA, based at St George's Hospital. These teams liaise closely with local urological cancer teams which are responsible for some aspects of the diagnosis and treatment of these cancers.

1.3.4 Members of specialist urological cancer teams

Each member of the specialist urological cancer teams has a specialist interest in urological cancer and all team members are expected to attend a majority of meetings, which are subject to audit by recording attendance in the attendance register.

The specialist urological cancer teams include one or more of each of the following individuals:

- urologist – there are at least two urologists in all teams
- clinical oncologist
- medical oncologist, except where the clinical oncologist has specific expertise in systemic treatment for urological cancers

- radiologist with expertise in urological cancers – all imaging investigations are carried out in accordance with Royal College of Radiologists' guidelines and LCA guidelines where appropriate (e.g. multiparametric magnetic resonance imaging (MRI) scanning in prostate cancer)
- pathologist – the LCA Urology Pathway Group has excellent pathology representation and has issued tumour-specific guidance on the requirements of pathology reporting to include all the information required by the current Royal College of Pathologists' minimum dataset for the relevant cancer
- clinical nurse specialist (CNS) – these specialist nurses have all attended the advanced communications course to reflect their importance in patient advocacy and provision of information and support for patients and carers; the CNS is typically the patient's key worker
- pain management and palliative care specialist(s)
- team coordinator, who organises the meetings and ensures that all documentation (such as patient lists and case notes) that may be required to inform discussion is available at each meeting
- someone to provide clerical support for the MDT, record decisions, and communicate information generated by the MDT to all those who may require it – in many instances this will be the MDT coordinator who enters data in real time into a cancer information system.

The team is required to maintain close contact with other professionals who may be actively involved in supporting patients or carrying out the management strategy decided by the team, so that rapid access to their services can be provided when required. These typically include the following:

- GPs/primary healthcare teams
- local urological cancer teams at linked cancer units
- thoracic/vascular/liver surgeons
- liaison psychiatrist
- clinical psychologist trained in psychotherapy and cognitive behaviour therapy
- counsellor with expertise in treating psychosexual problems
- infertility services (specifically for testicular cancer patients)
- stoma care nurse
- lymphoedema specialist
- specialist palliative care teams.

1.3.5 Organisation of multidisciplinary team meetings (local and specialist teams)

Meetings are arranged by the team coordinator, who should ensure that information necessary for effective team functioning is available at each meeting. This will include a list of patients to be discussed and copies of their case notes, along with diagnostic staging and pathology information. All new patients should be discussed, along with any other patients whose cases require discussion as their condition or treatment progresses. Straightforward cases may need very little discussion but they should nevertheless be included and the discussion documented.

1.4 Coordination between teams

Close coordination is required between primary care teams, diagnostic and treatment teams at cancer units and cancer centres, specialist palliative care teams, and patients and their families. Clearly defined arrangements should be in place to ensure that appropriate information (including the name of the clinician and CNS who are directly responsible for each patient) is communicated promptly to patients and others (such as GPs) who may require, or may benefit from, information about decisions concerning particular patients.

The LCA is trialling a new end of treatment summary and patient care plan for all tumour sites which will include details of the patient's disease and treatment, relevant MDT(s), clinical appointments, and details of who their consultant and key worker are (including contact details).

1.5 Key worker

All patients will be assigned a key worker (usually a CNS) at the time of diagnosis, and appropriate arrangements should be in place to facilitate easy access to the key worker during working hours and an appropriate source of advice in his/her absence. The LCA has produced a Key Worker Policy (see Appendix 2). This policy sets out the definition of a key worker and provides an overview of their role and responsibilities. All patients should be offered an holistic needs assessment (HNA) at diagnosis and subsequently if their disease status changes. Patients should be offered advice and support to address any immediate concerns – physical, mental, spiritual or financial – on completion of the HNA with onward referrals made as necessary.

1.6 Communication and support

Treatment and care should take into account the patient's needs and preferences. If a patient does not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – *Reference guide to consent for examination or treatment* (2001; available from www.dh.gov.uk). Healthcare professionals should also follow a code of practice accompanying the Mental Capacity Act 2005 (summary available from www.publicguardian.gov.uk).

The recommendations on communication and patient-centred care made in the two National Institute for Health and Care Excellence (NICE) cancer service guidance documents, *Improving outcomes in urological cancers* (2002) and *Improving supportive and palliative care for adults with cancer* (2004), should be followed throughout the patient journey. Patients should be offered individualised information tailored to their needs. This information should be given by a healthcare professional (e.g. a consultant or CNS) and may be supported by written and visual media (e.g. slide sets or DVDs). This information should be regularly reviewed to take into account changes in practice and guidance. Additionally, patients should be offered advice on how to access information and support from websites (e.g. the information prescription website at www.nhs.uk/IPG/Pages/IPStart.aspx), local and national cancer information services, and from cancer support groups locally.

Before choosing or recommending information resources for patients with cancer, healthcare professionals should check that the content is clear, reliable and up-to-date. Healthcare professionals should seek feedback from cancer patients and their carers to identify the highest quality information resources. The information should include action that patients can take to help themselves and sources of support for such action (e.g. quitting smoking, dietary modification).

When English is not the patient's first language, somebody who speaks the patient's language should be available to facilitate communication. Providers should not expect members of the patient's family to act as interpreters.

Healthcare professionals should discuss all relevant management options recommended in the LCA Urological Cancers Clinical Guidelines with patients and their partners or carers, irrespective of whether they are available through local services. Where necessary, the patient should be referred to another provider for the selected treatment if it is not available locally.

Healthcare professionals should ensure that mechanisms are in place to allow patients and their primary care providers to gain access to specialist services throughout the course of their disease.

1.6.1 Breaking bad news consultations

Patients should be encouraged to bring a close friend or relative to the 'bad news' consultation. The consultation should be with a senior member of the clinical staff who should have attended the advanced communication skills course. The 'bad news' consultation should be carried out in a private room without interruptions. The diagnosis should be explained clearly by the senior clinician, who must allow adequate time for explanation, and a CNS should be present. After the consultation, the CNS should offer to remain with the patient to provide support and further information tailored to individual needs. A summary of the information given to the patient should be recorded in the notes and communicated to the patient's GP, together with a comprehensive summary of the management plan, as quickly as possible so that primary care staff can provide additional support for patients and carers.

1.7 Survivorship

The Consequences of Cancer and its Treatment collaborative (CCaT, a Macmillan Community of Interest) produced a '10 Top Tips' guidance document for patients. These have formed the basis for the LCA Survivorship Guidelines[1], which cover the key components of good survivorship care. All providers of urological cancer care in the LCA are expected to familiarise themselves with, and address, these areas.

1.7.1 Self-managed follow-up

There is a move towards increased self-management and follow-up closer to home. This has clear benefits to patients including reduced anxiety in the lead-up to routine appointments and less interference in their day-to-day life caused by travelling to hospitals. In addition, research has shown than recurrence is more likely to be detected by the patient themselves between appointments, rather than at the outpatient appointment. By reducing unnecessary appointments, Trusts are able to see new patients more quickly and spend more time with more complex patients.

For self-management to be effective, patients need to be given the right information about signs and symptoms of recurrence, clear pathways to follow if they are concerned and the guarantee of a fast, explicit route to re-access services if necessary. The Urology Pathway Group embraces the concept of remote follow-up and is running a pilot for the remote PSA follow-up of patients undergoing radical prostatectomy, and hope to roll this out to other prostate cancer groups, including patients stable on hormonal treatment and patients with low-risk disease on active surveillance.

1.7.2 Treatment summary and care plan

There are two related but distinct documents which patients should be given at the end of their treatment:

- A **treatment summary** provides a summary of the cancer treatments received by the end of the first treatment, planned follow-ups (including mechanisms for these), and signs and symptoms of which to be aware. Their aim is to provide information not only to the patient, but also to the GP about possible consequences of cancer and its treatment, signs of recurrence and other important information.
- A **care plan** is generated as a result of a HNA and is the agreed plan between the patient and healthcare professional about how the identified areas of concern will be addressed. This may cover provision of information (e.g. through an information prescription), onward referral for specialist assessment and intervention (e.g. breathlessness management), or things which the patient themselves can do (e.g. contact their HR department about graduated return to work options).

Recommendation: An end of treatment consultation should be offered to every patient. This should include an end of treatment HNA and associated written care plan, and should also include the discussion and provision of a comprehensive treatment summary.

1.7.3 Supportive care

From the time of diagnosis, each patient should have access to a specialist cancer nurse who can offer psychosocial support and continuity of care.

Appropriate patients should be given information about organisations which offer specific forms of support. The CNS, or another member of each MDT, should be trained in counselling patients and couples who may have to live with impotence or other sexual problems, loss of fertility, incontinence or stomas after treatment for cancer. These issues should be specifically considered, possibly through counselling or when identified by the patient completing a HNA, and counselling should be available when required from an individual who has specific expertise in dealing with psychosexual and body-image issues; this should be available to help patients and their partners to cope with such problems after treatment and for as long as it is needed.

Patients who may have problems with urinary incontinence should be given information both about local continence services and the Continence Foundation.

Arrangements for cryopreservation of sperm should be explained to men whose ability to father children could be reduced by treatment. This is likely to be particularly relevant to men with testicular cancer.

1.7.4 Healthy lifestyle

There is a growing body of evidence which supports the adoption of a healthy lifestyle for those who have had a cancer diagnosis.

Smoking cessation

Tobacco smoking is the main cause of preventable morbidity and premature death in England. End of treatment provides an opportunity to deliver stop smoking interventions at a point at which an individual may be more susceptible to health advice and hence more motivated to quit.

Patients with bladder or kidney cancer should be asked if they smoke and smokers should be strongly advised to quit. The association between smoking and urological cancer should be explained, and the benefits of quitting explicitly linked with reduced risk of recurrence. Smokers should be given information about local initiatives designed to help them quit and be encouraged to participate.

Recommendation: All current smokers should be asked about their smoking habit, and offered smoking cessation advice with onward referral to local services as necessary.

Diet

The role that diet can play in cancer incidence has been widely documented. Research has now moved to look at its influence beyond treatment. The nutritional issues during or following treatment include weight loss or gain; changes in body composition (e.g. loss of muscle mass); particular eating difficulties (including swallowing problems or a limited capacity for food). There are also long-term symptoms (e.g. changes in bowel habits for those who have had pelvic radiotherapy).

Receiving advice from an appropriately trained professional has been shown to improve quality of life, reduce risk of recurrence and risk of developing a new primary or other chronic disease, such as heart disease or diabetes. The aim of dietary advice is also to counter the adverse effects of cancer treatment. To date, most of the work has been done in breast, colorectal and prostate cancer. The World Cancer Research Fund's (WCRF's) Second Expert Report – *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective* (2007) – recommends the following eight-point plan for all cancer survivors:

- be as lean as possible within the normal body weight range
- be physically active as part of everyday life
- avoid sugary drinks and limit the consumption of energy-dense foods
- eat mostly foods of plant origin
- limit intake of red meat and avoid processed meat
- limit alcoholic drinks
- limit consumption of salt; avoid mouldy cereals or pulses
- aim to meet nutritional needs by diet alone.

Recommendation: Patients are provided with dietary advice, based on the WCRF recommendations, at the end of treatment, with referral to specialist dieticians as required.

Physical activity

There has been a dramatic rise in the amount of high-quality published research on the role of exercise in cancer in recent years. Physical activity results in improvement in quality of life, fitness and function and symptoms related to cancer and its treatments. It reduces cancer recurrence, incidence of second cancers and reduces both all-cause and cancer-specific mortality.

There is wide consensus that cancer survivors should exercise to the same level as the general population for health benefits. Research suggests that a combination of cardiovascular and muscular strength training has important additional benefits over and above undertaking only one type of exercise.

Recommendations: Patients should be encouraged to maintain or increase their level of physical activity both during and after treatment in line with national guidance. They should be referred for specialist assessment by a physiotherapist as necessary.

Patients should also be offered access to a health promotion event, such as a health and wellbeing clinic, at the end of treatment.

1.7.5 Practical and social support

Many cancer patients are over 70 years of age and are likely to require long-term support. The primary and specialist palliative care teams have particularly important roles in coordinating with social services and ensuring that the needs of both patients and carers are identified and met.

Patients should be given information about sources of help, such as local and national support groups, and disability and benefits helplines, both verbally and in writing. Information about support groups of various kinds is provided by NHS Direct and by cancer charities.

Related NICE guidance

Improving outcomes in urological cancers. NICE cancer service guidance (2002) – available from www.nice.org.uk/csguc

Improving supportive and palliative care for adults with cancer, NICE cancer service guidance (2004) – available from www.nice.org.uk/csgsp

Referral guidelines for suspected cancer, NICE clinical guideline CG27 (2005) – available from www.nice.org.uk/CG027

1.8 Specialist palliative care

Patients with advanced urological cancer may require care from specialist palliative care teams and primary care teams. Specialist palliative care teams are available in all the cancer centres and units affiliated to the LCA. Criteria for referral for specialist palliative care are well established and there is specialist palliative care representation in many of the MDTs. Where this is not the case, there are protocols and policies in place for referral from the MDT to the specialist palliative care service. The LCA referral form for referral to specialist palliative care can be found in Appendix 3.

1.9 Data requirements and metrics

1.9.1 Nationally mandated datasets

Urological cancer services within the LCA are required to submit data to nationally mandated datasets for patients diagnosed with a urological cancer.

The Cancer Outcomes and Services Dataset (COSD)

The core dataset for all tumour types including urological cancer is mandated from January 2013, and the site-specific dataset is mandated from July 2013. Details of the dataset can be found on the National Cancer Intelligence Network (NCIN) website: www.ncin.org.uk/collecting_and_using_data/data_collection/cosd.aspx.

The local cancer registry will be collating this dataset using Trust data feeds which should include all these items. The feeds are:

- Trust PAS feed
- Trust pathology feed
- Trust radiology feed
- Trust MDT feed.

In line with the requirements set out in provider Trust contracts, this data should be submitted within 25 working days of the end of the month in which the activity took place.

National audits – British Association of Urological Surgeons (BAUS) Audit

This is a national urological surgery audit – submissions are not mandated but it is recognised as a priority and provider/individual surgeon submissions are strongly encouraged.

Systemic Anti-Cancer Therapy dataset (SACT)

Trusts that provide chemotherapy to patients are required to submit data to the SACT dataset. Details of the audit and the dataset requirements are available at the dataset homepage: www.chemodataset.nhs.uk/home.aspx.

Radiotherapy dataset (RTDS)

Trusts that provide radiotherapy to patients are required to submit data to the RTDS dataset. Details of the audit and the dataset requirements are available at the dataset homepage: www.canceruk.net/rtservices/rtds/.

Cancer Waiting Times Monitoring dataset

Trusts are required to submit data to the Cancer Waiting Times Monitoring dataset, which includes details of all patients with a referral under the 2 week wait (2ww) rule, and of all patients' treatments for cancer. Trusts are required to submit this data within 25 working days of the month in which patients were first seen for the 2ww target, or the month in which the patient was treated.

The Cancer Waiting Times Monitoring dataset can be found at: www.datadictionary.nhs.uk/data_dictionary/messages/clinical_data_sets/data_sets/national_cancer_waiting_times_monitoring_data_set_fr.asp.

1.9.2 Local data requirements

Local metrics have been developed by the LCA and scorecards for all LCA providers and tumour groups are collated on a quarterly basis. These metrics are used to support the identification of any quality issues facing LCA providers and to inform priority-setting for the Urology Pathway Group's ongoing work programme. The Pathway Group will be reviewing the incorporation of additional metrics (e.g. those specific to evaluating the impact of the implementation of the prostate best practice pathway) in this scorecard during the course of 2014/15.

1.10 Treatment of children, teenagers and young adults (TYA)

Children below the age of 16 years with a diagnosis of cancer or suspected cancer must be referred to the paediatric oncology team at the principal treatment centre (PTC) and must not be managed exclusively by adult site-specific teams.

The joint PTC for children aged 1 to 16 years for South Thames is The Royal Marsden Hospital Sutton site)/St George's Hospital.

- Penile cancer patients under 19 years will have their surgery at St George's Hospital and adjuvant therapy at The Royal Marsden. Patients over the age of 19 should be offered a choice of being managed at a PTC of a designated hospital (please see TYA section below).
- The PTC for North Thames (including North West London) is Great Ormond Street Hospital/University College London Hospital (UCLH).
- **All** patients under 1 year from both North and South Thames should be referred to Great Ormond Street Hospital.

For certain tumour types that are uncommon in children (e.g. skin, melanoma, head and neck, thyroid, gastrointestinal, hepatobiliary), the paediatric oncology team should liaise with the appropriate site-specific MDT for advice about management and to agree surgical interventions, but overall responsibility for managing the patient remains with the paediatric oncology team.

Please see Appendix 5 for contact information for the children's PTCs.

For teenagers and young adults, teenagers **aged 16–18** should be managed at a PTC for TYA cancers, and those **aged 19–24** are given the choice of being managed at a PTC or TYA designated hospital.

- The PTC for TYA for South Thames is The Royal Marsden Hospital Sutton site.
- The PTC for TYA for North Thames (including North West London) is UCLH.

All patients within this age range, regardless of place of care, should be referred to the TYA MDT at the relevant PTC.

Please see Appendix 6 for information about making a referral and for contact information for the PTC and TYA designated centres in the LCA.

[1] www.londoncanceralliance.nhs.uk/media/68896/LCA%20Survivorhsip%20Guidelines%20Sept%202013.pdf

2 Penile Cancer

2.1 Introduction

The purpose of these clinical guidelines is to provide a framework for the management of penile tumours within the supra-network based at St George's Hospital on behalf of the LCA. This is the only supra-network penile cancer team within the LCA.

Penile cancer is a rare condition affecting 1 in 100,000 men per annum, with similar numbers of penile pre-cancers; 95% are squamous cell carcinomas (SCCs). In the LCA, this represents 50–60 new cases each year. The peak age is 60 years, with incidence increasing with advancing years. There has been a 20% increase in detected cases since 1990.

Centralisation of penile cancer services into supra-network teams occurred in 2002. The 5-year cancer-specific survival has increased by around 10% over this time to 80–85%.

This guideline is closely based on the supra-network guideline reviewed annually by the team at St George's Hospital. The author of the LCA guidance also authors the supra-network guideline, the European Association of Urology (EAU) guideline and the European Society of Medical Oncology (ESMO) guideline. The development process begins with detailed evidence collection at the EAU guidelines office, with rating of levels of quality of the data and a 5-yearly update. Therefore, the recommendations at LCA level closely follow the EAU 2009 report.

There are several key differences that reflect the local healthcare system and also the large catchment area from which cases are referred. For treatment of the primary tumour, radiation therapy is not recommended. Management of the non-palpable lymph nodes relies on sentinel node biopsy not prophylactic groin dissection; follow-up is carried out with a risk-adapted approach and for most patients ends at 3 years (not 5 as per the EAU guideline). Finally, sections relating to non-penile genital malignancies (e.g. penile urethral SCC, extra-mammary Paget's disease and scrotal carcinoma) are included but are not covered in the EAU document.

This guideline is intended to direct referrals from GPs, dermatologists, genito-urinary (GU) medicine physicians and urologists to the appropriate centre without unnecessary delay or inappropriate investigation. It also informs the local and specialist centres of their role in the patient pathway with respect to delivery of radio/chemotherapy when necessary after definitive primary treatment at the supra-network centre.

2.1.1 Background

Penile carcinoma and pre-malignant lesions of the penis are rare and a typical consultant urological practice would expect to identify 1 or possibly 2 cases per annum. Cases may also become apparent through dermatology clinics and GU medicine clinics.

As a general rule, patients referred by GPs to urologists have clinically obvious lesions, which may not necessarily need biopsy confirmation before referral.

However, patients seen in dermatology and GU medicine clinics are often less clear-cut initially and a biopsy may be required in these cases before referral. It is quite likely that in these instances patients are

referred initially to a local consultant urologist because of a lack of awareness of a supra-network for the management of these tumours.

The catchment area for this supra-network covers most of South East England, Wessex and Dorset, with a population of 9–10 million.

2.1.2 Facilities at St George's Hospital and referral of patients

A specialist clinic runs every week at St George's Hospital for the management of penile cancer. We aim to see all referred patients within a week of receipt of the referral. The clinic is led by the consultant surgeons with clinical nurse specialist (CNS) support. In rare circumstances, when the patient is unable to travel, histology and imaging (if available) can be reviewed by the specialist team and advice given regarding management.

Referrals should be faxed to 020 8725 2915 directly to the urology office and marked **'suspected penile cancer'**. Referrals should state explicitly whether the patient has been told of the referral and possible diagnosis.

On receipt of the fax, the patient will be contacted (provided that he has already been told of the anticipated referral and a tentative diagnosis). Any patient referred from a local GP with suspected penile cancer will be seen under the 2 week wait (2ww) referral guidelines.

There is a weekly supra-network multidisciplinary team (MDT) meeting at which all new patients and post-operative patients are discussed with a dedicated histopathologist, two surgeons, CNS, medical oncologist, radiation oncologist and radiologist. Any patient referred from a local GP with suspected penile cancer will be seen under the 2ww referral guidelines.

The patient's original histology blocks and slides will be requested from the referring laboratory. The St George's urology secretary will send a histology review request form together with a copy of the histology report by fax to the histology office (fax 020 8767 7984). The pathologist will add the case to the next penile cancer MDT list on receipt of the slides and/or blocks.

The patient is given instructions on how to get to St George's Hospital; the appropriate clinic and priority is given to patients travelling from some distance, offering an early appointment to ensure an easier journey home.

The aim is to see all patients within 1 working week of receipt of the faxed referral.

There is a weekly operating list for inpatient surgery and our target is to offer all patients surgery within three weeks but in certain patients with more severe or rapidly growing lesions we aim to offer surgery within 1 week. All surgery is carried out at St George's Hospital. Patients can choose later booking for treatment if agreed with the team that it is safe to do so.

On this basis, the following referral recommendations are made:

1. Any suspected penile cancer seen by a consultant urologist can be referred without histological diagnosis or staging investigations directly to the department. All patients should be referred within 1 week of first appointment to provider.

2. Any suspected penile cancer or pre-malignant lesion referred to a consultant urologist via a dermatologist or GU medicine physician with histological diagnosis can be referred directly to the department without further investigation. All patients should be referred within 1 week of first appointment to a urologist.
3. Any suspected penile cancer that becomes apparent at the time of a circumcision should be referred directly without histology results.
4. Any patient with a suspicious but not diagnostic lesion should have a generous deep biopsy for confirmation. Scrapings and/or punch biopsies are not usually adequate in these cases.
5. Patients who are deemed unfit to travel or are unwilling to travel for whatever reason could be discussed directly with the consultant in charge and advice given accordingly.
6. It is not mandatory to arrange further staging investigations; however, if imaging has been performed and/or arranged this information should be sent with the referral.

2.2 Clinical guidelines on the diagnosis of penile cancer

2.2.1 Primary lesion

Detailed physical examination of the penis is carried out, noting the size, nature and position of the primary tumour, if this is possible. A deep biopsy of the lesion is mandatory in equivocal cases and in cases where there is a tight phimosis, a dorsal slit may be necessary to perform this. Cytological scrapings are usually inadequate and frequently under-stage the disease. Ultrasound and magnetic resonance imaging (MRI) scanning of the penis have been used for staging, but their role has not been fully established and they should be considered optional.

2.2.2 Regional nodes

Physical examination of the inguinal nodes will categorise people into clinically positive (palpable nodes) and clinically negative (impalpable nodes). In the case of clinically positive groin nodes, fine needle aspiration (FNA) or preferably ultrasound-guided FNA is recommended. A computed tomography (CT) scan of the thorax, abdomen and pelvis (TAP) should be performed. If the aspiration is negative and there is still a high index of suspicion, open biopsy of the lymph node is recommended.

Patients with moderate or high-risk disease (T1 G2 or greater) with clinically negative inguinal nodes are offered a dynamic sentinel lymph node study and ultrasound aspiration of suspicious nodes, preferably at the time of treatment of the primary lesion.

2.2.3 Staging CT scan

A staging CT scan of the TAP is recommended in the following circumstances:

- any node positive disease, i.e. clinically or pathologically involved lymph nodes
- any patient with symptoms suggestive of possible metastatic disease.

2.3 Guidelines on treatment of penile cancer

2.3.1 Treatment of the primary lesion

Stage TiS (carcinoma in situ)

Lesions on the penile shaft skin are most commonly Bowen's disease or Bowenoid papulosis. These lesions can be excised with a small margin of surrounding normal penile skin and patients should be advised on regular follow-up. If the foreskin and glans are otherwise normal, circumcision is optional.

Erythroplasia of Queyrat (penile intraepithelial neoplasia (PeIN))

This is typically a red velvety lesion on the glans and/or inner prepuce or sometimes a more diffuse flat or raised moist red patch. This has a higher incidence of conversion to invasive disease and should be managed differently. A circumcision is recommended. Careful examination of the glans with 5% acetic acid staining together with deep biopsy are recommended. Inspection of the distal urethra is recommended. Primary treatment includes a course of a topical chemotherapy agent such as 5% 5-fluorouracil, or imiquimod. Incomplete responders could be offered a second course of topical chemotherapy. Alternative options include partial or total glans resurfacing with partial thickness skin. Close follow-up is recommended in the centre. The follow-up protocol will be individualised.

Verrucous hyperplasia (PeIN)

A penile preserving treatment is recommended. Options include circumcision if the lesion is solely on the prepuce. For lesions on the glans, wide local excision for smaller lesions or total glans resurfacing or glansectomy for larger lesions is recommended.

T1 lesions

Solitary T1 lesions of the prepuce can be treated by a circumcision and close follow-up. T1 lesions of the glans are managed with a penile preserving surgical procedure such as wide local excision with or without grafting, glans resurfacing or glansectomy and skin grafting. Radiotherapy is an optional treatment that is currently not recommended within the LCA.

T2/T3 lesions

Larger distal tumours invading the glans and/or corporal heads can be managed with penile preserving surgery in most cases. Frozen section analysis of the margins is performed in selected cases. Either glansectomy and skin graft reconstruction or glansectomy and distal corporectomy and reconstruction are recommended. For large proximal shaft tumours, consideration should be given to penile preservation with a possibility of a penile lengthening procedure. In selected cases, partial amputation and delayed phalloplasty should be considered. If penile preservation is not considered possible, radical penectomy with perineal urethrostomy is recommended.

T4 lesions

Radical penectomy and formation of perineal urethrostomy are usually the only option. Down-staging with neo-adjuvant chemotherapy can be considered (see Annex 2.2 for details of appropriate regimens). In selected cases, radiotherapy can be considered for local control.

2.3.2 Comment

Very frail patients could be considered for more limited surgical options such as a conventional partial penectomy but this should only be agreed after discussion with the cancer centre. The network database figures suggest that this may be necessary in only 2–3% of all patients referred. Currently, over 85% of all referred patients receive a penile preserving procedure.

2.4 Management of the regional nodes

2.4.1 Clinically inguinal node negative at presentation

Ta G1, T1 G1 lesions

Patients who have a negative ultrasound FNA are observed. They are at very low risk of nodal disease.

T1 G2, T1 G2/3 T2 G1–3 or greater lesions

Patients who have a negative ultrasound FNA and a negative dynamic sentinel node study scan are offered surveillance. Patients who are advised or elect surveillance are followed up 3-monthly for the first year, 4- monthly for the second year and then considered for discharge. Surveillance includes physical examination and ultrasound examination with or without FNA of the groins. No CT scan is required at initial assessment unless there are specific clinical indications.

Patients in whom ultrasound FNA and/or dynamic sentinel lymph node study are positive undergo modified radical inguinal node dissection on the ipsi-lateral side. The contra-lateral groin is then observed.

Patients who are node positive should have a staging CT scan of the TAP and repeat scan every 3–6 months for 3 years according to disease stage (see below).

2.4.2 Clinically inguinal node positive at presentation

Patients in whom FNA and open biopsy are negative should still be considered for modified radical inguinal node dissection based on their risk status. Patients in whom any of the investigative tests are histologically positive should have a modified radical inguinal node dissection on the ipsi-lateral side and a dynamic sentinel node study on the contra-lateral side. A CT scan of the TAP is recommended. Other imaging is required only if clinically indicated.

Patients who elect for observation in the presence of negative histology should undergo repeated FNA every 2 months in the first year.

N1 disease

Patients with a single positive node without extracapsular extension should then be kept on surveillance with CT scans every 6 months for 3 years.

N2 disease

Patients with more than two unilateral or bilateral superficial nodes without extracapsular extension should be considered for bilateral pelvic node dissection after appropriate cross-sectional imaging. In those patients who are not surgically up-staged, regular surveillance with CT scans every 3 months for 2 years and 6-monthly for year 3.

N3 disease

N3 disease is classified as inguinal node(s) with extracapsular disease or pelvic node disease of any type. For inguinal disease, an ipsi-lateral pelvic node dissection is recommended. Down-staging with neo-adjuvant chemotherapy can be considered (see Annex 2.2 for details of appropriate regimens). Subsequently, adjuvant radiotherapy with chemo-sensitisation is delivered to the nodal basins with extracapsular involvement (see Annex 2.3 for regimens).

Chemotherapy

Adjuvant chemotherapy is not given on a routine basis. Recruitment to clinical trials of systemic therapy, where available, is encouraged. Outside a clinical trial, adjuvant systemic therapy is considered in the MDT on a case-by-case basis according to the pathological risk status, particularly for those with positive lymph nodes. This should include consideration of full adjuvant chemotherapy for those with positive nodes and extracapsular spread who also undergo adjuvant chemo-irradiation (see Annex 2.2 for regimens).

Positive pelvic nodes

Small volume disease should be managed by complete pelvic node dissection followed by adjuvant radiotherapy for extracapsular nodal extension; adjuvant chemotherapy can be considered. For patients with large volume disease at presentation, surgery is optional and consideration should be given to primary chemo-irradiation or primary chemotherapy followed by consolidation radiation depending on response (see Annex 2.2).

Fixed or fungating inguinal nodes

Careful assessment should be made by the MDT before a final decision is made. It may be possible to down-stage patients with primary chemotherapy and render the patients operable (see Annex 2.2 for details of regimen). Sometimes, with the help of a vascular surgeon or plastic surgeon, it is possible to remove nodes. However, in truly inoperable situations, palliative radiotherapy would be appropriate (see Annex 2.3).

Delayed presentation of positive groin nodes

In this situation, ipsi-lateral modified inguinal node dissection is appropriate. Assessment of the contra-lateral groin is advisable but the nodes are usually not involved. The subsequent management depends on the number of nodes affected.

Metastatic disease

Palliative chemotherapy can be helpful in slowing the progression of metastatic disease and is administered with the aim of minimising symptoms and maximising the duration of good quality of life. Chemotherapy should be offered subject to performance status, oncology advice and patient preference and within a clinical trial where possible (see Annex 2.2 for regimens).

Chemotherapy may be administered either at the supra-regional centre at St George's or locally in conjunction with the local penile cancer oncology service. Local administration, in accordance with the supra-regional network guidelines, is encouraged particularly for patients not suitable for treatment within a clinical trial and/or for those undergoing treatment in the palliative setting.

Following completion of chemotherapy for metastatic penile carcinoma, follow-up is 3-monthly with clinical examination and CT scans of the TAP, or as clinically indicated.

Additional lines of chemotherapy for second or subsequent relapses with metastatic disease are not delivered routinely but may be useful in disease control and symptomatic palliation in select cases. Clinical trials, including of novel agents in the context of early phase trials, should be considered in this situation for patients of good performance status.

Re-challenging with a platinum-based chemotherapy regime may be considered for patients with documented platinum sensitivity. For those with platinum-refractory or resistant disease, other regimens are available (see the list in Annex 2.2).

Palliation may be difficult for patients with cutaneous metastases or fungating nodal masses and radiotherapy can be considered. Early involvement with the palliative care team and a specialist nurse is recommended. Radical surgical treatments should be reserved for selected cases where there is a clear expected palliative benefit as life expectancy is generally short. Median survival is a few months only and 5-year survival is <10%.

2.5 Pathology protocols for penile and urethral cancer (supra-network)

2.5.1 Purpose of examination/clinical relevance

Description, dissection and block selection of penile and urethral specimens

References

RCPath minimum Data Sets

Penis 2006

Urothelial 2007

Urological Tissue Pathways

WHO Genetics and Histopathology of Urogenital Tumours

TNM/UICC 2009 (Version 7)

WHO Grading of Urothelial Tumours 1973

2.5.2 Penis and penile urethra

Punch and excision biopsies of the glans penis are handled in the same way as similar skin biopsies. For larger resections such as glans resurfacing, glansectomies and penectomies, the specimen must be dissected to allow assessment of tumour extent and margins. Large specimens should be photographed after fixation and before inking.

All reports on invasive tumours of penis and urethra, including reviews, should include a minimum dataset report (quickcode: Penis).

Stage using TNM 7 (2009) with the local modifications pT2 : pT2a – corpus spongiosum; pT2b – corpus cavernosum; and pT3 : pT3a – urethra within glans; pT3b – more proximal urethra/shaft.

For glansectomies, malignant foreskins and small specimens, submit entire tissue where practical in sequential transverse sections with margins inked. Orientation may be difficult particularly with foreskins so 1 to 2 sections only are placed in each block. Dissect glansectomies and larger specimens longitudinally

and put at least one section in a large block if necessary. Photograph resection specimens en face and transverse section if appropriate.

Record tumour type and grade (see proforma below). For mixed tumours record all tumour types present. If sarcomatoid areas are present this is not a separate subtype but should be recorded in the text/comment. Associated conditions such as lichen sclerosus dysplasia/carcinoma in situ (CIS) and viral changes should be recorded.

Distal urethral tumours are reported using the penile minimum dataset but the TNM differs (see proforma for penis below).

For lymph node dissections, take at least one section of each node, noting in the macro how many nodes are present. If an orientation suture is present, then dissect down from this end in sequence. Note if tumour is present at or close to margins and selectively ink these areas but do not ink the entire specimen.

For sentinel nodes, the whole specimen should be sliced into 2mm sections and examined. If obvious tumour is present, immunohistochemistry is irrelevant; for negative or suspicious nodes, all sections should be stained with CK8/18, CK5 and AE1/3 in the first instance if the tumour is an SCC, which should be ordered at cut up. For melanomas the panel is S100, Melan A and HMB 45.

Extranodal spread should be noted and measured and the maximum size and position of the metastases recorded for each separate nodal specimen as well as any involvement of surgical margins.

Dr CM Corbishley
July 2004, updated September 2004, February 2006, February 2007, July 2008, February 2011, August 2012

2.5.3 Penile cancer pathology minimum dataset (quickcode: Penis) (including penile urethra)

Type of specimen

(Punch biopsy/excision biopsy/circumcision/glansectomy/partial or total penectomy/other)

Size of tumour Width mm Depth mm

Type of tumour

(SCC/usual type/verrucous/papillary/basaloid/warty/mixed/TCC/melanoma/other)

Growth pattern (Exophytic/endophytic)

Grade Well 1 / Moderately 2 / Poorly 3

Stage (penile) modified TNM 7 (2009)

CIS, mucosa only 1a (not poorly differentiated and/or no LVI) 1b (poorly differentiated and/or with LVI), corpus spongiosum 2a, corpus cavernosum 2b, urethra 3a within glans, proximal urethra and prostate 3b, other organs 4.

Distance from margins

Nearest lateral/epithelial	mm (position if known)
Deep	mm
Circumferential (shaft)	mm
Lymphovascular invasion	yes/no

Perineural invasion	yes/no
Urethral involvement	yes/no
Urethral margin clear	yes/no
Associated pathology	
Lichen sclerosus	yes/no
Dysplasia present	yes/no
Grade of dysplasia	mild/moderate/severe/carcinoma in situ/PeIN
Dysplasia at margin	yes/no (including position of margin if specimen orientated)
Viral features	yes/no

Comments

Photograph taken yes/no

Conclusion

Penis (type of specimen): Squamous cell carcinoma of …….. Type, G……pT……
Pathological stage (modified TNM 7, 2009)
The same form and format should be used for penile urethral tumours which may be either urothelial or squamous. However, the TNM differs as follows:

Stage (penile urethra)

TX not assessable, CIS, Ta non-invasive papillary urothelial, T1 sub-epithelial connective tissue, T2a corpus spongiosum, T2b prostate, periurethral muscle, T3 corpus cavernosum, beyond prostatic capsule, anterior vaginal wall, bladder neck. T4 other adjacent organs
For melanoma use TNM 7 staging for melanocytic tumours with comment on extent of spread within penis. However, the TNM differs as follows. Melanocytic tumours should be joint reported with the skin team.
Lymph node dissection in carcinoma of the penis
Type of specimen (each to be reported separately):
(Left/right superficial or deep inguinal nodes, sentinel node)
Number of nodes present in each specimen:
Number of nodes involved:
Size and position of largest metastatic deposit:
Extranodal spread: yes/no
Immunohistochemical confirmation of tumour (state panel used):
Margin status:

Conclusion

NX	Cannot be assessed
N0	No nodal metastasis
N1	Metastasis in a single superficial inguinal node without ECS
N2	Metastasis in multiple or bilateral superficial inguinal lymph nodes without ECS
N3	Metastasis in deep inguinal or pelvic lymph node(s) unilateral or bilateral or any node with ECS

Dr CM Corbishley
July 2004, updated September 2004, March 2006, February 2007, July 2008, February 2011, August 2012

2.6 Follow-up arrangements

2.6.1 Introduction

The guiding principle of these recommendations is to allow the best possible care for each patient in the most convenient location. That will sometimes mean the patient has to travel further than their nearest hospital for access to specialist treatment.

Having received specialist treatment, the network has been structured so that follow-up can usually be provided at the nearest cancer centre if chemo-radiotherapy is required. This has been accomplished by specifying the appropriate intervals and investigation for follow-up of patients at different stages of their cancer journey, and by establishing a link with a named penile oncologist at cancer centres more local to the patient.

Patients not requiring additional treatment are offered surveillance at St George's, primarily to identify recurrence and manage surgical complications. If a patient finds travel difficult, we endeavour to provide care at the local unit if possible but anecdotally few patients request this in the 1–2 years of follow-up.

2.6.2 Sites of follow-up

Locations in which follow-up of patients currently takes place are as follows:

- St George's Hospital specialist clinic – any patient if advised or on patient request
- any cancer centre which has agreed to deliver radiotherapy and/or chemotherapy will review those specific treated patients in close collaboration with the supra-network centre.

Cancer centre sites in the LCA in which adjuvant therapies are given include:

- St George's Hospital (lead – Dr Lisa Pickering)
- Guy's Hospital (lead – Dr Simon Choudhury)
- St Thomas' Hospital (lead – Dr Simon Hughes)
- The Royal Marsden Hospital, Fulham Road (lead – Dr Vincent Khoo)
- The Royal Marsden Hospital, Sutton (lead – Dr Lisa Pickering).

Details of follow-up arrangements are given in the chapters relating to each tumour type, but an outline is given below.

2.6.3 Follow-up according to disease stage

The principles of follow-up are as follows:

- detection/management of early and late sequelae of treatment
- detection of new local disease occurrence
- detection of local recurrence (of residual disease).

Detection of regional or distant disease progression

It is important to recognise that re-occurrence of local disease can happen if there is residual glans/preputial or distal urethral epithelium as a field change effect is likely. This is particularly the case if human papilloma virus (HPV) is implicated in the original disease.

Low risk of disease recurrence and/or progression

- Any glans-confined tumour removed with clear margins by glansectomy or total glans resurfacing and pathologically staged N0 by sentinel node biopsy or prophylactic node dissection.
- 3-monthly review year 1 and 4-monthly review year 2. Clinical examination only, unless specifically indicated. Discharge if no late sequelae of treatment.
- Any pre-cancer removed completely from the foreskin, with a normal glans epithelium or treatment by total glans resurfacing with clear margins.
- 3-monthly review and consider self-examination thereafter (see below).

Intermediate risk of disease progression

- Any patient staged N1 disease.
- Monthly review with CT TAP year 1 and 6-monthly year 2. Clinical review 6-monthly, year 3. Consider discharge on an individualised basis at end of year 3.

High risk of local recurrence

- Any patient with a close or involved pathological margin, or in whom the margin status cannot be confirmed.
- Any patient with features of embolic disease in primary specimen.
- If the MDT recommends surveillance then 2-monthly review in the centre for 1 year is recommended. Subsequent follow-up can be arranged according to overall stage/grade.

High risk of disease progression

- Any patient with N2 or N3 disease.
- 3-monthly review with CT TAP for 2 years; 3-monthly review with CT 6-monthly in year 3. Continue surveillance for further 2 years for N3 disease, with CT if clinically indicated.

Indeterminate risk of disease recurrence

Patients with residual glanular and/or preputial epithelium affected by viral wart disease or lichen sclerosus and those with immunosuppression have potential for malignant change but there is no good evidence for the timeframe in which this might occur. We offer tailored surveillance on a case-by-case basis as discussed at the MDT and also encourage the self-examination protocol (see below).

2.6.4 Self-examination protocol

Patients with the following conditions will be instructed on self-examination in conjunction with an advice booklet; a telephone helpline will also be available.

- Any patient with residual glanular epithelium who has completed the required follow-up protocol and has been discharged with no evidence of local or regional recurrence.
- Any patient with a genital dermatosis of uncertain malignant potential.

The telephone helpline is currently the extension of the patient's key worker/CNS.

2.7 Specialist palliative care

All the cancer units have access to specialist palliative care expertise, and this will be provided locally, in the community, the local hospital or hospice.

There may be occasions when patients with advanced disease and poor performance status are considered for novel treatments at the centre, and continuity of specialist palliative care arrangements will be ensured by coordination with the patient's key worker and the centre specialist palliative care team.

Inpatients requiring specialist palliative care will be managed with the support of the hospital specialist palliative care team.

2.7.1 Centre-delivered palliation

- Surgical management of fungating inguinal node masses or genital recurrences (St George's only)
- Novel chemotherapy as part of a clinical trial (St George's or The Royal Marsden Hospital only)
- Palliative radiotherapy (all network centres)
- Palliative chemotherapy (all network centres).

2.7.2 Unit-delivered palliation

This provides supportive care for wound management, pain control and end of life pathway issues.

2.8 Research

The network has the highest number of patients treated annually in any of the penile networks in the UK. Clinical audit and research are ongoing in many areas of care of penile cancer patients.

The unit has a nurse responsible for facilitating patient recruitment, and the MDT is aware of 'open' studies and will identify suitable patients when they are discussed, so that entry into the study can be offered to patients when they are seen in clinic.

The network has a National Cancer Research Institute (NCRI) funded lead research nurse, who attends the Tumour Working Group (TWG) meetings and is responsible for keeping TWG members informed about the status of clinical trials into which its patients can be recruited.

The unit runs a tissue bank in conjunction with the Bart's Cancer Institute and is active in basic science research with clinicians from the centres, working collaboratively on a number of projects.

There are currently no NCRI trials open for penile cancer.

Annex 2.1: Members of the Supra-network Penile Cancer Team

Team member	Named lead	Cover
Team leader/Consultant surgeon	Mr Nick Watkin	Mr Ben Ayres
Consultant surgeon	Mr Ben Ayres	Mr Nick Watkin
Consultant histopathologist	Dr Cathy Corbishley (lead) Tel: 0208 725 5277 Fax: 0208 725 7984	Dr Brendan Tinwell Dr Ramzi Rajab
Nurse specialist	Janice Minter RGN Tel: 0208 725 0393 janice.minter@stgeorges.nhs.uk	Mary van Zyl RGN
Consultant medical oncologist	Dr Lisa Pickering lisa.pickering@stgeorges.nhs.uk Secretary, tel: 020 8725 3829	Specialist Registrar
Consultant clinical oncologist	Dr Vincent Khoo Secretary, tel: 020 8725 3829	Specialist Registrar
Consultant radiologists	Dr Mike Gonsalves Dr Sue Heenan	Dr James Pilcher
MDT coordinator	Louis Lot-Thomas Louis.Lot-thomas@Stgeorges.nhs.uk	
Patient liaison	Janice Minter RGN	Mary van Zyl RGN
Service improvement lead	Mr Nick Watkin	

Extended team members

Team member	Named lead	Cover
Consultant plastic surgeon	Mr Martin Vesely	Mr Mark Soldin
Consultant dermatologist	Professor Chris Bunker	
Consultant in palliative medicine	Dr Catherine McGowan	
Psychosexual counsellor	Remziye Kunelaki	
Counsellor	Caroline Armstrong	

Annex 2.2: Penile chemotherapy regimens and indications

Decisions to offer chemotherapy should be made only by a consultant oncologist in urological malignancies or by a specialist registrar in oncology who has been deemed competent to make such decisions. Consenting for chemotherapy and prescribing of chemotherapy are also limited to these groups.

Neo-adjuvant chemotherapy for T4 disease

Local standard therapy is a fluoropyrimidine (capecitabine or 5FU by continuous infusion) in combination with cisplatin. Carboplatin should be used in place of cisplatin in patients with:

- impaired renal function (creatinine clearance (CrCl) by ethylenediaminetetraacetic acid (EDTA) or Cockroft and Gault calculation of <60ml/minute)
- significant hearing impairment
- impaired cardiac function – patients with a confirmed or suspected history of cardiac failure or ischaemic heart disease should have an echocardiogram or multiple-gated acquisition (MUGA) scan prior to chemotherapy. Cisplatin should be avoided in patients with left ventricular ejection fraction (LVEF) <50%.

Cisplatin: 75mg/m^2, day 1 of 21-day cycle.

Capecitabine: 1,000mg/m^2, days 1–21 of 21-day cycle.

Cisplatin: 75mg/m^2, day 1 of 21-day cycle.

5-fluorouracil: 2,000mg/m^2 / day, day 1 of 21-day cycle.

Carboplatin: AUC 5. Day 1 of 21-day cycle.

Capecitabine: 1,000mg/m^2, days 1–21 of 21-day cycle.

Carboplatin: AUC 5. Day 1 of 21-day cycle.

5-fluorouracil: 2,000mg/m^2/ day, day 1 of 21-day cycle.

PMB

PMB is used as an alternative regimen in patients in whom fluoropyrimidines are contraindicated by virtue of a history of coronary artery disease/ischaemic heart disease.

All patients should have pulmonary function testing prior to commencing bleomycin and this should be repeated after 3 cycles of treatment or at any other time that the patient develops unexplained breathlessness. If significant deterioration, bleomycin should be omitted for the remaining chemotherapy cycles.

Cisplatin: 75mg /m^2, day 1 of 21-day cycle.

Methotrexate: 25mg/m^2, days 1 and 8 of 21-day cycle.

Bleomycin: 10,000 units, days 1 and 8 of 21-day cycle.

Carboplatin should be used in place of cisplatin for patients with impaired hearing, renal function or cardiac function as above.

Carboplatin: AUC 5. Day 1 of 21-day cycle.

Methotrexate: 25mg/m^2, days 1 and 8 of 21-day cycle.

Bleomycin: 10,000 units, days 1 and 8 of 21-day cycle.

Other regimens

Taxane-containing regimens have also been shown to have activity in case series both in the neo-adjuvant setting and in advanced disease. Such regimens can be considered on a case-by-case basis but are off-protocol and can be prescribed only with the agreement of the oncology pharmacy and clinical lead.

Indications for listed chemotherapy regimens in penile carcinoma:

	Neo-adjuvant	Adjuvant	Locally advanced first-line	Metastatic first-line	LA/ metastatic second-line
Cis + Cape	✓	✓	✓	✓	✓
Carbo + Cape	✓	✓	✓	✓	✓
Cis + 5FU	✓	✓	✓	✓	✓
Carbo + 5FU	✓	✓	✓	✓	✓
PMB	✓	✓	✓	✓	✓
PMCarbo	✓	✓	✓	✓	✓
Paclitaxel					✓
TIP	✓				

Joerger M, Warzinek T, Klaeser B et al. (2004), Major tumor regression after paclitaxel and carboplatin polychemotherapy in a patient with advanced penile cancer, *Journal of Urology* **63:**778–780.

Carboplatin dosing and creatinine clearance

Carboplatin is dosed according to an 'area under the curve' (AUC) calculation. The majority of regimens use a dose level of AUC 5 or 6 although there are exceptions.

Dose of carboplatin = (creatinine clearance + 25) x AUC

CrCl should be calculated by EDTA although for first cycle and emergencies the CrCl may be calculated by the Cockroft and Gault formula as follows:

$$\frac{\text{Constant} \times (150 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine}}$$

Constant: males = 1.23

females = 1.04

Annex 2.3: Penile radiotherapy cancer guidance (The Royal Marsden NHS Foundation Trust)

Adjuvant or post-operative radiotherapy

Indications

Radical radiotherapy is offered according to the indication(s) outlined in the main protocol document.

Treatment planning

All radical radiotherapy is CT planned.

Planning volumes

The clinical target volume (CTV) is defined according to the region at risk and can vary depending on the clinical case. For nodal pelvic regions, a surgical template for lymphovascular coverage is used to define the CTV.

Generally, a 1cm planning target volume (PTV) margin is used for all regions except nodal regions where a 0.5cm PTV margin is used. Different plan phases may be needed for boosting of disease.

Dose is 50 Gy for adjuvant irradiation, 54 Gy for microscopic disease and 60 Gy for macroscopic disease.

Fractionation is 2 Gy per fraction, treating 5# per week.

NB: Altered fractionation schemes can be considered but should be biologically equivalent to the standard fractionation scheme above.

Radiation is given with concomitant cisplatin at 40mg/m^2 if the patient is medically fit and suitable.

On-treatment monitoring

Patients should be reviewed weekly with on-treatment visits and blood test monitoring.

Follow-up

This is defined according to the main protocol.

Palliative radiotherapy

Indications

Palliative radiotherapy can be offered according to the indication(s) outlined in the main protocol document. This may be for symptom control or growth restraint.

Treatment planning

This can be achieved by any suitable method for the region(s) in question such as clinical mark-up for palliative skin radiotherapy to CT-simulation for more complex soft tissue disease.

The dose, beam energy, field arrangement may vary depending on treatment intent from 20 Gy in 5#, 30 Gy in 5# to single fraction radiotherapy.

Annex 2.4: Request for histopathological material from other hospitals (St George's Healthcare NHS Trust)

St George's Healthcare NHS
NHS Trust

Department of Cellular Pathology

Level 01, Jenner Wing

London SW17 0RE

General Enquiries: 0208 725 5264

REQUEST FOR HISTOPATHOLOGICAL MATERIAL FROM OTHER HOSPITALS FOR REVIEW

For the attention of Consultant Pathologist

Name of patient

D.O.B Hosp. Number

Ref. Consultant

Ref. Hospital/Address

Reason for review

Type of biopsy

Date of biopsy Place of biopsy

Signed Date

(Please attach a copy of the report if possible)

PLEASE FAX COMPLETED FORMS TO 0208 767 7984

Annex 2.5: LCA penile imaging guidelines

Cancer Area: Urology **Cancer Type:** Penile Cancer

	Imaging modality	Indications and notes
Diagnosis	No essential diagnostic investigation	US of groin and/or MRI of penis/pelvis are optional investigations
Staging	US of groin Nuclear medicine (Sentinel node study) CT of TAP	US and nuclear medicine studies carried out at centre CT TAP carried out only in those with palpable nodes at presentation
Surveillance	US groin CT TAP	US in those with high-risk disease but no nodal disease at surgery CT TAP in those with proven nodal/disseminated disease at presentation (annual study)

Techniques:

CT	Area scanned	Oral contrast	IV contrast Vol/sec	Delay(s)	Max slice thickness	Notes
	TAP	1 litre water	100ml at 3ml/sec	Porto-venous phase scans	5mm (reformat from 1.25–2.5mm for MDCT)	

MRI	Area scanned	Sequence	Plane	Slice thickness	Notes
	Abdomen	T1W T2W T2W T1W + Fat Sat +/- Gad	Axial Axial Coronal Cor +/or Ax		Either as 2D or 3D. Reformat 3D as coronals
Other					

3 Testicular Cancer

3.1 Introduction

Testicular cancer is an uncommon condition affecting 7 in 100,000 men per annum, although it is the commonest cancer in young adults. In the LCA, this represents around 350 new cases each year. The peak age is 30–35 years and there has been a 120% increase in detected cases since 1975.

Centralisation of testicular cancer services into supra-network teams occurred in 2002. The 5-year cancer-specific survival rate has increased steadily to over 95%.

This guideline is specifically related to the management of newly presenting testicular cancers to primary care providers and local centres within the LCA. Onward referral after primary treatment is the responsibility of three supra-network centres that are linked to different sectors of the LCA. Each of these has its own guideline reviewed annually. North West London (NWL) refers to Charing Cross or Mount Vernon, South West London (SWL) refers to The Royal Marsden Hospital (RMH) and South East London (SEL) to Bart's/Guy's. The local care guideline is based on the recommendations of the European Association of Urology (EAU) guideline (2011). It also reflects the recent National Institute for Health and Care Excellence (NICE) guidance on fertility (and cancer treatment) and use of testicular prosthesis after orchidectomy.

The critical review of this guidance begins with peer review at the EAU level. The supra-network review is carried out by named surgeons/clinical/medical oncologists annually. This guidance is based on the recommendations of the EAU and NICE guidance. This guidance was circulated to all members of the Urology Pathway Group for comments before amendments and sign off. The group recognises that there are subtle differences in the follow-up regimes within the supra-networks and have advised that the leads of these centres work towards a unified pathway over time.

This guideline is meant to direct referrals from GPs, radiologists and urologists to the appropriate centre without unnecessary delay or inappropriate investigation. It also informs the local and supra-specialist centres of their role in the patient pathway with respect to delivery of radio/chemotherapy when necessary after definitive primary treatment at the local centre.

3.1.1 National guidelines for the management of testicular cancers

These guidelines are based on existing peer-reviewed documents produced by the EAU (2013), with the most recent version completed in 2011, and local modification reflecting the established referral pathways in London to supra-network specialist centres.

3.1.2 Referrals: primary care to unit

These are detailed in the NICE *Referral Guidelines for suspected cancer* published in 2005 (Clinical Guideline 27, available at: www.nice.org.uk).

A patient with the following symptoms, signs or findings of investigations should be referred under the 2 week wait (2ww) rule:

- swelling or mass in the body of the testis
- suspicious testicular lesion found on imaging.

3.1.3 Referrals: unit to supra-network multidisciplinary team

All patients who meet the appropriate criteria should be referred to the supra-network centre:

- all patients diagnosed with testicular cancer post-orchidectomy
- high-risk patients (multiple lung metastases, brain metastases or gross elevation of markers prior to orchidectomy).

Supra-networks for testicular cancer:

- North West London (host – Charing Cross)
- South West London (host – RMH)
- South East London (host – Guy's and St Thomas' (GST)).

3.2 Diagnosis

Patients presenting with a swelling in the scrotum should be examined carefully and an attempt made to distinguish between lumps arising from the body of the testis and other scrotal swellings.

In those cases in which there is sufficient clinical suspicion, a 2ww referral should be made to the local urology unit.

Any patient with doubtful epididymo-orchitis or orchitis not resolving within 2 weeks should have an urgent scrotal ultrasound and be referred under the 2ww rule if suspicion is raised.

3.2.1 Unit assessment

Physical examination confirms the solid mass in the testis and assessment of contra-lateral testis determines size and consistency; abdominal palpation to exclude large retroperitoneal mass; observe for gynaecomastia; screen for distant disease.

- Ultrasound confirmation
- Blood taken for alpha-fetoprotein (AFP), beta human chorionic gonadotrophin (BhCG) and lactate dehydrogenase (LDH)
- Total testosterone, luteinising hormone (LH), follicle-stimulating hormone (FSH)
- Chest X-ray
- Other staging investigations should be deferred until review at the supra-network centre.

Offer advice and referral for sperm banking to an agreed centre, subject to local funding arrangements.

Advice regarding a testicular prosthesis – it is recommended in separate NICE guidance that this should always be discussed with the patient.

3.3 Primary surgical management

Orchidectomy through an inguinal incision with division of the cord at the internal ring.

The testis blood supply should be occluded with non-crushing clamps on the spermatic cord prior to mobilisation and delivery of the testis into the wound.

If the patient has elected to have a testicular prosthesis, it should be inserted through the inguinal wound.

Biopsy of the contra-lateral testis is advised for:

- contra-lateral testicular atrophy (<12ml)
- history of maldescent
- contra-lateral microlithiasis
- severe oligospermia
- **not required in patients over 40 years old.**

A small open biopsy through the scrotum with fixation in Bouin's solution.

3.4 Pathological assessment

All pathology reporting should comply with the Royal College of Pathologists (RCPath) tumour pathways and datasets and staged according to TNM 7. The version of TNM used must be clearly stated in all pathology reports.

- www.rcpath.org/publications-media/publications/datasets
- www.uicc.org/resources/tnm/publications
- *TNM Classification of Malignant Tumours* (7th edition) – Edge SB, Byrd DR, Compton CC et al. (eds) (2010), *AJCC Cancer Staging Manual* (7th edition). New York: Springer.

The RCPath guidelines, published in October 2007, are now published (May 2014) and is reflective of the guidance set out below.

Tumour typing should be performed according to the WHO guidelines (2004). The use of the British Testicular Tumour Panel (BTTP) system is no longer recommended.

- Eble J, Sauter G, Epstein J and Sesterhenn I (2004), *Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs.* Lyon: IARC Press.

Reports should also include the size of the tumour, the presence or absence of rete involvement and the estimated percentages of each tumour sub-type if more than one type is present and has been shown to have prognostic implications.

3.4.1 Summary dataset for testicular tumour reports

(based on draft RCPath testis dataset, December 2013)

The core macroscopic data items are as follows:

- specimen type
- tumour location
- tumour description
- macroscopic tunica vaginalis invasion
- cord invasion
- multifocality
- maximum tumour size.

The core microscopic data items are as follows:

- tumour type(s) including % of each sub-type of germ cell present
- maximum tumour diameter (if not assessed macroscopically)
- lymphovascular invasion
- rete testis stromal invasion
- hilar soft tissue or direct spermatic cord invasion (pT3)
- tumour at spermatic cord margin
- microscopic tunica vaginalis invasion
- intratubular germ cell neoplasia (ITGCN) identified
- margin status (partial orchidectomy)
- tumour viability (post-chemotherapy)
- pT stage (TNM 7)
- SNOMED coding.

3.4.2 Pathology review

All testicular tumour cases referred to the central testicular multidisciplinary team (MDT) must have a pathology review at the specialist central laboratories (RMH, GST and Imperial/Charing Cross). Pathology from metastases and nodal dissections etc. must also be reviewed if not reported by the specialist team. Pathologists must ensure that cases, usually as blocks plus pathology reports and photographs, are sent in a timely manner (i.e. as soon as the local report is completed) to the central referral laboratory specifically stating that they are for the testicular MDT meeting.

A copy of the pathology review report must be sent to the originating pathologist at the time of review so that any discrepancies can be noted locally. Original slides and blocks must be returned within a maximum of 12 weeks to the local laboratory.

3.4.3 Quality assurance and External Quality Assessment

Lead urological pathologists must undertake the National Urological Pathology External Quality Assessment (EQA) and provide evidence of participation to their local and/or specialist MDTs. Other pathologists undertaking urological pathology reporting should either participate in the UK National Urological Pathology EQA or a local scheme which includes urological cases. Laboratories undertaking diagnostic work must have Clinical Pathology Accreditation.

3.5 Referral to the supra-network centre

- All patients should be referred to the centre within 24 hours of surgery (unless they are in the high-risk category).
- Pathological blocks should be referred directly.
- All patients will be reviewed at the supra-network centre within 7 working days of receipt of the faxed referral.

- All patients will be reviewed within 2 weeks of surgery.
- Tumour markers should be repeated 5–7 days post-orchidectomy.

3.6 Organ-sparing surgery

Although it is not recommended in the presence of a non-tumoural contra-lateral testis, surgery can be considered in specific circumstances when the tumour volume is less than 30% testis volume:

- synchronous bilateral testicular tumours
- metachronous contra-lateral tumours
- tumour in a solitary testis
- suspected testicular stromal tumour or other indeterminate lesions.

Referrals to be centralised:

- NWL – Mr Jonathan Ramsay
- SWL – St George's andrology team (Mr Ben Ayres and Mr Nick Watkin)
- SEL – Guy's andrology team (Mr Majed Shabbir (GST) and Mr Gordon Muir (King's)).

There should be discussion at the weekly andrology/testis MDT meeting in the agreed centres for indeterminate lesions and further review at supra-network for suspected testicular tumours.

3.7 Testicular stromal tumours

These tumours account for 4–5% of adult testicular neoplasms and include Leydig cell, Sertoli cell and epidermoid tumours.

They are diagnosed following:

- incidental ultrasound finding
- infertility investigations
- hormonal disorder e.g. gynaecomastia.

They are frequently small and often misinterpreted as germ cell tumours. It is recommended that an organ-preserving approach is adopted for all small intra-parenchymal lesions in order to obtain histological diagnosis, provided the remaining parenchyma is sufficient for endocrine function.

Around 90% of stromal tumours are benign (and all epidermoid tumours). Features suggestive of malignancy include:

- size >5cm
- cytological atypia
- increased mitotic activity
- necrosis, infiltration and vascular invasion.

For benign tumours, a risk-adapted surveillance is recommended in the absence of clinical evidence of a suitable follow-up regime.

For malignant tumours, referral to the supra-network is recommended for computed tomography (CT) staging and a tailored management plan.

3.8 Retroperitoneal node dissection

The recommendations for this surgery are detailed in the supra-network guidelines for each of the three networks that link with the LCA.

It is anticipated that the surgery will be delivered on an east–west axis within the combined LCA/LC boundaries, in two centres by two teams of surgeons.

3.9 Chemotherapy

For chemotherapy, the supra-regional network guidance will continue to be used. This guidance can be found in Annex 3.1.

3.10 Follow-up

All patients are followed up under the supervision of the testicular supra-network to which the patient was referred. There are subtle differences between the teams and at the time of writing the follow-up pathways have not been unified for LCA patients. There is a plan to review this over the next 12 months.

- Annex 3.2: Follow-up guidelines for the South East London supra-regional testicular cancer network hosted by Bart's Health (Anglia, North East London, North Central London and South East London)
- Annex 3.3: Follow-up guidelines for the North West London supra-regional testicular cancer network
- Annex 3.4: Follow-up guidelines for the South West London supra-regional testicular cancer network.

3.11 Research and trials

One of the great opportunities of the integrated cancer system is to improve patient access to clinical trials and research. There are already many trials and research projects running in individual centres in the LCA, usually with a list of available trials on individual Trust websites. In the absence of this information, patients should be encouraged to ask about their eligibility for trial entry. This is particularly relevant in the chemotherapy setting.

It is the intention of the Urology Pathway Group to standardise the availability of National Cancer Research Institute (NCRI) trials across the LCA in due course, and to publicise unbadged single centre research projects where these are available in individual sites. The ultimate aim of the Pathway Group is to populate and regularly update a list of trials open to recruitment on the urology section of the LCA website.

Annex 3.1: Testicular guidelines for systemic therapy

These guidelines refer to the systemic treatment of testicular cancer in the adjuvant and metastatic settings. Further information and evidence are available from the supra-regional testicular guidelines for the North West London Cancer Network, the South West London Cancer Network and the Anglian Testicular Cancer Group (hosted at St Bartholomew's). Only systemic therapy will be discussed in this section and other treatment options for these patients are discussed in the relevant sections of the network guidelines.

Management depends on the histological type and stage of the disease. WHO Classification (2009) is used to define stage and prognosis:

- *UICC TNM Classification of Malignant Tumours* (7th Edition) (2009), 249–254.

The possibility of the patient entering into a clinical study will be discussed at the MDT meeting. International Germ Cell Cancer Collaborative Group (IGCCCG) prognostic groups are available in the supra-regional guidelines.

The standard treatments are as follows.

Seminoma

Spermatocytic seminoma are rare and occur in an older population (> 60 years). They never metastasise unless they show sarcomatoid change and are managed with a policy of surveillance.

Stage I seminoma

Standard treatment: chemotherapy:

Carboplatin (AUC x 7) x 1 cycle. An EDTA clearance is required to determine glomerular filtration rate (GFR).

IGCCCG – Good prognosis (metastatic seminoma)

There is no consensus on the treatment of metastatic seminoma:

- 3- or 5-day BEP (bleomycin, etoposide and cisplatin) (generally acceptable for patients with >50mm abdominal masses)*
- 4 cycles of EP (equivalent to 3 cycles of BEP in one trial) can also be considered
- carboplatin AUC 10 (3 or 4 cycles depending on whether or not complete response (CR)was achieved after the first cycle) is an acceptable option for patients with contraindications to (B)EP
- for Stage IIa and b excellent results have been reported in small series after giving a single cycle of carboplatin AUC 7 followed 3–4 weeks later by limited para-aortic radiotherapy 30 Gy in 15#
- for older patients, particularly those who smoke, it is probably wise to consider avoiding bleomycin
- radiotherapy alone to a dog-leg field should only be considered where chemotherapy is contraindicated.

IGCCCG – Intermediate prognosis (metastatic seminoma)

More advanced cases of seminoma which fall into the intermediate prognosis category should receive 4 cycles of standard 3- or 5-day BEP or VIP (vinblastine, ifosfamide and cisplatin) if patients have pre-existing impaired pulmonary function.

Non-seminomatous germ cell tumours (NSGCT)

Stage I NSGCT

Patients are categorised into high (40%) or low (20%) risk of recurrence according to the presence or absence of lymphatic or vascular invasion as defined by histological review by the designated pathologist.

Low-risk cases

These patients will enter the surveillance protocol unless they specify that they wish to have adjuvant chemotherapy or surgery (see below).

High-risk cases

There are three options for these patients:

1. Surveillance – associated with a relapse rate of 40% (within 3 years).
2. Adjuvant therapy – 2 cycles of BEP (etoposide 360mg/m^2) or 1 cycle of BEP (etoposide 500mg/m^2).
3. Primary retroperitoneal lymph node dissection (RPLND) is a third option that carries a higher risk of recurrence than adjuvant chemotherapy. It is essentially a more accurate staging procedure. Many patients who are found to have pathological Stage II disease are offered adjuvant chemotherapy.

IGCCCG – Good prognosis metastatic NSGCT

- BEP (bleomycin, etoposide, cisplatin) 3- or 5-day[*] x 3 cycles over 9 weeks (total etoposide dose 500mg/m^2 per cycle).

IGCCCG – Intermediate and poor prognosis metastatic NSGCT

- BEP 3- or 5-day[*] x 4 cycles over 12 weeks (total etoposide dose 500mg per cycle).
- POMB/ACE[†]
- C BOP BEP (poor prognosis only).

NB: For those patients who have normal markers, particularly if their orchidectomy sample showed teratoma, consideration should be given to the possibility of nodal disease being teratoma. In this situation a negative positron emission tomography (PET) scan may be useful in guiding these patients to a primary template RPLND instead of proceeding to chemotherapy.

Relapsed disease

In relapse following first-line treatment, the localisation and histology of the primary tumour, the response to first-line treatment, the duration of previous remissions, as well as the level of the tumour markers AFP and hCG at the time of relapse or progression are known prognostic indicators.

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[*] There is no significant difference in long-term toxicity between 3- or 5-day BEP when 3 cycles are being given. If 4 are required, then there is an increased risk of ototoxicity when the 3-day BEP is given. This should be explained to the patient when they are making their decision.

[†] POMB/ACE is the name of a combination of chemotherapy drugs used to treat testicular cancer and other germ cell tumours. It is made up of the drugs: P – CisPlatin; O – Vincristine, which is also called Oncovin; M – Methotrexate; B – Bleomycin; A – Actinomycin, which is also called Dactinomycin; C – Cyclophosphamide; E – Etoposide, which is also known as Eposin, Etopophos or Vepesi

Relapse management is therefore dependent upon previous therapy, time to relapse and site of the relapse. Please refer to the relevant supra-regional guidelines for chemotherapy regimens and recommendations for referral for high-dose chemotherapy.

Non germ cell tumours of the testis

Epidermoid cysts

This is a rare diagnosis in adolescents. It is difficult to entirely exclude monomorphic teratoma differentiates. Recommend CT staging and then limited follow-up to 5 years.

Sertoli cell tumours and Leydig cell tumours

These are indolent malignant tumours which rarely metastasise. Recommend CT staging and then limited follow-up for 5 years. The optimum management for metastatic disease is uncertain. In those with Stage I disease and adverse histological features (high mitotic rate and/or vascular invasion), consideration of a primary RPLND is recommended.

Testicular lymphoma

This requires urgent referral to the regional specialist and should be managed in accordance with relevant lymphoma protocol.

Annex 3.2: South East London testicular cancer follow-up management protocols

Supra-regional follow-up management protocols for patients in SEL

All patients should be followed up on protocol by the designated oncology team. The supra-regional MDT has agreed a minimum follow-up schedule.

Patients at high risk of intratubular germ cell neoplasia (ITGCN) in the remaining testis (i.e. under 30 years of age at primary diagnosis and with a testicular volume less than 12ml, or with a history of testicular maldescent), who did not have a biopsy at the time of orchidectomy, should be offered the opportunity to consider a contra-lateral biopsy 2 years after completion of treatment if they have not recovered fertility.

The purpose of this document is to form the basis of an agreed follow-up strategy for the testicular supra-network.

The schedule has been split between Stage I and metastatic patients. Within the Stage I group there are groups with differing relapse risk. Attention has been paid as to whether or not a patient has had adjuvant therapy.

General

- Blood pressure and weight should be measured annually.
- At 5 and 10 years – hormone and lipid profile should be measured.
- If patient has had chemo: full blood count (FBC), urea and electrolytes (U&E), liver function tests (LFTs) – annually if normal.

Stage 1 seminoma – surveillance

Year 1:

- tumour markers every 6 weeks (AFP and hCG and LDH)
- CT abdomen – 3 months and 1 year (scan pelvis only if prior history of scrotal or other pelvic surgery).

Year 2:

- tumour markers every 12 weeks
- CT abdomen – 2 years.

Year 3:

- tumour markers every 4 months.

Years 4 and 5:

- tumour markers every 6 months, hormone profile and lipids and blood pressure
- CT abdomen – 5 years.

Years 6–10:

- tumour markers annually.

Stage 1 seminoma – received adjuvant carboplatin

Year 1:

- 1 month post-chemotherapy – FBC, U&E, LFTs and tumour markers
- then tumour markers 3-monthly
- CT abdomen – 1 year.

Year 2:

- tumour markers 4-monthly
- CT abdomen – 2 years.

Year 3:

- tumour markers 6-monthly.

Years 4–5:

- tumour markers 6-monthly.

Years 6–10:

- tumour markers annually.

Non-seminoma – Stage 1 surveillance

Low risk – no vascular invasion; high risk –with vascular invasion.

Year 1:

- low risk – tumour markers every 6 weeks
- high risk – tumour markers every 4 weeks
- CT abdomen – 3 months and 1 year.

Year 2:

- tumour markers 8-weekly
- CT abdomen – 2 years.

Year 3:

- tumour markers 3-monthly.

Year 4:

- tumour markers 4-monthly.

Year 5:

- tumour markers 6-monthly.

Years 6–10:

- tumour markers annually.

Non-seminoma – Stage 1 (adjuvant chemotherapy or primary RPLND)

Year 1:

- tumour markers 3-monthly
- CT abdomen – 1 year.

Year 2:

- tumour markers 3-monthly
- CT abdomen – 2 years.

Year 3:

- tumour markers 4-monthly.

Year 4:

- tumour markers 6-monthly.

Year 5:

- tumour markers 6-monthly.

Year 6–10:

- tumour markers annually.

Metastatic disease

Year 1:

- tumour markers 2-monthly (monthly if not normalised or post-relapse therapy)
- CT post-treatment; if normal – further scan of affected area at 1 year
- if not normal – repeat every 4–6 months until stops changing and consider resection.

Year 2:

- tumour markers 3-monthly (2-monthly if post-relapse)
- CT abdomen or of any involved area at 2 years.

Year 3:

- tumour markers 4-monthly (3-monthly if post-relapse).

Years 4–5:

- tumour markers 6-monthly (4-monthly if post-relapse in year 4 , 6-monthly in year 5).

Years 6–10:

- tumour markers annually.

				Year 1	Year 2	Year 3	Year 4	Year 5	Years 6–10
Seminoma	**Stage 1**	Surveillance	Tumour markers	6 weeks	12 weeks	4 months	6 months		Annually
			Hormone profile				6 months		
			Blood pressure				6 months		
			CT abdomen	3 months and 1 year	2 years		5 years		
		Received adjuvant carboplatin	FBC, U&E, LFTs	1 month					
			Tumour markers	1 month then 3-monthly	4-monthly	6-monthly	6-monthly		Annually
			CT abdomen	1 year	2 years				
Non-seminoma	**Stage 1**	Surveillance	Tumour markers	*Low risk – every 6 weeks **High risk – every 4 weeks	8 weeks	3 months	4 months	6 months	Annually
			CT abdomen		2 years				
		Received adjuvant chemo or 1° RPLND	FBC, U&E, LFTs	1 month					
			Tumour markers	3 months	3 months	4 months	6 months	6 months	Annually
			CT abdomen	1 year	2 years				
Metastatic disease Good prognosis			FBC, U&E, LFTs	1 year	2 years	3 years	4 years	5 years	6–10 years
			Tumour markers	2-monthly or monthly if not normalised or post-relapse therapy	3-monthly or 2-monthly if post-relapse	4-monthly or 3-monthly if post-relapse	6-monthly or 4-monthly if post-relapse	6-monthly	Annually
			CT	Post-treatment CT – if normal, 1 year	2 years – CT abdomen or any involved area				
				Post-treatment CT – if not normal, every 4–6 months until it stops changing and consider resection					

Annex 3.3: North West London testicular cancer follow-up management protocols

North West London Testicular Cancer Supra-network

Stage I seminoma – 10-year surveillance protocol							
Orchidectomy date		Pre-op AFP		Pre-op hCG		Pre-op LDH	

At each attendance check neck and abdominal lymph nodes, nipples, contralateral testis and ask about backache and if patient is performing testicular self-examination.

Appointment schedule	Date	Next appointment	CT	CXR	AFP	hCG	Late effects
Baseline		1 month	TAP	✓	✓	✓	
1 month		2 months		✓	✓	✓	
3 months		3 months		✓	✓	✓	
6 months		3 months	Abdomen	✓	✓	✓	
9 months		3 months		✓	✓	✓	
1 year		3 months	Abdomen	✓	✓	✓	
15 months		3 months		✓	✓	✓	
18 months		3 months		✓	✓	✓	
21 months		3 months		✓	✓	✓	
2 years		4 months	Abdomen	✓	✓	✓	✓
28 months		4 months		✓	✓	✓	
32 months		4 months		✓	✓	✓	
3 years		6 months	Abdomen	✓	✓	✓	
3.5 years		6 months		✓	✓	✓	
4 years		6 months		✓	✓	✓	
4.5 years		6 months		✓	✓	✓	
5 years		1 year		✓	✓	✓	✓
6 years		1 year		✓	✓	✓	
7 years		1 year		✓	✓	✓	
8 years		1 year		✓	✓	✓	
9 years		1 year		✓	✓	✓	
10 years		1 year		✓	✓	✓	✓

Notes:

1. CT scan of thorax, abdomen and pelvis (TAP) at initial staging.
2. CTs subsequently are routinely of the abdomen only unless clinically indicated that pelvis is at high risk.
3. In seminoma, tumour markers should be checked just at the clinic visits.

Stage I NSGCT – 10-year surveillance protocol							
Orchidectomy date		Pre-op AFP		Pre-op hCG		Pre-op LDH	

At each attendance check neck and abdominal lymph nodes, nipples, contralateral testis and ask about backache and if patient is performing testicular self-examination.

Appointment schedule	Date	Next appointment	CT	CXR	AFP	hCG	Late effects
Baseline		1 month	TAP	✓	✓	✓	
1 month		1 month		✓	✓	✓	
2 months		1 month		✓	✓	✓	
3 months		1 month	Abdomen	✓	✓	✓	
4 months		1 month		✓	✓	✓	
5 months		1 month		✓	✓	✓	
6 months		1 month		✓	✓	✓	
7 months		1 month		✓	✓	✓	
8 months		1 month		✓	✓	✓	
9 months		1 month		✓	✓	✓	
10 months		1 month		✓	✓	✓	
11 months		1 month		✓	✓	✓	
1 year		2 months	Abdomen	✓	✓	✓	
14 months		2 months		✓	✓	✓	
16 months		2 months		✓	✓	✓	
18 months		2 months		✓	✓	✓	
20 months		2 months		✓	✓	✓	
22 months		2 months		✓	✓	✓	
2 years		3 months		✓	✓	✓	✓
27 months		3 months		✓	✓	✓	
30 months		3 months		✓	✓	✓	
33 months		3 months		✓	✓	✓	
3 years		4 months					

Appointment schedule	Date	Next appointment	CT	CXR	AFP	hCG	Late effects
40 months		4 months					
44 months		4 months					
4 years		6 months					
4.5 years		6 months					
5 years		6 months					✓
5.5 years		6 months					
6 years		1 year					
7 years		1 year					
8 years		1 year					
9 years		1 year					
10 years		Discharge					✓

Notes:
1. CT scan of TAP at initial staging.
2. CTs subsequently are routinely of the abdomen only unless clinically indicated that pelvis at high risk.
3. In NSGCT, tumour markers should be checked just at the clinic visits.

Post-chemotherapy follow-up protocol (seminoma and NSGCT)

At each attendance check neck and abdominal lymph nodes, nipples, contralateral testis and ask about backaches and if patient is performing testicular self-examination.

Appointment schedule	Date	Next appointment	CT	CXR	AFP	hCG	Late effects
1 month post-therapy		1 month	Sites of disease	✓	✓	✓	
2 months		1 month			✓	✓	
3 months		1 month		✓	✓	✓	
4 months		2 months			✓	✓	
6 months		2 months		✓	✓	✓	
8 months		2 months			✓	✓	
10 months		2 months		✓	✓	✓	
1 year		3 months	Abdomen/Sites of disease		✓	✓	
15 months		3 months		✓	✓	✓	
18 months		3 months			✓	✓	
21 months		3 months		✓	✓	✓	

Appointment schedule	Date	Next appointment	CT	CXR	AFP	hCG	Late effects
2 years		4 months	Abdomen/Sites of disease		✓	✓	
28 months		4 months		✓	✓	✓	✓
32 months		4 months			✓	✓	
3 years		6 months	Abdomen/Sites of disease	✓	✓	✓	
3.5 years		6 months			✓	✓	
4 years		6 months		✓	✓	✓	
4.5 years		6 months			✓	✓	
5 years		1 year		✓	✓	✓	✓
6 years		1 year					
7 years		1 year		✓			
8 years		1 year					
9 years		1 year		✓			
10 years onwards		1 year		CXR alternate visits			✓

Notes:
1. If post-treatment CT scan is not normal the case must be discussed at the supra-network MDT.
2. Late effects parameters to be assessed at the indicated clinic visits include: blood pressure, height and weight, urea and creatinine, fasting cholesterol (HDL and LDL) triglycerides, fasting glucose, FSH, LH and testosterone.

Stage I seminoma post-adjuvant treatment follow-up

Standard follow-up protocol

Stage I seminoma follow-up after adjuvant chemotherapy or radiotherapy

Clinic visits:

- year 1: 3-monthly clinic visits
- years 2–5: 6-monthly clinic visits
- year 6 onwards: annual visits.

Imaging:

- CT scan of TAP should be performed at 18–24 months
- chest X-ray (CXR) should be performed at alternate visits and stopped at the end of year 3.

Tumour markers:

- follow-up post-adjuvant therapy for Stage I seminoma
- serum AFP, hCG and LDH at clinic visits only.

Late effects:

- investigations at years 2, 5 and 10
- blood pressure, height and weight
- urea and creatinine, fasting cholesterol (HDL and LDL) triglycerides, fasting glucose, FSH LH and testosterone.

Annex 3.4: South West London testicular cancer follow-up management protocols

The guiding principle of these guidelines is to allow the best possible care for each patient in the most convenient location. That will sometimes mean the patient has to travel further than their nearest hospital for access to specialist treatment. Having received specialist treatment, the network has been structured so that follow-up can usually be provided at the nearest cancer unit. This has been accomplished by specifying the appropriate intervals and investigation for follow-up of patients at different stages of their cancer journey, and by ensuring that surgeons and oncologists working at the centre also attend the unit MDT and joint cancer clinic from which the patients have been referred.

Due to the intensive nature of follow-up, and the high proportion of these patients entered into clinical trials, most of them will require follow-up at RMH. This should present less of a problem for this patient group, as they are typically young men with good performance status, for whom travelling is not a major problem.

Follow-up schedules

In each case:

- markers – AFP, hCG and LDH
- CT scans should be of abdomen only unless stated.

Late effects are assessed after chemotherapy and radiotherapy at 2 and 5 years. Patients on follow-up after 5 years – assess every 5 years subsequently.

Non-seminoma germ cell tumour: Stage I – surveillance

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical	X		X		X		X		X		X	X
Markers	X	X	X	X	X	X	X	X	X	X	X	X
CXR	X		X		X		X		X		X	X
CT abdo			X									X
Year 2								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical			X			X			X			X
Markers			X			X			X			X
CXR			X			X			X			X
CT abdo												X
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR				X				X				X
CT												
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR						X						X
CT												
Year 5												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR						X						X
CT												

* Late effects:

– Clinical examination including blood pressure measurement, height and weight

– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Discharge after 5 years.

Follow-up after adjuvant chemotherapy

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical	X		X			X			X			X
Markers	X		X			X			X			X
CXR			X			X						X
CT abdo						X						
Year 2								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR												X
CT												
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 5								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												

* Late effects:

– Clinical examination including blood pressure measurement, height and weight

– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Discharge after 5 years.

Seminoma Stage 1 – surveillance

CT scans of abdomen only unless pelvis is at high risk.

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical			X			X			X			X
Markers			X			X			X			X
CXR						X						X
CT						X						X
Year 2											*late effects**	
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical			X			X			X			X
Markers			X			X			X			X
CXR						X						X
CT						X						X
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR												X
CT												X
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												X
Year 5												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												X

* Late effects:

– Clinical examination including blood pressure measurement, height and weight

– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Seminoma Stage I: single agent carboplatin

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical	X		X			X			X			X
Markers	X		X			X			X			X
CXR						X						X
CT												X
Year 2						*late effects**						
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR												X
CT												X
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 5								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												X

* Late effects:

– Clinical examination including blood pressure measurement, height and weight

– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Annual follow-up until 10 years, clinical and markers.

Seminoma follow-up: para-aortic radiotherapy

CT of pelvis only unless there is a clinical reason to scan abdomen.

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical			X			X			X			X
Markers			X			X			X			X
CXR			X			X			X			X
CT pelvis												(X)
Year 2								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR				X				X				X
CT pelvis												(X)
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 5								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT pelvis												(X)

* Late effects:
– Clinical examination including blood pressure measurement, height and weight
– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Discharge after 5 years.

Seminoma: Stage IIa/b – follow up after carboplatin and radiotherapy

CT scans should be abdomen/pelvis.

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical			X			X			X			X
Markers			X			X			X			X
CXR			X			X						X
CT			X									X
Year 2								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR												X
CT												X
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												
Year 5								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												X

* Late effects:
– Clinical examination including blood pressure measurement, height and weight
– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Annual follow-up until 10 years, clinical and markers.

Metastatic NSGCT and seminoma Stage IIc–IV post chemotherapy

CT until CR with or without surgery, frequency determined by MDT.

Year 1												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical		X		X		X		X		X		X
Markers		X		X		X		X		X		X
CXR				X				X				X
CT												
Year 2								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical				X				X				X
Markers				X				X				X
CXR				X				X				X
Year 3												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
Year 4												
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
Year 5								*late effects**				
Month	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Clinical						X						X
Markers						X						X
CXR												X
CT												X

* Late effects:
– Clinical examination including blood pressure measurement, height and weight
– Cardiac history, U&E, fasting cholesterol (HDL and LDL), triglycerides, fasting glucose

Discharge seminoma patients at 5 years. For NSGCT patients follow up annually until 10 years and then bi-annually. Stop performing CXRs at 10 years.

4 Bladder Cancer

4.1 Introduction

Bladder cancer is an uncommon cancer and one which is frequently overlooked. About 10,000 new cases per annum will be diagnosed in England and Wales. Across the LCA, 25% of Londoners will die within the first year of diagnosis. It is widely accepted that bladder cancer is one of the most expensive cancers to treat in terms of time, resources and finance.

This guideline is closely based on the European Association of Urology (EAU) Guideline (2013). It also amalgamates the South and West London cancer network guidelines from the previous cancer networks. It has been developed by the LCA Urology Pathway Group.

The guidelines are designed as a reference for local urology departments, central cancer units and to inform purchasers about what to expect from their local service. Suggestions for local audits to continually improve the service and knowledge outcomes are included. They are designed to be practical with the appropriate use of resource.

There are several key areas that reflect the local healthcare system. The use of Bacillus Calmette-Guérin (BCG) therapy is recommended for 1 year and the role of mitomycin C as an instillation in all cases is questioned. Patients should be seen by urologists with a special interest in bladder cancer in appropriate clinics and surveyed on cystoscopy lists by urology subspecialty teams with modern cystoscopic techniques to maximise diagnosis and treatment of early tumours. High-risk cancers should be identified and managed by teams with an interest in bladder cancer to ensure prompt treatment with intravesical instillations or by radical surgery. Muscle invasive disease needs referral to centres equipped to provide information regarding chemotherapy, radiotherapy and surgery. Practical advice on follow-up after major intervention is also included.

4.2 Management of non-muscle invasive bladder cancer

4.2.1 Urothelial carcinoma of the urinary bladder

Diagnosis

Some 80% of patients with a bladder tumour will present with painless visible haematuria. These patients should be referred urgently to a haematuria clinic.

Presentations via other symptoms (e.g. irritative voiding symptoms, recurrent urine infections) may have been referred urgently, or via general urology clinics. The receiving clinician can upgrade the referral to an urgent suspected cancer if they so wish.

Audit recommendations:

- number of cases upgraded to a 2 week referral (2ww)/urgent suspected cancer (USC) by the department.

4.2.2 Haematuria

Haematuria should be divided into visible (VH) and non-visible haematuria (NVH). Haematuria should be assessed via a dedicated haematuria clinic.

Structure of haematuria clinic

Ideally, a haematuria clinic should provide urinalysis, history, examination, upper tract imaging and endoscopy at one visit, with time afterwards to explain the findings and any further action needed to the patient.

Urinalysis: a fresh, voided urine sample should be sent for microscopy and culture if abnormalities are detected on dipstick testing.

History: specific enquiry should be made about occupational exposure and smoking habits.

Relevant details of the presenting complaint and past history including medication should be noted.

Smoking cessation advice should be given and documented.

Examination: including abdominal, genital and rectal examination.

Investigations for VH

- Upper tract imaging: a computed tomography (CT) urogram should be arranged for the primary investigation of VH.
- Cystoscopy: flexible cystoscopy under local anaesthesia will be performed. In the presence of heavy haematuria, or when the imaging has shown an obvious bladder tumour, urgent general anaesthetic cystoscopy/transurethral resection of bladder tumour (TURBT) should be arranged.

Investigations for NVH

- Upper tract imaging: both urinary tract ultrasound and kidney, ureter and bladder (KUB) X-ray should be performed.
- Cystoscopy: flexible cystoscopy under local anaesthesia will be performed.
- If no cause for haematuria is found: blood pressure and urinary dipstick should be assessed for signs of renal disease and the patient referred accordingly.

If all normal the patient can be reassured and discharged.

Role of urine cytology

Cytology has high sensitivity for high-grade urothelial carcinoma and carcinoma in situ (CIS), but very low sensitivity for low-grade lesions. It is user-dependent and expensive. A negative result does not rule out the presence of a urothelial cancer and, as such, it does not have a role in routine haematuria clinics as a primary investigation.

4.2.3 Treatment

When a bladder tumour is seen on flexible cystoscopy or imaging, the patient should be booked on to an appropriate general anaesthetic list for TURBT. The National Cancer Plan specifies a time from initial referral to first definitive treatment of 62 days for 2ww referrals and from diagnosis to treatment of 31 days for all new cancers and subsequent treatments.

First therapeutic cystoscopy

This is an important step in both diagnosis and treatment. All findings should be accurately documented, and a bladder map produced for the notes.

Under anaesthesia (a general anaesthetic or spinal), a bimanual examination should be performed to assess the bladder. The urethra, prostate and bladder should be carefully inspected and size and location of tumours documented.

The bladder epithelium should be inspected, and visualisation of the ureteric orifices documented. All tumours should be completely resected, and their base biopsied with cold cup forceps and sent separately for histological analysis.

Areas of abnormal mucosa should be biopsied with cold cup biopsy forceps. Following resection, the bimanual examination should be repeated if a mass was felt pre-operatively.

Pathology reporting should follow the Royal College of Pathologists' recommendations (see section 4.9).

Audit recommendations:

- number of new patients
- number of samples at first resection
- base of tumour biopsies at first resection
- muscle in the specimen.

4.2.4 Imaging

Following diagnosis of a bladder tumour, the original urinary tract imaging should be reviewed and a CT urogram should be employed to fully assess the urinary tract as a baseline for all new urothelial carcinomas.

4.3 Management of non-invasive disease (pTa, pT1a/b CIS)

This represents 70–80% of newly diagnosed bladder cancers.

4.3.1 Prognostic groups

Non-muscle invasive bladder cancer can be divided into three prognostic groups: low, intermediate and high risk. Management of the groups differs, and high-risk tumours should be referred for discussion at the specialist multidisciplinary team (MDT) meeting.

Features allowing stratification are as follows:

- number of tumours at diagnosis: single, 2–7, >8
- recurrence at first review cystoscopy: <1 recurrence per year, >1
- size of tumours: <3cm, >3cm
- histology: Ta, T1
- presence of CIS: no, yes
- tumour grade: G1/G2, G3.

Recurrence and progression scores can be found at www.eortc.be/tools/bladdercalculator/.

4.3.2 Management of low-risk group

Low grade: <3cm, low number of tumours (single), Ta, no CIS, G1/G2.

- Single instillation of 40mg mitomycin C in 50ml saline within 24 (ideally 6) hours of resection.
- First review cystoscopy at 3 months, subsequent cystoscopy at 9 months; thereafter annually for 5 years.
- Any recurrences, reclassify and treat as per protocol.

Patients should be discharged after 7 years of clear cystoscopies.

Mitomycin C is a potent chemotherapy agent. The meta-analysis shows its role in decreasing rates of recurrence in low-risk bladder cancers, especially in those patients with a solitary small lesion. Mitomycin C should be given where possible in this group. Severe complications can arise in those patients who have a bladder perforation, significant resections or where there is bleeding. In these cases, or if there is doubt, the mitomycin C should be omitted as the risk outweighs the benefit to that patient.

4.3.3 Management of intermediate-risk group

Intermediate grade: >3cm, 2–7 tumours, recurrences, Ta/T1, G1/G2, no CIS.

- Re-scope under general anaesthetic at 3 months.
- If clear, continue 3-monthly cystoscopies until clear for 1 year, then 6-monthly for 3 years; thereafter annually for 10 years.
- Any recurrences, reclassify and treat as per protocol.
- If multiple recurrences, consider a course of mitomycin. If recurrences persist after mitomycin C course, or patient factors dictate (e.g. allergy), then consider course of BCG for one year.

4.3.4 Management of high-risk group

High grade: any size, G3, CIS, any T.

- If there is any doubt about the completeness of resection, or if the pathologist cannot positively identify muscle in the specimen, second look TURBT and epithelial biopsies are indicated 2–6 weeks after initial resection.
- Cystoscopy should be carried out on a specialist operating list by a dedicated bladder cancer surgeon using specialist cystoscopic imaging such as fluorescence cystoscopy or narrow band imaging.
- Following complete resection of all exophytic tumour, a course of BCG should be offered as below.
- Freshly voided urine cytology and review cystoscopy under general anaesthesia should be performed at 3 months.
- Targeted and random mucosal biopsies and biopsies of the prostatic urethra should be obtained.

G3 pT1 with multifocal CIS are at a particularly high risk and primary cystectomy should be discussed.

All high-risk tumours should be discussed at the central MDT, with histopathological review.

4.3.5 BCG therapy

Much discussion surrounds the use of BCG therapy at the time of writing.

BCG as a maintenance course has greater efficacy than just an induction course.

The 'SWOG' protocol of 30 instillations over 3 years is widely used but only 17% of patients make it through a course of this nature. A maintenance schedule is recommended but the optimal scheme is not known.

A recent meta-analysis recommends at least 1 year of BCG therapy.

We recommend an induction 6-week course followed by a 3-weekly course at 3 months, 6 months and 12 months post-TURBT. Further treatment should be discussed with the patient and depends upon tolerability and side effects as the therapeutic benefits after 1 year are not substantial.

Partial responders (fewer biopsies with CIS, fewer tumours) could have a second course of BCG (weekly x 3) but should be advised about the poor prognosis of BCG-resistant disease, and should also be counselled re cystectomy.

Non-responders should be advised that cystectomy is the safest option for them.

Non-responders unfit for surgery may be offered hyperthermia mitomycin C.

Definition of BCG failure:

- Muscle-invasive disease at any time during course of treatment (disease progression).
- Persistent disease at 3 and 6 months (additional BCG at 3 months can be of use but discuss with the patient the lower outcomes).
- Worsening of disease, development of CIS, or increase in number of tumours.

Audit recommendations:

- number of patients per unit with high-risk disease
- number of patients receiving BCG
- number of patients receiving intravesical chemotherapy
- rate of recurrences
- rate of progression to cystectomy/radiotherapy.

4.3.6 Role of second-look cystoscopy/re-resection

- When there is doubt about complete resection.
- When there are multiple or large tumours present.
- When there is no muscle present (especially in high-grade lesions).
- When further staging is required to determine treatment, e.g. prostatic urethral biopsies.

Re-resection should be carried out by a specialist bladder cancer surgeon who may be involved in the next step of management (e.g. cystectomy surgeon, surgeon aligned to radiotherapy team). This may require referral away from the unit to the cancer centre.

It cannot be overstated that the early intervention in high-risk non-muscle invasive bladder cancer may lead to better outcomes and every effort should be made to identify this risk group and ensure the multidisciplinary approach to the management accordingly.

4.4 Upper tract monitoring

4.4.1 Low- and intermediate-risk groups

Regular upper tract imaging is not indicated.

Imaging should be considered if symptoms occur, e.g. haematuria.

4.4.2 High-risk group

A CT urogram is required for baseline staging.

These are repeated annually for 5 years.

A computed tomography urography (CTU) or retrograde pyelogram should be performed in any patient with:

- unexplained haematuria
- frequent tumour recurrences near one ureteric orifice
- loin pain or evidence of upper tract obstruction
- positive cytology with a normal cystoscopy and negative bladder biopsies
- when a change in treatment policy is being considered (e.g. cystectomy).

4.5 Muscle-invasive bladder cancer

Muscle invasive, non-metastatic disease pT2 (at least) (T3, T4a on imaging) N0/1 M0.

4.5.1 Staging

- Initial management includes TURBT of the exophytic lesion to establish the diagnosis with random mucosal biopsies and loop resection biopsies of the prostate at 5 and 7 o'clock to fully locally stage the disease. A careful exam under anaesthesia must be performed.
- Staging should include CT of the thorax, abdomen and pelvis (TAP). An MRI of the pelvis may give more accurate local clinical staging.
- A bone scan should be performed if there is clinical suspicion of bone metastases, or if the alkaline phosphatase is elevated.

4.5.2 Neo-adjuvant chemotherapy

Neo-adjuvant chemotherapy has been shown in an individual patient data meta-analysis of randomised studies to confer a survival benefit, and should be offered to patients with muscle-invasive disease (T2–T4a), prior to definitive treatment with either surgery or radiotherapy, who fit the following criteria:

- Eastern Cooperative Oncology Group performance status (ECOG PS) 0 or 1
- normal renal function (glomerular filtration rate (GFR) >60ml/min)
- no major contraindication to chemotherapy.

Patients with bilateral hydronephrosis are not usually appropriate for neo-adjuvant chemotherapy. Selected patients with unilateral hydronephrosis may be appropriate after stenting of the affected kidney.

Appropriate standard treatment options for neo-adjuvant chemotherapy are:

- gemcitabine 1,000mg/m^2, days 1 and 8
- cisplatin 70mg/m^2

Repeated on 21-day cycle for a total of 3–4 cycles.

Accelerated MVAC:

- methotrexate 30mg/m^2
- vinblastine 3mg/m^2
- doxorubicin 30mg/m^2
- cisplatin 70mg/m^2
- repeated on 14 day cycle with granulocyte colony stimulating factor (G-CSF) support.

Chemotherapy alone is not recommended for primary therapy of localised bladder cancer as it rarely produces durable complete responses.

Adjuvant chemotherapy after radical cystectomy is under debate and is not currently considered a standard approach. However, it may be considered for patients with muscle-invasive bladder cancer where neo-adjuvant chemotherapy was not possible or appropriate.

Enrolment in clinical trials of neo-adjuvant and adjuvant chemotherapy is encouraged where available.

4.5.3 Local treatment

Patients should be offered one of three options for control of the disease in their bladder. There is no current evidence that any one option is superior to any of the other options in terms of survival. Entry into a suitable trial is strongly encouraged. Patients should be counselled about the risks and benefits of each approach and discuss options with the surgical and non-surgical oncologists undertaking each treatment.

Possible options are as follows.

Cystectomy

This is particularly suitable for fit patients with hydronephrosis (and mandated for those with bilateral hydronephrosis), bulky disease, severe irritative symptoms and with CIS unresponsive to BCG, and for patients unable to receive radiotherapy

Radiotherapy

May be offered as alternative to cystectomy in most patients. It is the best alternative for frail or elderly patients.

Selective bladder preservation

In patients receiving neo-adjuvant chemotherapy, selection of modality according to the response at repeat cystoscopy after 3 cycles of chemotherapy. Patients with good response (pT0 or pT1 disease at cystoscopy)

undergo radiotherapy while those with residual muscle invasive disease or widespread CIS undergo immediate cystectomy.

Cystectomy

Patients whose disease does not preclude it, and who are physically and mentally suitable, should be offered all types of urinary diversion. The modern reconstructions commonly available are ileal conduit and ileal neobladder.

Less common approaches such as recto-sigmoid reconstruction and Mitrofanoff ileal neobladder may be considered in patients wishing to avoid a stoma, but in whom urethral disease precludes orthotopic bladder replacement.

Those patients not suitable or willing to undergo a continent reconstruction will need an ileal conduit.

Involvement of the stoma therapist and/or urology clinical nurse specialist soon after diagnosis is essential. Patients should be offered the opportunity to meet a patient who has had a cystectomy and urinary diversion to help the decision-making process.

Pelvic lymph node dissection is also carried out to various levels according to the individual patient pathology and performance status.

Cystectomy should be performed within 31 days of decision to operate (or within 6 weeks of last chemotherapy if used).

Patients not receiving neo-adjuvant chemotherapy should be considered for post-cystectomy adjuvant chemotherapy.

4.5.4 Follow-up

The purpose of following up patients with invasive bladder cancer after radical exenterative surgery (and radiotherapy) is to detect the presence of local or distant recurrences as early as possible in order to be able to offer additional treatment when indicated. It is evident that patients who have symptomatic recurrence/progression also have a poor performance status and are less likely to be able to tolerate further treatment.

Follow-up after radical cystectomy

Follow-up should address the risks of recurrent disease and the complications of the reconstructive surgery. The risk of disease progression depends upon the tumour stage, e.g.:

- pT1 G3 50%
- pT4 N2 90+%.

Recurrence may develop in the pelvis or distantly and new tumours may occur in the remaining urothelium of the upper tracts and male urethra if not removed. The risk of recurrence is highest in the first 2 years after cystectomy and reduced in the third year to a low level after 3 years.

Disease developing in the upper tracts occurs in 5–15% of cases and 50% of these develop in the first 12 months after cystectomy. The most common site of new urothelial tumour occurrence is the male urethra if it has not been removed; the incidence is 5–13%. The risk of new urothelial tumours developing does not reduce with time, therefore lifelong follow-up and surveillance are required.

Urinary diversions are associated with mechanical problems due to the re-implantation of the ureters and monitoring needs to assess reflux, stenosis and associated renal function decline.

There are also metabolic consequences of urine diversion:

- vitamin B12 deficiency developing in 3–5 years
- hyperchloraemic acidosis (less common with ileal diversions)
- mild acidosis associated with ammonia absorption (with ileal diversions)
- increased incidence of stones
- reduced renal function.

Follow-up after urinary diversion

Year 1 – at 3–4-monthly intervals:

- metabolic checks
- ultrasound of the upper tract/residual
- electrolytes, creatinine levels and alkaline phosphatase
- base excess
- disease recurrence
- CT TAP – 6-monthly
- urethroscopy (or washout cytology)
- urine cytology – annually.

Years 2–3 – at 6-monthly intervals:

- ultrasound of the kidneys and reservoir
- electrolytes, creatinine levels and alkaline phosphatase
- base excess
- CT TAP
- urethroscopy (or washout cytology)
- urine cytology – annually.

Year 4 – at yearly intervals:

- ultrasound of the kidneys and reservoir
- electrolytes and creatinine levels
- base excess
- vitamin B12 levels
- CT TAP, 12-monthly
- urethroscopy (or washout cytology)

- urine cytology.

Year 5 and thereafter – at yearly intervals:

- ultrasound of kidneys and reservoir
- electrolytes and creatinine levels
- base excess
- vitamin B12 level
- colonoscopy in patients with ureterosigmoidostomy
- urethroscopy (or washout cytology)
- urine cytology.

Patients who have undergone radical radiotherapy or bladder preservation combined therapy should follow the same protocol, but omitting the ultrasound to assess upper tract dilatation and residual urine in reconstruction and the base excess estimation, and including regular cystoscopy.

New tumours may occur in the remnants of the urinary tract such as the urethra and the upper tract (ureters and renal pelvis). The risk of detecting new tumours in the urothelial remnants (5–15%) does not decrease with time.

Examination of the urethra, either endoscopic or by cytology following lavage with saline, should be lifelong. Although upper tract tumours are found infrequently after cystectomy, they are often advanced when detected. This and the need to survey the upper tracts for ureteric dilatation due to stenosis or stricture make upper tract imaging useful after cystectomy.

Tumour progression may be local, in regional lymph nodes or as distant metastatic spread. Some 15–20% of all cases of relapse after surgery occur locally in the true pelvis, while another 10–15% occur in the pelvic and retroperitoneal lymph nodes. Therefore, cross-sectional imaging of the abdomen and pelvis will detect up to 35% of all cases of progression.

While distant metastatic disease can be found in any organ, lung, bone and liver are the most common sites. More than 50% of patients who progress will do so with distant metastatic disease. Therefore, it would seem sensible to add cross-sectional imaging of the chest to that of the abdomen and pelvis.

Frequency of scans CT TAP:

- 6 months
- 12 months
- 24 months
- 36 months
- 48 months
- 60 months.

4.5.5 Radiotherapy

This is given to a minimum dose of 64 Gy over a 6.5-week period.

Patients not suitable for daily fractionated treatment may receive 30–36 Gy in 5–6# given weekly.

The BC 2001 trial has shown that concomitant 5-fluorouracil (500mg/m^2/day x 5 days as continuous infusion weeks 1 and 4) plus mitomycin (12mg/m^2, day 1) reduces invasive recurrence after radiotherapy by 50% and should be offered to all suitable patients.

Following radiotherapy, cystoscopy under general anaesthetic with biopsies of the scar and/or any residual disease should be performed, initially 6–8 weeks after radiotherapy. If clear, flexible cystoscopy should be performed at 6-monthly intervals. If the bladder does not appear normal then cystoscopy under anaesthesia should be carried out for a longer period to allow for biopsies to be taken.

CT follow-up imaging may be performed at 1, 2 and 5 years.

Patients with residual invasive disease who are fit enough can be treated with salvage cystectomy.

4.6 Bladder cancers other than urothelial carcinoma

Urothelial carcinomas account for 90–95% of bladder tumours seen in the UK.

Other histological types include the following.

4.6.1 Squamous cell carcinoma

Urothelial carcinoma may exhibit squamous differentiation, but pure squamous cell carcinomas (SCCs) may occur, often associated with chronic urinary tract infections, long-term catheterisation or schistosomiasis. These tumours are usually invasive at presentation. In non-metastatic patients, cystectomy is the treatment of choice. The role of adjuvant or neo-adjuvant chemotherapy has not been defined. Pre-operative radiotherapy could be considered in otherwise fit patients with high-risk disease (cT3b/T4 disease) to minimise the risk of local recurrence.

4.6.2 Adenocarcinoma of the bladder

This may arise in a urachal remnant (~30%) or de novo.

Careful imaging is required to exclude direct invasion of the bladder by a colonic primary.

Treatment is either partial or total cystectomy depending on the size and location of the tumour, and the fitness of the patient.

4.6.3 Small-cell carcinoma of the bladder

This is a rare, aggressive tumour with a poor prognosis. For localised small-cell carcinoma of the bladder, the best chance of disease control is primary chemotherapy and cystectomy or radiotherapy.
An appropriate chemotherapy regimen is carboplatin + etoposide (see Annex 4.1 for details).

Patients with metastatic small-cell carcinoma of the bladder should be offered palliative chemotherapy. Appropriate regimens are:

- carboplatin and etoposide
- CAV (cyclophosphamide, doxorubicin, vincristine).

4.6.4 Rhabdomyosarcoma

This is usually seen in children or young adults, and is managed by the paediatric oncology team.

4.7 Upper tract tumours

These may occur de novo, with no associated bladder tumour, or may present synchronously with a bladder tumour. The lifetime chance of a patient with a bladder tumour developing an upper tract tumour is about 4%, whereas a patient with an upper tract tumour has a 40% chance of developing a bladder tumour. The indications for monitoring the upper tracts in patients with a bladder tumour are given above.

Patients with an upper tract tumour should have regular cystoscopies following treatment of their tumour, initially at presentation, and then lifelong, with the frequency determined by the findings at previous cystoscopies.

4.7.1 Investigation of upper tract tumours

Patients with a suspected upper tract tumour should have a CTU, cystoscopy and ureteroscopy with biopsy of any suspicious lesions.

4.7.2 Management of upper tract tumours

This has traditionally been by nephroureterectomy, taking a cuff of normal bladder around the ipsilateral ureter. This remains the standard treatment, but with improving access to the upper ureter and collecting system endoscopically, more conservative treatment may be considered.

The Odmit C trial showed that a single dose of mitomycin C at the time of nephroureterectomy can reduce the risk of a subsequent bladder cancer from 23% to 13%.

The role of chemotherapy for localised, resected upper tract urothelial carcinoma is not defined but is being investigated in the POUT clinical trial. Recruitment to this (or other appropriate clinical trials) is encouraged.

4.8 Advanced urothelial cancer

Approximately 10–15% of patients with urothelial cancer have metastatic disease at diagnosis, while about 50% of those who present with localised, muscle-invasive disease will ultimately relapse with either locally advanced or metastatic disease.

In patients for whom a cure is not possible, consideration of quality of life and collaboration between MDT members is paramount.

4.8.1 Systemic therapy in advanced urothelial cancer

Systemic chemotherapy can achieve good response rates with improvement in symptoms, progression-free and overall survival in appropriately selected patients with good performance status. All National Institute for Health and Care Excellence (NICE) and Cancer Drugs Fund (CDF)-approved regimens should be made available to patients with urothelial cancer within their approved indications where clinically appropriate without waiting for an update of these guidelines.

First-line systemic therapy

Standard regimens in patients of ECOG PS 0 or 1 with GFR >60 ml/min are as follows:

- Gemcitabine and cisplatin (GC) (as described in section 4.5.2).
- MVAC (standard or accelerated with G-SCF) (as described in section 4.5.2).
- GC is often preferred as it is associated with less toxicity than MVAC. Accelerated MVAC with G-CSF is better tolerated than standard MVAC.
- The triple combination of paclitaxel, cisplatin and gemcitabine is associated with higher response rates than the gemcitabine and cisplatin doublet. In a randomised controlled trial, an improvement in overall survival was seen in the eligible (but not intention-to-treat (ITT)) population and in the ITT subgroup with primary bladder tumours with an increase in G4 neutropenia, febrile neutropenia and G-CSF use. It is not used frequently but could be considered in very carefully selected patients. For most patients the risk of adding paclitaxel to GC outweighs the benefits.

The value of chemotherapy is less certain in patients with impaired performance status (ECOG PS ≥2) and/or renal function (GFR <60ml/min). After careful consideration of the risks and benefits, carboplatin or taxane -based regimens, or single agent chemotherapy, could be used. Appropriate regimens are as follows:

- GC
- paclitaxel

Participation in clinical trials is encouraged for patients of adequate performance status where available.

Non platinum-containing regimens of paclitaxel and gemcitabine have also been investigated and have shown good response rates but have not been compared with standard cisplatin-containing therapy and so are not considered standard.

Second-line systemic therapy

The value of second-line chemotherapy is not clearly established and there is no standard regimen in this setting.

The following points should be considered:

- Patients who have responded to first-line chemotherapy for more than 6 months can be re-challenged with the same regimen.
- Patients of good performance status (ECOG PS 0 or 1) who have been treated with GC in the first-line setting and had a good response could receive MVAC in the second-line setting.
- Patients of good performance status (ECOG PS 0 or 1) who have been treated with MVAC in the first-line setting and had a good response could receive GC or gemcitabine and carboplatin (GemCarbo) in the second-line setting.
- Other regimens that may be considered include taxane-based regimens with carboplatin or as monotherapy.
- Given the paucity of robust data in this setting, all patients should be considered for entry into suitable trials where available.

4.8.2 Radiotherapy in advanced urothelial cancer

Advanced bladder cancer may cause distressing or life-threatening haematuria. This may be controlled with palliative radiotherapy (either 24–36 Gy in 4–6# weekly or 30 Gy in 10# over 2–4 weeks).

Metastatic urothelial carcinoma, whether renal or bladder in origin, may respond to radiotherapy if localised or symptomatic (e.g. bone secondaries). Patients with metastatic disease should be seen by a clinical or medical oncologist at the appropriate time.

4.8.3 Surgery in advanced urothelial cancer

Surgery may be considered in patients with advanced/metastatic urothelial cancer for palliative benefit.

A proportion of patients who undergo cisplatin-based chemotherapy for metastatic disease have an excellent response, particularly among those with lymph node only metastases. These patients with post-chemotherapy low volume disease may be considered for surgery to small volume residual disease on an individual basis as some will have long-term disease-free survival.

4.8.4 Palliative and symptomatic therapy in advanced urothelial cancer

A number of treatments are available that can alleviate pain and other symptoms such as haematuria.

Zoledronic acid and denosumab are both approved for metastatic bone disease in solid tumours, including urothelial cancers, for the reduction of skeletal-related morbidity and so should be considered for patients with metastatic bone disease.

All patients should have access to the best supportive care and the specialist palliative care team should be involved at an appropriate time.

4.9 Pathology

All pathology reporting should comply with the Royal College of Pathologists (RCPath) tumour pathways and datasets and staged according to TNM 7. The version of TNM used must be clearly stated in all pathology reports.

- www.rcpath.org/publications-media/publications/datasets
- RCPath Dataset for tumours of the urinary collection system (2nd edition, published April 2013): www.rcpath.org/publications-media/publications/datasets/urinary-collecting-system.htm
- www.uicc.org/resources/tnm/publications
- *TNM Classification of Malignant Tumours* (7th edition) – Edge SB, Byrd DR, Compton CC et al. (eds) (2010), *AJCC Cancer Staging Manual* (7th edition). New York: Springer.

Tumour typing should include both WHO 1973 and 2004 systems.

- Mostofi FK, Sobin LH, Torloni H (1973), *Histological Typing of Urinary Bladder Tumours*, vol. 10. Geneva: WHO
- Eble J, Sauter G, Epstein J and Sesterhenn I (2004), Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Lyon: IARC Press.

Reports should include the following dataset for urothelial and other primary mucosal tumours of all sites within the lower urinary tract. The use of the term pTX should be avoided if at all possible and where deep

tissue is not present the term ‘at least’ is preferred. The term transitional cell carcinoma (TCC) has been superseded by urothelial carcinoma (UC).

4.9.1 Summary dataset for tumour reports

The core macroscopic data items are as follows:

- site(s) and type(s) of specimens
- specimen size(s) and/or weight
- tissue sampling – all or partly sampled.

The core microscopic data items are as follows:

- type of tumour urothelial/squamous/adenocarcinoma/sarcomatoid/mixed etc.
- invasive yes/no
- growth pattern papillary/solid/inverted/micropapillary/nested etc.
- grade of urothelial tumour (WHO 1973) Grade 1/2/3
- grade of urothelial tumour (WHO 2004) PUNLMP/Low grade/high grade
- grade – other tumour types well/moderately/poorly differentiated
- Stage (TNM 7, 2009) pT
- lymphovascular invasion yes/no
- muscularis propria present yes/no/not assessable
- associated CIS present yes/no/not assessable
- SNOMED coding.

4.9.2 Pathology review

All cases of superficial high-risk bladder cancer (CIS, G3 pTa and G3 pT1) diagnosed at local hospitals must be reviewed centrally by the specialist pelvic (bladder) pathology team for discussion at the specialist MDT meeting unless an exception has been made following a diagnostic quality audit. Original blocks and/or slides must be sent together with a copy of the pathology report.

A copy of the pathology review report must be sent to the originating pathologist at the time of review so that any discrepancies can be noted locally. Original slides and blocks must be returned within a maximum of 12 weeks to the local laboratory.

Cases reported at specialist laboratories in other networks need not be reviewed but a copy of the full original report, not just a summary or correspondence, must be available to the specialist clinical team.

4.9.3 Quality assurance and External Quality Assessment

Lead urological pathologists must undertake the National Urological Pathology External Quality Assessment (EQA) and provide evidence of participation to their local and/or specialist MDTs. Other pathologists undertaking urological pathology reporting should either participate in the UK National Urological

Pathology EQA or a local scheme which includes urological cases. Laboratories undertaking diagnostic work must have accreditation with Clinical Pathology Accreditation.

4.10 Research and trials

One of the great opportunities of the integrated cancer system is to improve patient access to clinical trials and research. There are already many trials and research projects running in individual centres in the LCA, usually with a list of available trials on individual Trust websites. In the absence of this information, patients should be encouraged to ask about their eligibility for trial entry. This is particularly relevant in the chemotherapy setting.

It is the intention of the Urology Pathway Group to standardise availability of National Cancer Research Institute (NCRI) trials across the LCA in due course, and to publicise unbadged single centre research projects where these are available in individual sites. The ultimate aim of the Pathway Group is to populate and regularly update a list of trials open to recruitment on the urology section of the LCA website.

Annex 4.1: Bladder chemotherapy regimens

Some regimens can be prescribed and delivered according to slightly different protocols. Example protocols are included below but any recognised dosing regimen can be used.

Gemcitabine and cisplatin (GC)

A number of GC regimens are recognised, including regimens where the cisplatin dose is split over different days and/or the gemcitabine is given over days 1, 8 and 15 in a 28-day cycle. One commonly used regimen is:

Gemcitabine: 1,000mg/m^2 (or 1,250mg/m^2) IV, D1 and D8

Cisplatin: 70mg/m^2 IV, day 1 (given on day 2 in some protocols)

21-day cycle.

Neo-adjuvant/adjuvant therapy: 3–4 cycles
Palliative therapy in metastatic disease: 6–8 cycles.

Paclitaxel, cisplatin and gemcitabine

Paclitaxel: 80mg/m^2 IV, D1 and D8

Gemcitabine: 1,000mg/m^2, D1 and D8

Cisplatin: 70mg/m^2 IV, D1

21-day cycle.

Neo-adjuvant/adjuvant therapy: 3–4 cycles
Palliative therapy in metastatic disease: 6–8 cycles.

GemcCarbo (neo-adjuvant dosing)

Gemcitabine: 1,250mg/m^2, D1 and D8

Carboplatin: AUC 5

21-day cycle for 3–4 cycles.

GemCarbo (palliative dosing)

Gemcitabine: 1,000mg/m^2, D1 and D8

Carboplatin: AUC 5

21-day cycle for 6–8 cycles.

MVAC (standard)

Methotrexate: 30mg/m^2 IV, days 1, 15 and 22

Vinblastine: 3mg/m^2 IV, days 2, 15 and 22

Doxorubicin: 30mg/m^2 IV, day 2

Cisplatin: 70mg/m^2 IV, day 2

28-day cycle.

Neo-adjuvant/adjuvant therapy: 2 cycles
Palliative therapy in metastatic disease: 4 cycles.

MVAC (high-dose intensity)

Methotrexate: 30mg/m^2 IV, day 1

Vinblastine: 3mg/m^2 IV, day 2

Doxorubicin: 30mg/m^2 IV, day 2

Cisplatin: 70mg/m^2 IV, day 2

G-CSF (any approved regimen and dosage) 14-day cycle.

Neo-adjuvant/adjuvant therapy: 4 cycles
Palliative therapy in metastatic disease: 6–8 cycles.

Carboplatin and paclitaxel

Carboplatin: AUC 5 IV , day 1

Paclitaxel: 175mg/m^2 IV, day 1

21-day cycle for 6–8 cycles.

Paclitaxel (weekly)

Paclitaxel: 80mg/m^2/week IV

21-day cycle for up to 6 cycles (18 weeks).

Carboplatin and etoposide

A number of regimens exist. A commonly used one is:

Carboplatin: AUC 5 IV, day 1

Etoposide: 100mg/m^2 IV, day 1, PO days 2 and 3

21-day cycle for 6–8 cycles.

CAV

Cyclophosphamide: 800mg/m^2 IV, day 1

Doxorubicin: 50mg/m^2 IV, day 1

Vincristine: 1.4mg/m^2 IV, day 1

21-day cycle for 6–8 cycles.

Table of indications for regimens

Indications where regimens may routinely be considered according to histology, line of therapy, previous treatment, performance status, renal function and funding.

Urothelial cancer				**Small cell cancer**
Regimen	**Neo-adjuvant/ adjuvant**	**First-line metastatic**	**Second-line metastatic**	
GC	✓	✓	✓	
MVAC (accelerated)	✓	✓	✓	
MVAC (standard)	✓	✓	✓	
GemCarbo	✓	✓	✓	
CarboTaxol			✓	
Paclitaxel (weekly)			✓	
CarboEtop				✓
CAV				✓

5 Renal Cancer

5.1 Introduction

In 2010 there were over 9,639 newly diagnosed cases of kidney cancer (renal cell carcinoma (RCC)) in the UK. The crude incidence rate per 100,000 population is 15.9 in men and 9.6 in women. Cancer of the renal pelvis (urothelial cancer affecting the lining of the renal pelvis) is less common with around 500 cases per year. Relative survival estimates for kidney cancer (excluding renal pelvis) are similar for both sexes at 70% for males and 68% for females.

A separate operational guideline document has been developed by the LCA Urology Pathway Group and details how the number of specialist multidisciplinary teams (MDTs) has been reduced to two across the LCA to improve access to new treatments and trials. Furthermore, the guidance as to which patients should be discussed has been extended beyond the requirements of the Improving Outcomes Guidance because there is a concern that, historically, patients who would be suitable for nephron-sparing surgery may not necessarily have been offered this locally. This new guidance requires that all new cases of suspected renal cancer should be discussed at one of the two specialist MDTs, and where the recommended treatment is not available locally they should be referred on. This guidance will shortly be published pending final agreement on the template referral documentation.

Renal cancer surgery will continue to be provided in five centres, by surgeons who all attend the specialist MDT meetings and are recognised as having a specialist interest in renal cancer surgery by virtue of submission of their surgical data to the British Association of Urological Surgeons (BAUS) database. This data is published annually by the Healthcare Quality Improvement Partnership (HQIP).

As far as clinical care is concerned, all the individuals involved in the care of renal cancer patients are signed up to the European Association of Urology (EAU) guidelines on renal cancer and we have not attempted to reproduce this guidance. It is available at: www.uroweb.org/gls/pdf/10_Renal_Cell_Carcinoma_LR.pdf. Obviously there is separate UK National Institute for Health and Care Excellence (NICE) guidance on chemotherapy and when/how specific agents should be made available. Separate guidance on chemotherapy follows. This is written to supplement the excellent information in the EAU guidelines.

An area of relative weakness in the EAU guidelines is pathology reporting as there are specific UK requirements itemised in the Royal College of Pathologists' (RCPath) minimum dataset. We are grateful to Cathy Corbishley for developing a guideline for pathology reporting which forms part of these LCA Urological Cancer Clinical Guidelines.

5.2 Pathology

All pathology reporting should comply with the RCPath tumour pathways and datasets and staged according to TNM 7. The version of TNM used must be clearly stated in all pathology reports.

- www.rcpath.org/publications-media/publications/datasets
- The RCPath guidelines published in November 2006 are currently being revised
- www.uicc.org/resources/tnm/publications
- *TNM Classification of Malignant Tumours* (7th edition) – Edge SB, Byrd DR, Compton CC et al. (eds) (2010), *AJCC Cancer Staging Manual* (7th edition). New York: Springer.

Tumour reporting should comply with the WHO classification of tumours which has recently been updated with the new Vancouver guidelines.

Reports should include Fuhrman grading for clear cell and papillary RCC but it is not indicated for chromophobe tumours. Leibovich scores should be given for clear cell RCC.

- Eble J, Sauter G, Epstein J and Sesterhenn I (2004), Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Lyon: IARC Press
- Srigley JR, Delahunt B, Eble JN et al.; ISUP Renal Tumor Panel (2013), The International Society of Urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia, *American Journal of Surgical Pathology* 37(10):1469–1489
- Delahunt B, Cheville JC, Martignoni G et al.; Members of the ISUP Renal Tumor Panel (2013), The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters, *American Journal of Surgical Pathology* 37(10):1490–1504.

5.2.1 Summary dataset for renal tumour reports

The core macroscopic data items are as follows:

- specimen type
- location of tumour(s)
- size of tumour(s)
- adrenal included in specimen(s)
- invasion of perirenal fat within Gerota's fascia (pT3a)
- invasion of renal sinus (pT3a)
- invasion of renal vein or segmental branches (pT3a)
- invasion of vena cava below diaphragm (pT3b)
- invasion beyond Gerota's fascia and/or direct invasion of adrenal (pT4).

The core microscopic data items are as follows:

- tumour type(s)
- Fuhrman tumour grade (clear cell and papillary only)
- capsular invasion
- invasion of renal sinus
- lymphovascular invasion
- presence or absence of necrosis
- adrenal involvement (direct invasion, pT4, or metastatic, M1)
- margin status (state sites and extent of positive margins, and distance from margins where relevant such as in partial nephrectomies)
- tumour stage (TNM 7)

- Leibovich score (clear cell carcinoma only)
- SNOMED coding.

5.2.2 Pathology review

It is recommended that renal tumour biopsies reported at local hospitals be reviewed by the specialist renal pathology team for discussion at the central MDT meeting. Original blocks and/or slides must be sent together with a copy of the pathology report.

A copy of the pathology review report must be sent to the originating pathologist at the time of review so that any discrepancies can be noted locally. Original slides and blocks must be returned within a maximum of 12 weeks to the local laboratory.

Review of other pathology should be at the discretion of the specialist renal MDT.

5.2.3 Quality assurance and External Quality Assessment

Lead urological pathologists must undertake the National Urological Pathology External Quality Assessment (EQA) and provide evidence of participation to their local and/or specialist MDTs. Other pathologists undertaking urological pathology reporting should either participate in the UK National Urological EQA or a local scheme which includes urological cases. Laboratories undertaking diagnostic work must have Clinical Pathology Accreditation.

5.3 Systemic therapy

These guidelines refer to the treatment of RCC; transitional cell cancer (TCC) of the kidney will be managed with systemic therapy as detailed in the bladder cancer guidelines. Further information and evidence are available from the EAU guidelines for RCC.

5.3.1 First-line management of metastatic renal cell carcinoma

Patients may be managed by tyrosine kinase inhibitors (TKIs), surveillance or immunotherapy. The standard of care for first-line therapy of metastatic RCC is the use of a TKI, with the current choice between pazopanib or sunitinib. Sunitinib and pazopanib are both NICE approved for patients with advanced or metastatic RCC with an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1.

Pazopanib: 800mg PO given continuously

Sunitinib: 50mg PO given in a 6-week cycle (4 weeks on drug; 2 weeks off).

Surveillance is suitable for patients with good prognosis low volume disease or for patients with significant co-morbidities where the risks of treatment outweigh potential benefits. These patients should be actively monitored by the kidney cancer MDT.

Immunotherapy may be used with interleukin-2 or interferon alpha in highly selected cases. Interleukin-2 therapy is delivered only at specialist centres due to the complexity of treatment and level of support needed. Patients from the LCA are referred to St Bartholomew's Hospital, London, or the Christie Hospital, Manchester.

All patients should be considered for appropriate clinical trials.

5.3.2 Second- and third-line management of metastatic renal cell carcinoma

Patients should be considered for second- and third-line therapy. There are two current options: axitinib and everolimus. Both drugs need to be applied for via the Cancer Drugs Fund (CDF) in patients who meet the appropriate selection criteria. Axitinib is an oral TKI; everolimus is an oral mTOR (mammalian target of rapamycin inhibitor.

Axitinib dose to be titrated from 5mg BD to 10mg BD PO continuously.

Everolimus 10mg PO continuously.

NB: At present everolimus is available third line via the CDF but axitinib is not; please refer to the national CDF website for selection criteria: www.england.nhs.uk/wp-content/uploads/2014/02/ncdf-list-feb-14-fin.pdf.

All patients should be considered for appropriate clinical trials.

5.3.3 Regimens approved by NICE and the Cancer Drugs Fund

Systemic therapy for RCC is changing rapidly. Systemic therapies that are not NICE-approved may be available through the CDF. The list of approved regimens and indications is reviewed every 2 months and therefore may change regularly prior to the formal update of these guidelines. All NICE and CDF-approved regimens should be made available to patients with kidney cancer within their approved indications where clinically appropriate without waiting for an update of these guidelines.

5.3.4 Adjuvant systemic therapy

There is currently no evidence that renal cancer patients who have undergone nephrectomy for localised disease benefit from adjuvant treatment in terms of disease-free survival and overall survival. Therefore, adjuvant treatment should not be offered outside of approved clinical trials.

5.3.5 Neo-adjuvant systemic therapy

The use of systemic therapy prior to nephrectomy for localised disease is unproven and, outside clinical trials, is not recommended. The use of systemic therapy prior to cytoreductive nephrectomy (see below) is an evolving area with at present no level 1 evidence to support it. In selected cases it is reasonable to give systemic therapy and perform cytoreductive surgery at a later date. Such cases are complex and need to be discussed in the specialist MDT meeting at each point in the decision pathway.

5.3.6 Cytoreductive nephrectomy

Nephrectomy in the setting of metastatic disease is palliative for the majority of patients and systemic therapy will ultimately be required. Cytoreductive nephrectomy has shown a survival benefit with immunotherapy compared with immunotherapy alone. At present, only limited data is available addressing the value of cytoreductive nephrectomy combined with TKIs such as pazopanib and sunitinib. Two large randomised studies are ongoing that will address this area.

Cytoreductive nephrectomy is a suitable approach in selected cases that must be discussed in the MDT meeting. Suitable cases include:

- where the bulk of the tumour burden is in the primary

- to provide palliative benefit from local or systemic symptoms
- for prophylactic palliation of large primary tumours
- where surgery is deemed feasible and unlikely to significantly delay systemic therapy
- patients with good performance status (0–1)
- as part of a clinical trial protocol.

All patients should be considered for clinical trials.

5.3.7 Metastasectomy

There is no level 1 evidence to support metastasectomy but it is a reasonable approach in highly selected cases. Suitable cases include:

- solitary sites of disease
- patients with a minimum disease-free interval of 6 months
- patients with good performance status (0–1)
- where surgery is deemed feasible and safe.

All cases should be discussed in the MDT meeting and patients should be counselled about the level of evidence and the alternative options of active monitoring or systemic therapy.

All patients should be considered for the TRACER-X study looking at tumour profiling in RCC.

5.3.8 Palliative and symptomatic therapy in advanced renal cancer

Palliative care is integral to the care of metastatic renal cancer. A number of treatments are available that can alleviate pain, nausea, anorexia and other symptoms such as haematuria. Haematuria can be managed conservatively, with embolisation and ultimately with cytoreductive nephrectomy (see above).

Zoledronic acid and denosumab are both approved for metastatic bone disease in solid tumours including renal cancers for the reduction of skeletal-related morbidity and so should be considered for patients with metastatic bone disease. If used with TKIs, particular care should be taken to avoid osteonecrosis of the jaw.

All patients should have access to the best supportive care and the specialist palliative care team should be involved at an appropriate time.

5.4 Research and trials

One of the great opportunities of the integrated cancer system is to improve patient access to clinical trials and research. There are already many trials and research projects running in individual centres in the LCA, usually with a list of available trials on individual Trust websites. In the absence of this information, patients should be encouraged to ask about their eligibility for trial entry. This is particularly relevant in the chemotherapy setting.

It is the intention of the Urology Pathway Group to standardise the availability of National Cancer Research Institute (NCRI) trials across the LCA in due course, and to publicise unbadged single centre research projects where these are available in individual sites. The ultimate aim of the Pathway Group is to populate and regularly update a list of trials open to recruitment on the urology section of the LCA website.

6 Prostate Cancer

6.1 Introduction

Prostate cancer is a common cancer with 1 in 8 men being diagnosed at some point in their lifetime. It is now the most common male cancer in the UK and the incidence increases with age and a positive family history.

These guidelines have been written by the LCA Urology Pathway Group and have taken into consideration guidelines from the National Institute for Health and Care Excellence (NICE), the European Association of Urology (EAU) and previously agreed local network tumour working group guidelines.

These guidelines are designed as a reference for local urology departments, central cancer units and to inform purchasers what to expect from their local service. The guidelines serve as a basis for audit within the LCA and will be updated over time to account for changes in our understanding and treatment of the disease.

With increasing awareness of prostate cancer, more and more men are being diagnosed. In an attempt to avoid over-treatment, strategies to identify low-risk patients where active surveillance is most appropriate are discussed (e.g. the role of transperineal template biopsy). Magnetic resonance imaging (MRI) prior to a prostate biopsy in men with suspected prostate cancer is endorsed. This allows accurate staging in low-risk disease and can assist with the 62-day pathways in those where treatment in required.

Radiotherapy protocols for prostate cancer patients can be found in Annex 6.1.

6.1.1 National guidelines for the management of prostate cancer

NICE published the Improving Outcomes Guidance (IOG) for urological cancers in 2002, as part of the review of all tumour types, to implement the National Cancer Plan. The main recommendations made in the IOG document specific to prostate cancer are that:

- all new cancers are discussed by multidisciplinary teams (MDTs)
- radical surgery for patients with early prostate cancer should be managed at a centre by surgical teams performing 50 or more radical prostatectomies and cystectomies a year
- any individual surgeon performing less than five of either procedure a year should hand them on to colleagues who are doing more than five per annum.

6.1.2 Epidemiology of prostate cancers

Prostate cancer is the most common cancer in men, with about 33,000 new cases and 10,000 deaths in the UK each year. Prostate cancer is most common in older men, and post-mortem studies have shown foci of prostate cancer in 70% of men over 80.

6.1.3 Purpose of this document

This document was compiled with the help of members of the LCA prostate cancer guideline group and will be reviewed and updated over time. It sets out the guidance from the LCA and describes how the various healthcare professionals and organisations work together to provide care for an individual with prostate cancer.

6.2 The LCA urological cancer network

- Chelsea and Westminster Hospital NHS Foundation Trust
- Croydon Health Services NHS Trust
- Ealing Hospital NHS Trust
- Epsom and St Helier University Hospitals NHS Trust
- Guy's and St Thomas' NHS Foundation Trust*
- The Hillingdon Hospitals NHS Foundation Trust
- Imperial College Healthcare NHS Trust*
- King's College Hospital NHS Foundation Trust
- Kingston Hospital NHS Foundation Trust
- Lewisham and Greenwich NHS Trust
- Mount Vernon Cancer Centre (East and North Hertfordshire NHS Trust)
- The North West London Hospitals NHS Trust
- Royal Brompton & Harefield NHS Foundation Trust
- St George's Healthcare NHS Trust*
- The Royal Marsden NHS Foundation Trust*
- West Middlesex University Hospital NHS Trust

6.3 Referral guidelines

6.3.1 Primary care to unit with suspected prostate cancer

These are as laid down in the *Referral guidelines for suspected cancer*, published by NICE in June 2005 (Clinical Guideline 27, www.nice.org.uk). A patient with the following signs, symptoms or findings on investigations should be referred under the 2 week wait (2ww) rule:

- elevated age-specific prostate-specific antigen (PSA) with or without urinary symptoms with life expectancy >10 years
- in patients with significant co-morbidities, a discussion with the patient or carers and/or a specialist may be more appropriate than a 2ww referral
- with symptoms (e.g. bone pain) and a high PSA
- with a hard, irregular prostate typical of prostatic carcinoma.

* Specialist prostate cancer centres.

Age-specific PSA range

50–59 >3.0ng/ml

60–69 >4.0ng/ml

70+ >5.0ng/ml

(Source: Department of Health, Prostate Cancer Risk Management Programme)

An urgent referral is not needed if the prostate is simply enlarged and the PSA is within the normal range.

6.3.2 Criteria for discussion at specialist MDT in patients with prostate cancer

Patients who meet the following criteria should be discussed in the specialist MDT for review and discussion, some of whom will be referred on to specialist prostate cancer centres:

- all new patients with a diagnosis of prostate cancer
- patients presenting with relapsed or progressive disease after active surveillance or curative treatment
- patients failing second-line treatment to be considered for escalation of therapy
- patients for discussion of inclusion in trials.

6.4 Investigation and management of prostate cancer

6.4.1 Presentation

The Prostate Cancer Risk Management Programme materials, produced by the Department of Health, should be offered to men who are considering whether or not to have a PSA test.

Digital rectal examination (DRE) findings, age, family history and ethnicity help to inform the risk of detecting prostate cancer, and the need to test the PSA.

Any man over 50 presenting with persistent bone pain should have a DRE and a PSA test, as bone secondaries are one presentation of prostate cancer, although this as a mode of presentation is declining.

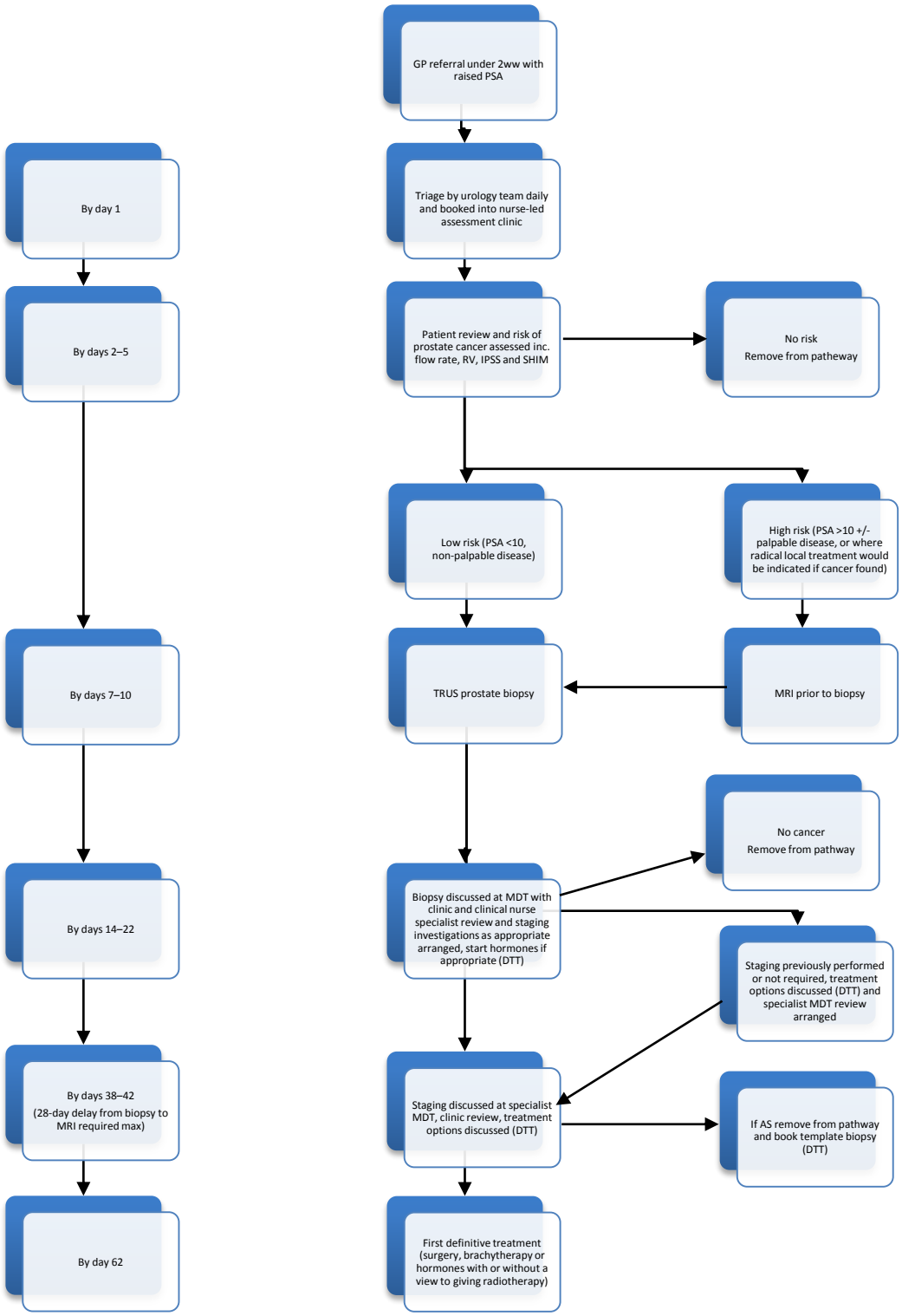
6.4.2 Diagnosis of prostate cancer

A man's decision whether or not to proceed to imaging of the prostate with MRI and prostate biopsy should be informed by the PSA level, estimate of prostate size, DRE findings, age, ethnicity and co-morbidities, together with any history of a previous urological evaluation (e.g. negative prostate biopsy). Serum PSA level alone should not automatically lead to a prostate biopsy. Nomograms such as that produced by the prostate cancer prevention trial provide a useful way to consider these factors.

Men and their partners or carers should be given information, support and adequate time to decide whether or not they wish to undergo investigation for prostate cancer. The information should include an explanation of the risks (including the significant increased chance of having to live with a prostate cancer diagnosis) and the benefits of having a diagnosis of prostate cancer.

It is good practice to assess the lower urinary tract with the international prostate symptom score (IPSS), flow rate, residual volume, the Sexual Health Inventory for Men (SHIM) score and a midstream specimen of urine at initial presentation as a baseline.

Figure 6.1: Prostate cancer pathway timeline



DTT – decision to treat
RV – residual volume
FR – flow rate
IPSS – international prostate symptom score
SHIM – sexual health inventory for men

Imaging

Multiparametric MRI

There is increasing use of multiparametric MRI as an initial investigation in men with a high PSA. It is particularly useful where the PSA >10, the rectal examination is abnormal or where local radical treatment would be indicated if a diagnosis of prostate cancer is made. Performing a prostate MRI before a biopsy allows a more seamless transition through the 2ww pathway, allowing patients and clinicians more time to discuss management options. Multiparametric MRI can be used to select biopsy route and accurately stage prostate cancer without the artefact produced by needle biopsy. It is not possible yet to completely exclude significant prostate cancer by MRI alone.

It should be noted that the evidence for pre-biopsy MRI for risk stratification is still experimental although many departments advocate this. The results of the PROMIS study (completion date August 2015, http://public.ukcrn.org.uk/search/Study Detail.aspx?StudyID=9941) are awaited and should influence recommendations.

If performed post-biopsy, it is necessary to allow at least a 4–6 week interval to reduce artefact from intraprostatic haemorrhage, although it is recognised that this artefact may remain for much longer.

Minimum requirements for multiparametric prostatic MRI

- Magnet: 1.5T adequate but 3T is optimal
- Coil: multichannel pelvic phased array coil (endorectal coil not necessary)
- Sequences:
  - small field of view T2 axial and coronal of prostate with NO angle with maximum slice thickness of 3mm, minimum in plane resolution of 0.7 x 0.7mm
  - large field of view T1 axial (maximum slice thickness 5mm)
  - sag T1w lumbar spine – optional but useful
  - diffusion weighted imaging – at least 3 b-values for calculation of the apparent diffusion coefficient (ADC) with highest of b = 1,000s/mm^2.

Optional

- Sag T1w lumbar spine
- Dynamic post-contrast images, pump injection at 3ml/s
- Use of anti-peristaltic drugs.

Minimum standards for reporting multiparametric prostatic MRI

Reports should include:

- prostate volume
- size and location of up to three lesions, each lesion given a PI-RAD score:
  1 – tumour highly unlikely
  2 – tumour unlikely
  3 – equivocal
  4 – tumour likely
  5 – tumour highly likely
- description of capsule, likelihood of breach, status of seminal vesicles, neurovascular bundles, bladder neck, rectum, lymph nodes and bones
- mark lesions on images or screen save images with a marker to indicate sites suspicious for disease to aid for targeted biopsies
- overall TNM stage.

Isotope bone scan

A bone scan should be performed in patients with high-risk localised (PSA >20ng/ml or Gleason score 8–10) or locally advanced disease where the presence of metastasis would change management. Single photon emission computed tomography (SPECT CT) can be used as appropriate where available at the time of the bone scan. There is no specific algorithm for the role of SPECT CT in prostate cancer and it is not available in all centres currently.

Choline positron emission tomography (PET)

Consider in high-risk patients prior to surgery to exclude metastases or in patients with biochemical relapse after curative treatment where the site of relapse is uncertain.

MRI spine

Use as appropriate in indeterminate cases of spinal metastasis on bone scan and when clinically appropriate to assess for metastases/spinal cord/cauda equina compression.

Prostate biopsy

If the clinical suspicion of prostate cancer is high because of a high PSA value and evidence of multiple bone metastases (identified by a positive isotope bone scan), prostate biopsy for histological confirmation should not be performed unless the patient is suitable for inclusion in clinical trials.

The transrectal route is the most commonly employed method for taking biopsies of the prostate. It is common practice to take a total of 12 cores, sampling apex, mid-gland and base on both sides of the prostate. In some circumstances limited biopsies to obtain a diagnosis of cancer is appropriate. Antibiotic prophylaxis should be given according to local microbiological advice.

There are some circumstances when a transperineal template biopsy of the prostate is indicated over a transrectal ultrasound (TRUS) biopsy including:

- previous negative TRUS biopsy and rising PSA

- anterior tumour on pre-biopsy MRI
- to assist in the risk stratification of patients electing to undergo active surveillance
- high risk for uro-sepsis such as poorly controlled diabetes.

The results of all prostate biopsies should be reviewed by a urological cancer MDT. This allows a discussion of positive biopsies and escalation to the specialist MDT and also a discussion of a negative biopsy where further imaging with MRI or repeat biopsy (transperineal template) may be appropriate (e.g. palpable nodule and high PSA).

6.5 Pathological assessment

All pathology reporting should comply with the Royal College of Pathologists (RCPath) tumour pathways and datasets and staged according to TNM 7. The version of TNM used must be clearly stated in all pathology reports.

- www.rcpath.org/publications-media/publications/datasets
- The RCPath guidelines published in October 2009 are currently being revised.
- www.uicc.org/resources/tnm/publications
- *TNM Classification of Malignant Tumours* (7th edition) – Edge SB, Byrd DR, Compton CC et al. (eds) (2010), *AJCC Cancer Staging Manual* (7th edition). New York: Springer.

Tissue handling, processing and reporting of prostate biopsies should comply with the PRCMP 2006 guidelines:

- www.cancerscreening.nhs.uk/prostate/pcrmp01.pdf

Gleason grading should comply with the modified Gleason grading system published in 2010:

- Epstein JI (2010), An update of the Gleason grading system, *Journal of Urology* 183(2):433–440.

6.5.1 Summary dataset for prostate biopsies including template biopsies

Core macroscopic items

Ideally, cores should be processed and cut individually, or at most 2–3 per cassette, so that they can be embedded and cut without core overlap or significant loss of core profile between levels. A standard diagram of core sites, in addition to the block key, may be helpful, particularly in template biopsies:

- individual biopsy site(s)
- individual core length(s).

Core microscopic items

Cores should be reported individually as a tabulated rather than text report for clarity and clinical preference. Free text should only be used to indicate features that are not itemised in tabulated reports.

Individual core data items for tabulated microscopy report are as follows:

- presence or absence of adenocarcinoma in each core
- Gleason grade for each core (including tertiary 5)

- percentage of individual core involvement (5–10% intervals)
- maximum tumour length within any individual core (mm).

Microscopic data items for overall case are as follows:

- tumour type – microacinar/other (state type)
- perineural invasion
- lymphovascular invasion
- extraprostatic extension (pT3a) – state site(s)
- seminal vesicle invasion (pT3b) – state left or right
- presence or absence of small cell component in high-grade tumours
- highest Gleason score (derived from tabulated individual core data items)
- SNOMED coding
- summary/conclusion to include overall Gleason score for entire case (overall score to include tertiary 5).

Report summary/conclusion (suggested format):

- prostate TRUS/template biopsies: adenocarcinoma
- overall Gleason (x + y) = z, in x/n cores
- maximum core involvement up to %
- maximum tumour length (mm).

NB: Measurement of the overall tumour involvement for the entire case as a percentage of the summary core lengths is no longer required as it does not influence any of the currently used treatment nomograms.

The highest Gleason score may also be included in the dataset but must also be able to be derived readily from the tabulated individual core reports.

Small cell carcinoma is high grade by definition and is not Gleason graded.

Overall Gleason score is most commonly used in treatment nomograms and therefore must be included in the report's conclusion.

6.5.2 Pathology review

All cases of prostate cancer deemed suitable for consideration of active surveillance or radical treatment diagnosed at local hospitals must be reviewed centrally by the specialist pelvic (prostate) pathology team for discussion at the specialist MDT meeting unless an exception has been made following a diagnostic quality audit. Original slides must be sent together with a copy of the pathology report.

A copy of the pathology review report must be sent to the originating pathologist at the time of review so that any discrepancies can be noted locally. Original slides and blocks must be returned within a maximum of 12 weeks to the local laboratory.

Cases reported at specialist laboratories in other networks need not be reviewed but a copy of the full original report, not just a summary or correspondence, must be available to the specialist clinical team.

6.5.3 Quality assurance and External Quality Assessment

Lead urological pathologists must undertake the National Urological Pathology External Quality Assessment (EQA) and provide evidence of participation to their local and/or specialist MDTs. Other pathologists undertaking urological pathology reporting should either participate in the UK National Urological Pathology EQA or a local scheme which includes urological cases. Laboratories undertaking diagnostic work must have Clinical Pathology Accreditation.

6.6 Staging

The TNM 7 classification is used.

Prostate TNM staging 1997

T1 – Not palpable or visible

- T1a 5%, T1b >5% of prostatic chips involved at transurethral resection of prostate
- T1c needle biopsy

T2 – Confined within prostate

- T2a one lobe
- T2b both lobes

T3 – Through prostatic capsule

- T3a extracapsular
- T3b seminal vesicles(s)

T4 – Fixed or invades adjacent structures (e.g. bladder neck, sphincter, rectum, levator muscles, pelvic wall)

N1 – Regional lymph nodes(s)

M1a – Non-regional lymph nodes(s)

M1b – Bones(s)

M1c – Other site(s)

In addition, localised (and some locally advanced) prostate cancer cancers are classified as low, intermediate or high risk:

- low risk: PSA <10ng/ml and Gleason score 6 and clinical stage T1–T2a
- intermediate risk: PSA 10–20ng/ml, or Gleason score 7, or clinical stage T2b or T2c
- high risk: PSA >20ng/ml, or Gleason score 8–10, or clinical stage T3–T4.

Urological cancer MDTs should assign a risk category to all newly diagnosed men with localised prostate cancer. Healthcare professionals should determine the provisional treatment intent (radical or not) before decisions on further imaging are made.

6.7 Management of prostate cancer

6.7.1 General considerations for all patients

Treatment and care should take into account the patient's needs and preferences. Men with prostate cancer should have the opportunity to make informed decisions about their care and treatment in partnership with their healthcare professionals. If men with prostate cancer do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines, *Reference guide to consent for examination or treatment* (2001; available from www.dh.gov.uk). Healthcare professionals should also follow a code of practice accompanying the Mental Capacity Act 2005 (summary available from www.publicguardian.gov.uk).

All men should be assigned a key worker (usually a clinical nurse specialist (CNS)) and should undergo a holistic needs assessment and any immediate concerns – physical, mental, spiritual or financial – should be addressed.

Communication and support

The recommendations on communication and patient-centred care made in the two NICE cancer service guidance documents, *Improving outcomes in urological cancers* (2002) and *Improving supportive and palliative care for adults with cancer* (2004), should be followed throughout the patient journey.

Men with prostate cancer should be offered individualised information tailored to their needs. This information should be given by a healthcare professional (e.g. a consultant or CNS) and may be supported by written and visual media (e.g. slide sets or DVDs).

Men with prostate cancer should be offered advice on how to access information and support from websites (e.g. Prostate Cancer UK http://prostatecanceruk.org and UK Prostate Link www.prostate-link.org.uk), local and national cancer information services, and from cancer support groups locally.

Before choosing or recommending information resources for men with prostate cancer, healthcare professionals should check that their content is clear, reliable and up-to-date. Healthcare professionals should seek feedback from men with prostate cancer and their carers to identify the highest quality information resources.

Healthcare professionals caring for patients with prostate cancer should ascertain the extent to which they wish to be involved in decision making and ensure that they have sufficient information to do so. A validated, up-to-date decision aid is recommended for use in all urological cancer MDTs. It should be offered to men with localised prostate cancer when making treatment decisions by healthcare professionals trained in its use.

Healthcare professionals should discuss all relevant management options recommended in this guideline with patients with prostate cancer and their partners or carers, irrespective of whether they are available through local services.

Healthcare professionals should ensure that mechanisms are in place to allow men with prostate cancer and their primary care providers to gain access to specialist services throughout the course of their disease.

Healthcare professionals should adequately inform men with prostate cancer and their partners or carers about the effects of prostate cancer and the treatment options on their sexual function, physical appearance, continence and other aspects of masculinity. Healthcare professionals should support men

and their partners or carers in making treatment decisions, taking into account the effects on quality of life as well as survival.

Healthcare professionals should offer men with prostate cancer and their partners or carers the opportunity to talk to a healthcare professional experienced in dealing with psychosexual issues at any stage of the illness and its treatment.

6.7.2 Management of localised disease

Localised prostate cancer incorporates stages T1–T2 N0 M0 disease. Patients with localised disease are suitable for the following treatment options depending on individual circumstances:

- watchful waiting
- active surveillance
- radical prostatectomy
- external beam radiotherapy
- brachytherapy.

High intensity focused ultrasound (HIFU) and cryotherapy are not recommended for men with localised or locally advanced prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions.

The specialist MDT should determine for each individual patient which of these options are applicable and the patient should be given a choice. Given the range of treatment modalities and their side effects, men with prostate cancer who are candidates for radical treatment should have the opportunity to discuss their treatment options with both a specialist surgical oncologist and a specialist clinical oncologist, along with a CNS.

Watchful waiting

Men who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care in accordance with locally agreed protocols. Their PSA should not be measured routinely, and the GP should be given clear directions when and how to access back into secondary care.

Active surveillance

Active surveillance is recommended for men with low- or intermediate-risk prostate cancer who wish to defer treatment with the aim of avoiding the unnecessary side effects of treatment. Active surveillance is not recommended for men with high-risk disease.

Criteria for inclusion into an active surveillance pathway include:

- PSA <10, clinical stage T1c/T2a, Gleason score 3 + 3
- less than 50% of biopsy cores involved and <10mm of any one core involved
- selected patients with low volume 3 + 4 disease where the level of pattern 4 cancer is <10%.

Men who start on an active surveillance pathway whose cancer shows signs of progression or who become uncomfortable with ongoing active surveillance are offered treatment. Whereas traditional watchful waiting in elderly or infirm men aims to avoid any treatment at all for as long as possible and excludes

radical treatment options, active surveillance of younger, fitter men tries to target curative treatment on those likely to benefit.

Men on active surveillance are monitored by serial PSA estimations, imaging and repeat prostate biopsy. Those who have evidence of disease progression, such as a significant rise in PSA or adverse findings on repeat biopsy or imaging, are offered curative radical treatment. The decision to proceed to radical treatment should be made in the light of the individual's personal preferences, co-morbidities and life expectancy.

To reduce the sampling error associated with the initial prostate biopsy, men who are candidates for active surveillance should have a repeat biopsy (ideally a transperineal template biopsy) and, if not previously performed, a multiparametric MRI.

Follow-up schedule

PSA testing in men on active surveillance can be performed through protocol-driven nurse-led clinics with urologist review only when required.

For men on active surveillance, follow-up should include as a minimum:

- PSA testing every 3–6 months during the first 2 years and 6-monthly thereafter; depending on local arrangements PSA testing can be performed via the GP and relayed to the responsible team via phone, email or letter
- repeat prostate biopsy performed intermittently – there is debate as to whether this should be via TRUS or a transperineal route; it should be performed after imaging with MRI to ensure abnormal areas are targeted and, as a minimum if the PSA is stable, the prostate should be re-biopsied every 2 years
- referral back to the GP with stable disease depending on local arrangements and availability of survivorship programmes – any patient discharged on active surveillance will need a plan for further PSA review and thresholds documented to trigger re-referral.

Follow-up with the GP with easy access back into secondary care is appropriate if local resources and expertise exist, and there is a robust way of remote monitoring. With the development of survivorship programmes within the LCA this will become easier over time.

Radical prostatectomy

Radical prostatectomy is appropriate for men with low-, intermediate- or high-risk localised prostate cancer and a life expectancy of greater than 10 years. Within the LCA, surgery for prostate cancer is performed minimally invasively, with or without robot assistance. There is no indication for neo-adjuvant androgen ablation.

Surgical centres include Imperial, St George's, The Royal Mardsen and Guy's and St Thomas' NHS Trust. Each centre performs over 100 cases per year.

A discussion with the patient following radical prostatectomy with analysis of the final specimen along with a super-sensitive PSA should occur 6–8 weeks following surgery so prognosis can be established and the need for adjuvant treatment discussed.

Men should be offered continence and psychosexual support if desired pre- and post-operatively. Men with persistent complications of surgery such as stress incontinence or erectile dysfunction should be referred early to an appropriate specialist for review.

Histopathological dataset for radical prostatectomy cases

Core macroscopic data items

The prostate should be processed and embedded in its entirety with use of large block sections as required. The apex and base should be coned not shaved and differential inking used to preserve information on laterality. Data items should include the following:

- description including prostate size in 3 dimensions
- prostate weight in grams with and/or without seminal vesicles
- block key including inking protocol to indicate method of dissection and blocking
- lymph node specimen sites, numbers of nodes and descriptions.

Core microscopic data items

These should include the following:

- tumour type – microacinar/other (state type)
- number and position of tumours (left/right, peripheral/central, posterior/anterior etc.)
- size of largest tumour focus
- tumour volume (ml)
- overall Gleason grade (including tertiary Gleason 5 if this is >10%)
- Gleason grade and position of dominant focus and/or highest Gleason score (optional)
- perineural invasion
- lymphovascular invasion
- extraprostatic extension – periprostatic fat and connective tissues
- seminal vesicle involvement – muscle and/or surrounding fat
- bladder neck involvement
- margin status (state whether extraprostatic or intraprostatic, apical, periurethral, circumferential, basal or bladder neck and measure extent in mm of each margin)
- grade of tumour present at positive margin (optional)
- nodal status including number of nodes, maximum tumour size and presence of extracapsular spread (ECS)
- TNM stage (TNM 7)
- SNOMED coding.

Positive margins should only be reported where tumour cells actually touch inked true surgical limits.

Tumour volume in ml should be estimated in all cases using the sum of tumour areas in individual blocks multiplied by block thickness.

Percentage of tumour involvement has not been found to be useful in patient management as it is subject to major subjective variations in estimation and varies considerably depending on the size of the prostate.

These guidelines will be reviewed when the next edition of the RCPath prostate guidelines are published.

Follow-up schedule

For men who have undergone a radical prostatectomy follow-up should include as a minimum:

- low risk for recurrence (T2, negative margins, PSA <0.1 at 8 weeks): 6-monthly PSA up to 3 years and then annually thereafter
- high risk for recurrence (T2/T3, positive margins, PSA <0.1 at 8 weeks): consider early adjuvant radiotherapy (+/- RADICALS trial), or 3-monthly PSA in first year, 6-monthly PSA up to 3 years and annually thereafter
- high risk for recurrence (T2/3, positive margins, and detectable PSA at 8 weeks): clinical oncology review for pelvic radiotherapy (+/- RADICALS trial), or androgen deprivation therapy depending on the PSA
- node positive patients should be discussed at the specialist MDT and considered for surveillance, androgen deprivation or trials as suitable.

The follow-up schedule of patients receiving additional radiotherapy will be at the discretion of the oncology team (depending on risk) or trial protocol.

All patients should ideally be evaluated using supra-sensitive PSA assays with accuracy to at least 0.1.

Referral to the specialist MDT should be made for rising PSA levels during follow-up.

Follow-up with the GP with easy access back into secondary care is appropriate if local resources and expertise exist and there is a robust way of remote monitoring. With the development of survivorship programmes within the LCA this will become easier over time.

External beam radiotherapy

External beam radiotherapy (EBRT) is appropriate for men with low- or intermediate to high-risk localised or locally advanced with regional disease prostate cancer. For men with low or intermediate stage, we would expect a life expectancy of greater than 10 years for these patients to benefit. In men with high-risk localised or locally advanced disease where the disease is more aggressive, a life expectancy of 5–8 years is reasonable.

EBRT is usually combined with 3–6 months of neo-adjuvant androgen deprivation for low to intermediate risk disease and 3 years of neo-adjuvant androgen deprivation for high-risk localised or locally advanced disease.

EBRT is given to the prostate and seminal vesicles; whole pelvis treatment including the lymph nodes is not standard practice although it is performed in some cases.

Dose options for EBRT include:

- 74 Gy in 37 fractions given 5# per week
- 55 Gy in 20 fractions given 5# per week
- 78 Gy in 39 fractions given 5# per week to
- 60 Gy in 20 fractions (both of these are usually in a trial but are starting to be used elsewhere in the country as standard).

Follow-up schedule

For men who have undergone radical EBRT, follow-up should include the following as a minimum:

- Patients should be reviewed with PSA every 6 months for 5 years and then annually to 10 years. Patients with a rise in their annual PSA level should have a subsequent 3–6monthly review depending on the level of PSA rise.
- Patients who have stable PSA levels 2 years from the end of radical combination therapy with androgen deprivation therapy or radiotherapy if this is used alone can be discharged back to primary care with the following re-referral guidelines listed below.
- Re-referral guidelines: patients suitable for local salvage will have had T1 or T2 disease at presentation and have a life expectancy of >10 years. These patients should be re-referred if there are two consecutive rises in PSA and the PSA is >2. All other patients re-refer if three consecutive rises and PSA 5 or symptoms develop which may represent recurrent or metastatic disease.
- Other patients with more advanced disease should be referred back if their PSA is greater than their threshold of nadir plus 2 and have three consecutive rises above this or if their PSA doubling time is less than 3 months.
- Toxicity management: the main toxicities after radiotherapy are rectal, urinary and erectile dysfunction. Any patient developing rectal or urinary (which includes any episode of rectal or urinary bleeding, even if minor) toxicity should have appropriate evaluation based on its merits. In particular, any rectal or urinary bleeding will need referral for endoscopic assessment. Urological symptoms should be evaluated by the local urological service.
- Most men will have received 3 months to 3 years of neo-adjuvant/adjuvant androgen suppression. For the latter group, clear guidance on the duration (i.e. when the last dose of luteinising hormone-releasing hormone analogue (LHRHa) should be given) of androgen suppression must be given; PSA levels are expected to rise a little as androgen levels recover which may be delayed 1–2 years after the last LHRHa depot.
- Bone density testing (DEXA scan) should be considered for all men at risk of osteoporotic complications for whom treatment is planned with androgen suppression for ≥2 years. National guidelines are awaited but assessment of bone density is particularly appropriate for men with a family history of osteoporosis or atraumatic or multiple bone fractures.

Follow-up with the GP with easy access back into secondary care is appropriate if local resources and expertise exist and there is a robust way of remote monitoring. With the development of survivorship programmes within the LCA this will become easier over time.

Brachytherapy

Brachytherapy is appropriate for men with low- or intermediate-risk localised prostate cancer and a life expectancy of greater than 10 years. Brachytherapy should be a day-case single stage treatment.

Criteria for men suitable for brachytherapy include:

- low- and intermediate-risk prostate cancer (PSA <20, clinical stage T1c–T2c, Gleason score 3 + 3 and 3 + 4)

- patients with PSA >15 or Gleason score ≥8 should only be treated in exceptional circumstances after cancer centre MDT discussion
- treatment can be given in specialist centres as an adjunct to EBRT
- if men are severely symptomatic, it may be necessary to perform a TURP prior to a 6-month delay in implanting.

Following brachytherapy, PSA levels may take up to 3 years to reach nadir. Follow-up is required to manage any complications (including sexual dysfunction) arising from the procedure, manage patient expectations and to evaluate tumour response and recurrence.

Follow-up schedule

For men treated with brachytherapy, follow-up should include as a minimum:

- year 1: 3-monthly review with PSA and assessment of urinary symptoms
- year 2: 6-monthly review with PSA and assessment of urinary symptoms
- referral back to GP after 2 years' follow-up if PSA levels are stable or <2ng/ml
- year 3: 6-monthly review with PSA and assessment of urinary symptoms
- years 4 and 5: 6-monthly review with PSA and assessment of urinary symptoms, and then annually for 10 years
- re-referral back to centre if any two consecutive rising PSA levels >0.5 ng/ml over a 3–6 month period or rise in PSA levels >1ng/ml or any patient with potential complications.

Follow-up with the GP with easy access back into secondary care is appropriate if local resources and expertise exist and there is a robust way of remote monitoring. With the development of survivorship programmes within the LCA this will become easier over time.

High dose rate brachytherapy

NICE guidelines advise that current evidence on the safety and efficacy of high dose rate (HDR) brachytherapy in combination with EBRT for localised prostate cancer appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. Within the LCA only a single centre performs this technique.

6.7.3 Management of locally advanced prostate cancer (T3–4 N0 M0)

In the absence of obvious metastatic disease on imaging (MRI, bone scan, CT, PET), in some cases after specialist MDT discussion it may be appropriate to offer local treatment in the form of radical prostatectomy or EBRT but not brachytherapy. Some patients, particularly younger men, may have a radical prostatectomy with planned adjuvant rather than salvage radiotherapy afterwards with curative intent.

Neo-adjuvant and concurrent LHRHa therapy for 3–6 months is recommended for men receiving radical radiotherapy for high-risk localised or locally advanced prostate cancer.

Immediate post-operative radiotherapy after radical prostatectomy is not routinely recommended if the PSA is undetectable other than in the context of the RADICALS trial. If margins are positive, irrespective of the PSA level, adjuvant radiotherapy should be discussed, preferably as part of the RADICALS trial.

6.7.4 Management of adverse effects after treatment

To provide good rehabilitation, an understanding of the patient's needs, goals and expectations should initially be established. The use of the holistic needs assessment form may be useful here to establish these grounds where needed (see Appendix 4). A baseline function of bladder, sexual and bowel symptoms should be assessed prior to treatment (including SHIM score), and where symptoms exist the patient should be given strategies to improve function prior to treatment. Advice should include appropriate fluid intake, pelvic floor exercises, bladder training, and avoiding constipation.

Radiotherapy toxicity

Bowel symptoms where present (e.g. constipation, obstructed defecation or faecal incontinence) should be discussed and advice to address these symptoms prior to treatment should be given. Patients presenting with symptoms consistent with radiation-induced enteropathy should be fully investigated, including flexible sigmoidoscopy, in order to exclude inflammatory bowel disease or malignancy of the large bowel and to ascertain the nature of the radiation injury. Particular caution should be taken with anterior wall rectal biopsy following brachytherapy because of the risk of fistulation. Steroid enemas should not be used for treating men with radiation proctopathy. Men treated with radical radiotherapy for prostate cancer should be offered follow-up with flexible sigmoidoscopy every 5 years.

Erectile dysfunction

Prior to treatment for prostate cancer it is essential that men are warned of potential changes to their sexual functioning including:

- inability to gain erection for sexual activity
- inability to sustain an erection
- There will be no ejaculation following prostate surgery; some younger men may want to undergo semen preservation – in these cases, referrals should be made to the appropriate fertility service to enable them to make informed decisions
- climacturia.

Men and their partners should have early and ongoing access to specialist erectile dysfunction services. Men with prostate cancer who experience loss of erectile function should be offered phosphodiesterase type 5 (PDE5) inhibitors to improve their chance of spontaneous erections. If PDE5 inhibitors fail to restore erectile function, or are contraindicated, men should be offered vacuum devices, intraurethral inserts or penile injections, or penile prostheses as an alternative.

Men who undergo radical prostatectomy with nerve sparing may benefit from the use of daily dosing of PD5 inhibitors and the daily use of a vacuum device as a form of penile rehabilitation.

Incontinence or bothersome lower urinary tract symptoms

Prior to treatment the patient should be made aware that there is a likelihood that there may be a decline in continence and a change in the way they void. These include:

- an increase in urinary frequency
- an increase in post-micturition dribble
- incontinence of urine with sit to stand, walking, coughing, lifting

- increase in bladder frequency during the day and at night
- the need to use pads following removal of the catheter.

Men with bothersome urinary symptoms after treatment should have access to specialist continence services for assessment, diagnosis and conservative treatment. This may include learning coping strategies, along with pelvic floor muscle re-education (bio-feedback), bladder retraining and pharmacotherapy (antimuscarinics). Men with intractable stress incontinence should be referred to a specialist surgeon for consideration of a sling or artificial urinary sphincter. The injection of bulking agents into the distal urinary sphincter is not recommended to treat stress incontinence.

Side effects associated with androgen deprivation therapy

Fatigue

Men starting androgen deprivation therapy should be informed that regular resistance exercise reduces fatigue and improves quality of life. Referral to physiotherapy and/or occupational therapy should be considered.

Hot flushes

Offer medroxyprogesterone acetate (20mg per day) to manage troublesome hot flushes caused by long-term androgen deprivation therapy. This should initially be for 10 weeks. Evaluate effectiveness at the end of that treatment period. In patients for whom medroxyprogesterone acetate is ineffective, cyproterone acetate or megestrol acetate can be considered.

Sexual dysfunction

- Before starting androgen deprivation therapy, tell men and, if they wish, their partner, that long-term androgen deprivation will cause a reduction in libido, and possible loss of sexual function.
- Ensure that men starting androgen deprivation therapy have access to specialist erectile dysfunction services and to psychosexual counselling if wished.
- Offer PDE5 inhibitors to men having long-term androgen deprivation therapy who experience loss of erectile function. If PDE5 inhibitors fail to restore erectile function or are contraindicated, other options should be offered, such as intraurethral inserts, penile injections, penile prostheses and vacuum devices.

Osteoporosis

Androgen suppression is associated with bone density loss. For men receiving long-term hormonal therapy, consideration should be given to performing a DEXA bone scan, particularly if there is a family history of osteoporosis, past history of atraumatic bone fracture or other risk factors for osteoporosis such as smoking and excess alcohol consumption. If osteoporosis is detected, treatment should be with intravenous or oral bisphosphonate or other approved bone-protecting agents together with calcium and vitamin D supplementation. Bisphosphonates are not recommended routinely for all men on long-term androgen deprivation therapy.

Gynaecomastia

Men starting long-term bicalutamide monotherapy (longer than 6 months) should be offered prophylactic radiotherapy to both breast buds within the first month of treatment. This is usually a single fraction of 8 Gy using orthovoltage or EBRT.

If radiotherapy is unsuccessful in preventing gynaecomastia, weekly tamoxifen should be considered.

6.7.5 Management following failure of primary curative treatment

Defining biochemical relapse

The definition of biochemical relapse differs depending upon the radical treatment. Radical surgery aims to remove all prostatic tissue. The serum PSA should drop to very low levels (typically <0.1ng/ml) and remain at that level. Radiation results in cell death and a fall in serum PSA but not to the levels seen after prostatectomy.

A rise in PSA during follow-up indicates the probability of prostatic cancer cells present either locally at the site of the prostate or at distant sites. However, this frequently does not translate into clinical recurrence or death from cancer. The rate at which PSA increases following radical treatment is an important predictor of subsequent prostate cancer-related mortality. Other factors such as Gleason score ≥8 and the timing of PSA rise after radical treatment are also useful measures of risk. The interpretation of biochemical relapse may be complicated by the variety of PSA assays available.

After radical prostatectomy

The presence of any detectable PSA in peripheral blood is often interpreted as indicating a clinically significant relapse, but this may be due to the presence of benign prostate tissue in a small proportion of men. The existence of residual disease, which may lead to clinical progression, can be recognised most reliably by serial PSA measurement. Most commonly a PSA of 0.2ng/ml or more would be considered a failure.

After radical radiotherapy

The PSA does not usually fall to zero after radical treatment with EBRT. The definitions of biochemical relapse with the best combination of sensitivity and specificity for clinical or distant relapse after radical treatment are those that use a fixed value above the nadir. This allows for the slight rise in PSA that is seen when neo-adjuvant or adjuvant hormonal therapy is discontinued. The 2005 American Society of Radiation Oncology (ASTRO) consensus definition (PSA greater than nadir + 2ng/ml) had a sensitivity of 74% and specificity of 71% for any clinical failure.

After low-dose brachytherapy

Typically the PSA level falls slowly after brachytherapy and does not normally reach zero. Indeed, the level may temporarily rise (the PSA bounce) after initial treatment. The most sensitive and specific predictors of persistent disease or relapse are, as with EBRT, nadir + 2ng/ml.

Restaging patients after biochemical relapse following failure of primary curative treatment is useful to exclude metastasis. Both CT, MRI and isotope bone scan can be used depending on the individual case. If available, PET CT has a role in the evaluation of lymph node and prostatic bed recurrence.

Biopsy of the prostatic bed should not be performed in men with prostate cancer who have had a radical prostatectomy. Biopsy of the prostate after radiotherapy should only be performed in men with prostate cancer who are being considered for salvage local therapy.

Biochemical relapse alone should not necessarily prompt an immediate change in treatment. Men with biochemical relapse after radical prostatectomy, with no known metastases, should be offered radical radiotherapy to the prostate bed, ideally within the RADICALS trial. A typical regime would be 66 Gy in 33 fractions.

Hormonal therapy is recommended for men with prostate cancer who have a biochemical relapse if they have:

- symptomatic local disease progression, or
- any proven metastases, or
- a PSA doubling time <3 months.

Intermittent hormone therapy should be considered if men are treated with androgen deprivation for PSA recurrence.

6.7.6 Management of metastatic prostate cancer

First-line therapy of metastatic prostate cancer

The standard of care for first-line therapy of metastatic prostate cancer is androgen deprivation therapy. There are a number of appropriate options for this:

- An LHRH analogue (such as leuprorelin or goserelin) is given with anti-androgen cover (e.g. cyproterone acetate or bicalutamide) to prevent testosterone surge and tumour flare.
- Bilateral subcapsular orchidectomy should be offered to all men with metastatic prostate cancer as an alternative to continuous LHRHa therapy.
- An LHRH antagonist such as degarelix should be considered for men who present with metastatic vertebral disease that could be at risk of causing spinal cord compression.

Combined androgen blockade is not recommended as standard first-line treatment for men with metastatic prostate cancer. All men should be considered for suitability for appropriate clinical trials such as STAMPEDE.

Toxicity considerations when prescribing first-line hormonal therapy

Anti-androgen monotherapy with bicalutamide (150mg daily) can be offered to men with metastatic prostate cancer who are willing to accept the adverse impact on overall survival and gynaecomastia in the hope of retaining sexual function.

Intermittent hormone therapy may be considered in men who require long-term androgen deprivation if they have a good response to primary hormone manipulation and find the side effects of treatment troublesome, provided they are appropriately informed and monitored. The 2014 NICE clinical guideline for prostate cancer (Clinical Guideline 175) recommends the following in regard to intermittent hormone therapy:

- men should be aware of the limited evidence regarding the reduction in side effects and the effect of intermittent therapy on the progression of prostate cancer
- PSA should be measured every 3 months
- androgen deprivation therapy should be restarted if serum PSA rises above 10ng/ml or if there is symptomatic progression.

Castration-resistant disease

Castration-resistant prostate cancer, sometimes referred to as androgen-independent prostate cancer, arises due to alterations in androgen signalling. Treatment options include further hormonal manipulation and cytotoxic chemotherapy.

When men develop castration-resistant disease, their treatment options should be discussed via the specialist MDT with particular reference to clinical trial recruitment and sequencing of addition therapies.

In the absence of prospective data, the modest potential benefits of continuing castration outweigh the minimal risk of treatment. Androgen suppression should therefore be continued indefinitely in these patients.

NICE's definitions of castration-resistant prostate cancer

Disease progression, despite traditional androgen-deprivation therapy, that may present as one or any combination of a continuous rise in serum levels of PSA, progression of pre-existing disease, or the appearance of new metastases.

The EAU guidelines' definitions of castration-resistant prostate cancer

According to EAU guidelines (2012):

- three consecutive rises of PSA, 1 week apart, resulting in two 50% increases over the nadir, with a PSA >2ng/ml
- castrate serum levels of testosterone (testosterone <50ng/dl or <1.7nmol/l)
- anti-androgen withdrawal for at least 6 weeks for bicalutamide[*]
- PSA progression, despite consecutive hormonal manipulations.[†]

Restaging imaging on progression

Restaging with MRI, CT and bone scan to assess disease burden should be performed where clinically indicated. Consideration should be given to the following points:

- the role of imaging in restaging is uncertain when the serum PSA remains less than 20ng/ml, but it can be of use in certain patients

[*] Either anti-androgen withdrawal or one secondary hormonal manipulation should have been done in order to fulfil the criteria for castration-resistant prostate cancer if patients have been treated with anti-androgens in the context of maximum androgen blockade, or step up therapy following PSA progression after failure of LHRH treatment.

[†] Progression of osseous lesions: progression or appearance of two or more lesions on bone scan or soft tissue lesions using RECIST (response evaluation criteria in solid tumours) and with nodes >2cm in diameter.

- imaging should be undertaken prior to initiating abiraterone, enzalutamide, or cytotoxic chemotherapy with docetaxel or cabazitaxel to ensure that the patient meets the appropriate criteria for therapy and to enable an appropriate assessment of response
- MRI scan should be considered for patients with extensive vertebral metastatic disease who may be at risk of metastatic spinal cord compression (MSCC), but it is not routinely recommended; MRI is essential for men with known spinal disease who develop any spinal symptoms.

Second-line hormone therapies

There are a number of appropriate current options for second-line hormone therapy. The choice of approach will depend on patient factors including prior therapy, duration of response to prior therapy, co-morbidities, toxicity and patient wishes. The following are all considered appropriate and are generally available without application to the CDF:

- Bicalutamide 50mg OD (or other equivalent anti-androgen) in addition to androgen deprivation therapy (ADT) as maximal androgen blockade. **Regimen: Bicalutamide 50mg PO OD.**
- Corticosteroids. **Regimen: e.g. dexamethasone 0.5mg OD or prednisolone 20mg OD.**
- Oestrogens. **Regimen: e.g. diethylstilbestrol 1–3mg OD.**

Abiraterone acetate in chemotherapy-naive patients

Abiraterone acetate is available through the CDF for men who meet all of the following criteria:

- castration-resistant metastatic prostate cancer
- chemotherapy-naive for metastatic disease
- ECOG PS 0 or 1
- asymptomatic or mildly symptomatic patients
- chemotherapy not yet indicated
- application made and first cycle prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.

Regimen: Abiraterone acetate 1,000mg PO OD and prednisolone 5mg BD.

Docetaxel chemotherapy

Docetaxel is recommended, within its licensed indications, as a treatment option for men with castration-resistant prostate cancer provided they have ECOG performance status of 0–2 (Karnofsky performance status score ≥60%). **Regimen: Docetaxel 75mg/m^2, day 1, 21-day cycle.** It is recommended that treatment with docetaxel should be stopped:

- at the completion of planned treatment of up to 10 cycles, or
- if severe adverse events occur, or
- in the presence of progression of disease as evidenced by clinical or laboratory criteria, or by imaging studies.

Post-docetaxel treatment options

A number of regimens are approved for use after docetaxel chemotherapy. The choice or sequence of regimens will depend on consideration of prior therapy, duration of response to prior therapy, co-morbidities, toxicity and patient wishes. The following are all considered appropriate within their approved indications:

- Abiraterone is recommended by NICE for use in men who have metastatic castration-resistant prostate cancer that has progressed on or after one docetaxel-containing chemotherapy regimen and who have not had prior abiraterone therapy. **Regimen: Abiraterone acetate 1,000mg PO OD and prednisolone 5mg BD.**
- Enzalutamide is licensed for use after docetaxel and is available through the CDF for men with metastatic castration-resistant prostate cancer who have not had prior abiraterone therapy and have an ECOG performance status of 0–2. In November 2013, NICE issued an appraisal consultation document recommending the use of enzalutamide in men who have metastatic castration-resistant prostate cancer that has progressed on or after one docetaxel-containing chemotherapy regimen and who have not had prior abiraterone therapy, provided the manufacturer adheres to the agreed discount scheme. (In practice, this currently means that men who have not had abiraterone prior to chemotherapy can have either abiraterone or enzalutamide post-chemotherapy but not both sequentially.) **Regimen: Enzalutamide 160mg PO OD, continuous.**
- Cabazitaxel is licensed for use after docetaxel and is available through the CDF for men with castration-resistant metastatic prostate cancer who have had prior treatment with docetaxel. This is available to men who have had prior therapy with either abiraterone or enzalutamide. **Regimen: Cabazitaxel 25mg/m^2 IV day 1, 21-day cycle.**
- All treatment options listed in 'Second-line hormone therapies' above can be considered post-docetaxel if not previously used.

Regimens approved by NICE and the Cancer Drugs Fund

Systemic therapies that are not NICE-approved may be available through the CDF. The list of approved regimens and indications is reviewed every 2 months and therefore may change regularly prior to formal update of these guidelines.

All NICE and CDF-approved regimens should be made available to men with prostate cancer within their approved indications where clinically appropriate without waiting for an update of these guidelines.

6.7.7 Supportive therapies in advanced prostate cancer

- Bisphosphonates for pain relief may be considered for men with hormone-refractory prostate cancer in conjunction with other treatments (including analgesics and palliative radiotherapy) or when other treatments have failed. The route of administration should be chosen according to convenience, tolerability and cost.
- The use of bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-refractory prostate cancer is not routinely recommended but may be considered if a high fracture risk is apparent.

- Bisphosphonates should not be used routinely to prevent osteoporosis in men with prostate cancer receiving androgen withdrawal therapy.
- Corticosteroids and radiotherapy should be considered for men with symptomatic metastatic prostate cancer for palliation of bone metastases and other symptoms.
- Strontium-89 should be considered for men with hormone-refractory prostate cancer and painful bone metastases, especially those men who are unlikely to receive myelosuppressive chemotherapy.
- Urological input may be required for lower urinary tract symptoms and so where possible these men should be managed in a multidisciplinary setting. Decompression of the upper urinary tract by percutaneous nephrostomy or by insertion of a double J stent should be offered to men with obstructive uropathy secondary to hormone-refractory prostate cancer.
- The option of no intervention should also be discussed with men with obstructive uropathy secondary to castration-resistant prostate cancer and remains a choice for some.
- Radiotherapy:
  - EBRT is appropriate treatment for symptomatic metastatic lesions located in soft tissue, nodes or bones. The fractionation schedule can range from a single fraction of 8 Gy to 20 Gy in 5 fractions. The single fraction may be repeated if pain control is not achieved.
  - EBRT may also be used in the palliative setting to achieve local control of disease. In these situations, high dose radiotherapy over 3–6 weeks may be used to achieve local control. The dose will need to be discussed with the clinical oncology team and is often individualised to the clinical circumstances.

6.8 Spinal cord compression

Men who are suspected of having spinal cord compression should be treated according to the LCA spinal cord compression pathway which is described within the Acute Oncology Guidelines: www.londoncanceralliance.org.uk/media/56533/FINAL%20LCA%20Acute%20Oncology%20Clinical%20Guidelines%20September%202013.pdf. The guidelines contain the contact details for MSCC services in the LCA.

In brief, whole spine MRI is the investigation of choice. If an MRI is absolutely contraindicated, then spinal CT is an alternative; however, it is inferior in this setting. Imaging must be performed within 24 hours of presentation for any patient with spinal pain suggestive of spinal metastases and with neurological signs or symptoms suggestive of MSCC, or more urgently if there is clear neurological deficit or deterioration.

Patients should be initiated on dexamethasone 16mg PO or intravenous (IV) stat. All patients with radiologically confirmed MSCC must be discussed urgently with a consultant clinical oncologist, consultant neuro- or spinal surgeon and, where possible, the treating oncology consultant prior to definitive treatment decisions. All patients should be referred to the MSCC coordinator and discussed at the specialist spinal MDT.

6.9 Specialist palliative care

All cancer units have access to specialist palliative care expertise, and this will be provided locally, in the community, the local hospital or hospice.

There may be occasions when patients with advanced disease and poor performance status are considered for novel treatments at the centre, and continuity of specialist palliative care arrangements will be ensured by coordination between the patient's key worker and the centre's specialist palliative care team. Inpatients requiring palliative care will be managed with the support of the hospital specialist palliative care team.

Men with metastatic prostate cancer should be offered tailored information and access to specialist urology and palliative care teams to address their specific needs and to discuss any significant changes in their disease status or symptoms as these occur. The regular assessment of needs (described in the NICE guidance on *Improving supportive and palliative care for adults with cancer*) should be applied systematically to men with prostate cancer.

Men with metastatic prostate cancer should be given the opportunity to discuss their therapy and information needs with members of both the urology and the specialist palliative care teams when there are significant changes in their disease status or symptoms.

Palliative interventions at any stage should be integrated into coordinated care, and any transitions of care settings should be facilitated as smoothly as possible.

Men with metastatic prostate cancer, their partners and carers should be consulted as early as possible in respect of their values and preferences for palliative care. Treatment/care plans and preferred place of care should be tailored accordingly. Healthcare professionals should ensure that specialist palliative care is available when needed and not limited to being available only at end of life. It should not be restricted to being associated with hospice care.

6.10 Research

All men with prostate cancer, at all stages of disease, should be offered the opportunity to participate in clinical research trials where available. While the list of open trials will vary to some extent across the hospitals within the LCA, all hospitals treating men with prostate cancer will have access to clinical trials either themselves or by referring to other hospitals within the LCA should they and their patients wish.

An updated list of clinical trials will be available through local urology research leads and through lead research nurse/managers.

Annex 6.1: Prostate systemic therapy regimens: indications and doses

1. LHRH analogues

Indications: Intermediate-, high-risk localised and locally advanced prostate cancer as neo-adjuvant/adjuvant therapy.

Metastatic prostate cancer – first line and as ongoing therapy following progression.

Doses:

Leuprorelin: 3.73mg SC 4-weekly or 11.25mg SC 12-weekly

Goserelin: 3.6mg SC 4-weekly or 10.8mg SC 12-weekly

Triptorelin: 3.73mg SC 4-weekly or 11.25mg SC 12-weekly

2. LHRH antagonists

Indications: First-line treatment of metastatic prostate cancer. Usually for men at high risk of spinal cord compression.

Doses:

Degarelix: first dose 240mg (as 2 x 120mg SC doses) followed by 80mg SC 4-weekly

3. Anti-androgens

Indications:

1. To prevent androgen flare on initiation of LHRH analogues.

2. In combination with androgen deprivation therapy as maximal androgen blockade.

3. First line for intermediate-, high-risk localised and metastatic/locally advanced prostate cancer in men who select anti-androgens for toxicity reasons.

Doses:

Cyproterone acetate: 100mg TDS (for 4–6 weeks when given to prevent flare)

Bicalutamide in combination with androgen deprivation therapy: 50mg OD

As monotherapy: 150mg OD or 50mg TDS

4. Corticosteroids as monotherapy

Indications: Castration-resistant prostate cancer.

Doses:

Prednisolone: 20mg OD

Dexamethasone: 0.5mg OD

5. Diethylstilbestrol

Indication: Castration-resistant prostate cancer.

Dose:

1, 3 or 5mg OD and aspirin 75mg OD

6. Abiraterone acetate

Indications: Castration-resistant prostate cancer. Pre-docetaxel for patients with ECOG PS 0–1 and no visceral disease. Post-docetaxel for patients with PS 0–2.

Dose:

1,000mg OD and prednisolone 5mg BD

7. Enzalutamide

Indications: Castration-resistant prostate cancer. Post-docetaxel for patients with PS 0–2.

Dose:

160mg OD

8. Docetaxel and prednisolone chemotherapy

Indications: Castration-resistant metastatic prostate cancer, for patients with PS 0–2, visceral and non-visceral disease.

Doses:

Docetaxel: 75mg/m^2, day 1, 21-day cycle. Can be dose reduced to 60mg/m^2

Prednisolone: 5mg PO BD throughout treatment (omit on days of dexamethasone pre-med)

9. Cabazitaxel chemotherapy

Indications: Castration-resistant prostate cancer, post-docetaxel for patients with PS 0–2.

Doses:

Cabazitaxel: 25mg/m^2, day 1, 21-day cycle. Can be dose reduced to 20mg/m^2

Prednisolone: 5mg PO BD throughout treatment (omit on days of dexamethasone pre-med)

10. Mitoxantrone and prednisolone chemotherapy

Indications: Castration-resistant prostate cancer, alternative to docetaxel in those who are intolerant of/have hypersensitivity to taxanes.

Doses:

Mitoxantrone: 12mg/m^2 IV, day 1, 21-day cycle. Can be dose reduced to 10mg/m^2

A maximum cumulative dose of 160mg/m^2 mitoxantrone should be given

Prednisolone: 5mg PO BD throughout treatment (omit on days of dexamethasone pre-med)

Annex 6.2: Radiotherapy treatment protocol for prostate cancer

Purpose

To define the treatment policy for the management with external beam radiotherapy where the treatment aim is local tumour control and cure in patients with localised disease. To ensure integration and appropriate cross-referencing of employers' procedures under the Ionising Radiation (Medical Exposure) Regulations and the quality management system.

1. Procedure

Radiotherapeutic management of patients with carcinoma of the prostate depends on the stage of disease, tumour grade, PSA level, and the age and co-morbidities of patient.

1.1. Staging

Routine tests:

- PSA
- FBC
- U&E
- Ca ++
- alkaline phosphatase
- histology review (Gleason score)
- local staging: DRE +/- TRUS +/- MRI
- nodal staging: MRI or CT*
- metastases staging: bone scan*

1.2. Treatment policies (local policies incorporate NICE Guidelines, 2014)

- Low risk of recurrence: T1–T2a and Gleason ≤6 and PSA <10ng/ml.
- Intermediate risk of recurrence: T2b–T2c or Gleason 7 or PSA 10–20ng/ml.
- High risk of recurrence: T3a or Gleason 8–10 or PSA >20ng/ml.
- Very high risk of recurrence: T3B/T4.

Patients in the low-risk group may be considered for active surveillance, radical prostatectomy, brachytherapy and conformal/intensity modulated external beam radiotherapy with a dose of 74 Gy (± short course androgen suppression) or for SBRT 36.5 Gy. Radiotherapy volume is prostate ± base of seminal vesicles (SV) only (may exclude SV in non-trial low risk of recurrence patients).

For **patients in the intermediate group**, active surveillance may be considered if PSA ≤15ng/ml and ≤50% of core biopsies are positive. Brachytherapy may be considered if one risk factor is present. For most patients, management will be either radical prostatectomy or conformal/intensity modulated radiotherapy to a dose of 74 Gy with 4–6 month androgen suppression.

* If Gleason score <6 and PSA <10, scans are not indicated.

Radiotherapy volume is determined by risk of seminal vesicle involvement (risk = PSA + (Gleason score -6) x 10).

For **high-risk patients**, external beam radiotherapy (or, rarely, prostatectomy) is the preferred option. If risk of seminal vesicle involvement ≤30%, radiotherapy as for intermediate-risk group but with 6 months' androgen suppression. If risk of seminal vesicle ≥30% consider for both (i) pelvic and prostate radiotherapy and (ii) 3 years' neo-adjuvant/adjuvant androgen suppression.

Very high-risk patients: as for high-risk patients with seminal vesicle risk ≥30%. Patients with involved lymph nodes may be treated with primary hormonal therapy only, combination hormone plus pelvic radiotherapy.

Post-prostatectomy, adjuvant or salvage external beam radiotherapy to the prostate bed using IMRT should be considered, potentially within the RADICALS trial. For patients with high-risk features, consider pelvic radiotherapy.

2. Radiotherapy treatment planning

2.1. General principles

Hormone cytoreduction should be given for at least 3 months prior to radiotherapy and continue until the completion of radiotherapy.

All patients are seen by a clinical oncologist and consented before they are booked in for radiotherapy. At this clinic appointment, they should have baseline bloods including FBC, U&E, liver and bone profile, glucose and PSA. If the PSA has not fallen by >90% from baseline and the patient has been on hormone therapy for at least 8 weeks, then combined androgen blockade should be considered. In addition, an international prostate symptom score (IPSS) or equivalent questionnaire should be completed and medication considered if the patient is moderately to severely symptomatic. Patients' bowel habits should be assessed and rectal size reviewed on diagnostic MRI. If the rectum is greater than 4cm in the AP diameter, enemas should be prescribed. CT planning scan with empty rectum, full bladder and patient supine is requested at the assessment of patient at least 6 weeks after commencement of hormone cytoreduction for radiotherapy planning. Bladder filling and bowel emptying instruction sheet to be given to patient in outpatients.

Patient is positioned supine with arms across chest using the Combifix™ for immobilisation. Anterior midline and lateral tattoos are placed at the superior edge of the pubic symphysis. Scout views are performed, followed by a short axial scan starting superiorly at the level of the pubic symphysis to assess rectal distension (due to gas/content) before proceeding with the full helical scan. If the rectal diameter is greater than 4cm in the AP plane at the level of the prostate the scan should be aborted at this stage and the patient commenced on enemas and booked for a rescan. If the rectal diameter is less than 4cm, the full helical scan should be acquired, scanning levels are from the L3/4 interspace, ensuring that the entire bladder is included, to 2cm below the ischial tuberosities.

Normal tissues outlined will include bladder, rectum, penile bulb and femoral heads. The normal tissues will be outlined as solid organs by defining the outer wall of rectum, bladder and bowel. Bladder should be outlined from base to dome. The rectum should be outlined from the anus (usually at the level of the ischial tuberosities or 1cm below the lower margin of the PTV, whichever is more inferior) to the recto-sigmoid junction. The recto-sigmoid junction can usually be identified on the CT slice where the bowel turns anteriorly and to the left. This will give a length of 10–12cm in most cases. Any additional bowel in the

volume should be outlined separately. Dose volume data to normal tissues will be tabulated and should meet the dose constraints specified in Table A6.2.1.

All target volumes are reviewed at audit/individually prior to proceeding to planning. The proposed treatment plan and dose prescription should be documented in the clinical notes and also on planning referral. Any modification to treatment design will also be clearly stated on the planning referral and in the medical notes.

Patients with localised disease who are having treatment to the prostate ± all or base of SV and prostate bed will usually be planned with an IMRT 5 field inverse-plan or a multi-segment 3-field forward-plan. All patients having pelvic lymph node treatment should normally have IMRT or VMAT.

2.2. Target volumes

Volumes will be defined according to:

- ICRU Report 50 (1993) and supplement report ICRN 62: Prescribing, Recording and Reporting Photon Beam Therapy; *Journal of the ICRU*
- ICRU Report 83 (2010), Prescribing, recording and reporting photon beam intensity-modulated radiotherapy (IMRT), *Journal of the ICRU* 10(1) (for IMRT prescriptions).

Table A6.2.1: Summary of target volume definitions for localised disease

	fp-IMRT	**ip-IMRT**
GTV	Prostate-only (P)	P/P + base SVs/ P + SVs
CTV	P + base SVs/ P + SVs	P + base SVs/ P + SVs
High dose boost volume	PTV3 = GTV + 5mm/0mm post and exclude rectum	PTV2 = CTV + 3mm/5mm ant/0mm post and exclude rectum
Standard dose	PTV2 = PTV3 + 5mm	PTV1 = CTV + 10mm/8mm post
Treatment of SVs	PTV1 = CTV + 10mm	Included above

2.3. Dose and fractionation

Localised disease

- Standard dose: 74 Gy/37#/7.5 weeks.

Prostate and pelvic radiotherapy

- Prostate (plus involved SVs): 74 Gy/37#/7.5 weeks
- SV and LN: 55–60 Gy/37#/7.5 weeks

- Nodal boost: 60–65 Gy/37#/7.5 weeks
- (Nodal doses for off trial are 55 Gy for uninvolved and 60–65 Gy for involved nodes)
- In case of excess bowel dose, reduce LN to 55 Gy and nodal boost to 60 Gy.

Post-prostatectomy

- CTV to include prostate bed and remnant of seminal vesicles if present. Outlining will conform to RADICALS protocol. Standard is with CFRT/IMRT.
- PTV = CTV + 1cm (0.7–1.0cm posterior margin depending on rectal area which should be defined on each CT planning slice).
- Dose = 66 Gy in 2 Gy fractions. For patients with a high risk of lymph node involvement, consider treating the pelvic lymph nodes in addition to the prostate bed.

2.4 Variations to dose and fractionation

Alternative fractionation schedules may be used following discussion and informed consent from patients.

Moderate hypofractionation may be selected by men having radical treatment for localised disease using 3 Gy/# as in the CHHiP trial giving a total dose of 60 Gy or 57 Gy in 20 or 19 fractions. Safety of these schedules has been reported (Dearnaley et al Lancet Oncol 2012) but efficacy data is awaited. Planning will be identical to men receiving standard fractionation with appropriate dose constraints as used in the CHHiP trial.

Extreme hypofractionation giving 36 Gy in 6 fractions may be used in men with a reduced performance status who would find daily fractionation practically very difficult, or to control localised disease in castration-resistant prostate cancer. Similar planning methods and appropriate dose constraints should be employed. Patients are reviewed weekly prior to treatment delivery.

3. Pre-treatment standard procedures

Repeat pre-treatment imaging may be required after evaluation if the initial dataset is unsuitable for treatment planning or delivery. The requirement for repetition of pre-treatment imaging is justified when optimisation of patient position or immobilisation is required, or if patient motion and organ/contour deformation are observed. Entitled radiographer operators are therefore able to authorise one repeat planning CT scan in these circumstances. Any extraordinary requirements for additional pre-treatment imaging should be justified by a practitioner.

4. Treatment geometric verification

This is performed following the specific clinical unit protocol, by radiographers entitled as operators.

The use of an imaging modality not specified as routine by this protocol requires justification by a practitioner.

Radiographers, entitled as practitioners for concomitant exposures, may refer and justify a patient for additional off-protocol images.

5. Follow-up

On treatment: patients are seen on alternate weeks. Patients with no early toxicity may be seen starting from week 4 of treatment. Trial patients are reviewed alternate weekly.

Post-treatment patients are seen in 1 month, then 6-monthly to 5 years, then annually. PSA should usually be arranged prior to 6-monthly and subsequent follow-up visits. Non-trial patients should be referred back to the cancer unit (immediately after completion of radiotherapy) or GP (after 2 years).

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Horwitz EM, Bae K, Hanks GE et al. (2008), Ten-year follow-up of radiation therapy oncology group protocol 92–02: a phase III trial of the duration of elective androgen deprivation in locally advanced prostate cancer, *Journal of Clinical Oncology* 26(15):2497–2504.

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Thompson IM, Tangen CM, Paradelo J and Scott Lucia M (2009), Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term follow up of a randomized clinical trial, *Journal of Urology* 181: 956–962.

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Appendix 1: Urgent Suspected Urological Cancers Referral Forms

LCA UROLOGY URGENT SUSPECTED CANCER REFERRAL FORM

Date of GP decision to refer: / /20 **No. pages faxed:**

PLEASE COMPLETE THIS FORM AND FAX TO THE RELEVANT URGENT REFERRAL TEAM WITHIN 24 HOURS

PATIENT DETAILS – *please provide multiple contact details*

Last name: **First name:**

Gender: M / F

Address:

Telephone No (daytime):

Telephone No (evening):

Mobile No:

Email:

DOB: **Interpreter: Y / N**

Language: **Ethnicity:**

NHS No:

GP DETAILS

GP name and initials:

Practice code:

Address:

Telephone No:

Fax No:

Practice email address:

INVESTIGATIONS REQUIRED FOR REFERRAL

PSA (required for urgent referrals criteria 1 & 2)

First PSA: **Second PSA:**

MSU (required for urgent referrals criteria 1 – 5):

Creatinine level (request at time of referral required for all urgent referral criteria)*:

***Please tick if creatinine result to follow:** ☐

Urgent referrals criteria (tick category)

1. Clinically malignant prostate on rectal examination. PSA result to be sent with referral ☐
2. Age related raised PSA (50-60 >3, 60-69 >4, 70+ >6.5, 85+ >20) on 2 occasions 4 weeks apart, unless the prostate feels malignant or the PSA is over 20 when immediate referral appropriate ☐
3. Visible haematuria in adults >18 years old ☐
4. Non visible haematuria greater than a trace on dipstick in adults > 50 years old ☐
5. Symptoms of UTI with persistent sterile pyuria >50 years old ☐
6. Palpable renal mass, or renal lesion which is suspicious for malignancy identified clinically or radiologically ☐
7. Testicular lump which appears to be intratesticular or solid suspicious of cancer ☐
8. Raised/suspicious penile lesion or phimosis with discharge and/or palpable/hard area beneath prepuce ☐

PATIENT MEDICAL HISTORY

Current medication:**

Existing conditions*:

***Otherwise please fax current medication list and medical history*

Other information or symptoms:

DISCUSSIONS WITH PATIENT PRIOR TO REFERRAL

1. **Has the patient been told it is a suspected cancer referral?** ☐
2. **Has the patient been given the urgent referral leaflet?** ☐
3. **Have you told the patient where they are being referred to?** ☐
4. **Have you told the patient they need to be seen within 14 days?** ☐

LCA TRUST CONTACT DETAILS FOR URGENT UROLOGICAL CANCER REFERRALS

Chelsea and Westminster NHS Foundation Trust Fax: 020 3315 8814 Tel: 020 3315 2679	**Croydon Health Services NHS Trust** Fax: 020 8401 3337 Tel: 020 8401 3986	**Epsom and St Helier NHS Trust** Fax: 020 8296 2741 Tel: 020 8296 2742
Guy's & St Thomas' Fax: 020 7188 0923 Tel: 020 7188 0902	**Hillingdon Hospital NHS Trust** Fax: 01895 279807 Tel: 01895 279698 Alternative Fax: 01895 279890	**Imperial College Healthcare NHS Trust** Fax: 020 3312 1580 Tel: 020 3312 1527
Kingston Hospital NHS Foundation Trust Fax: 020 8934 3306 Tel: 020 8934 3305 Email: Khn-tr.OPReferrals@nhs.net	**King's College Hospital NHS Foundation Trust** Fax: 020 3299 1515 Tel: 020 3299 1516 Email: kch-tr.cancerdata@nhs.net	**Lewisham and Greenwich University Hospitals NHS Trust (Queen Elizabeth's)** Fax: 020 8836 4035 Tel: 020 8836 5964/5
North West London Hospitals NHS Trust Fax: 020 8235 4188 Tel: 020 8235 4293	**Princess Royal** Fax: 01689 863187 Tel: 01689 865676	**The Royal Marsden NHS Foundation Trust** Fax: 020 8661 3149 Tel: 0800 731 2325 Email: rmh-tr.referrals@nhs.net
St George's Healthcare NHS Trust Fax: 020 8725 0778 Tel: 020 8725 1111 Email: cancerreferraloffice@stgeorges.nhs.uk	**West Middlesex University Hospital NHS Trust** Fax: 020 8321 5157 Tel: 020 8321 6776	

CLINICAL GUIDANCE FOR URGENT UROLOGICAL CANCER REFERRALS

Patients with any of the following symptoms should be referred urgently using this proforma:

- Painless visible haematuria in adults
- Recurrent (>3 episodes in 6 months) or persistent (on-going despite minimum of 2 weeks antibiotics) urinary tract infection associated with pyuria in patients aged over 50 years
- Unexplained non visible haematuria greater than a trace in patients aged over 50 years
- An abdominal mass identified clinically or radiologically that is thought to arise from the urinary tract
- Swellings in the body of the testis
- Symptoms or signs of penile cancer, including progressive ulceration or a mass in the glans or prepuce or involving the skin of the penile shaft
- Raised or rising age-specific PSA – in men with other co-morbidities or life expectancy <10 years, consider discussion with patient/carers and/or a specialist before urgent referral
- Clinically malignant prostate on DRE. Prostate-specific antigen (PSA) should be measured and the result should accompany the referral

In male or female patients with symptoms suggestive of a urinary infection and macroscopic haematuria, diagnose and treat the infection before considering referral. If infection is not confirmed, refer them urgently.

Investigations in primary care required for referral:

- **PSA**
  - If initial PSA result is >20, then an immediate urgent referral should be made.
  - Raised or rising age-specific PSA (in men with other co-morbidities or life expectancy <10 years), consider discussion with patient/carers and/or a specialist before urgent referral.
  - Where possible and at the discretion of the referrer, two PSA tests should be obtained, 4 weeks apart, unless the prostate feels malignant upon examination or the first PSA test is >20.
- **Creatinine**
  - All Trusts operate a ‘one stop’ clinic for urgent referrals. Receipt of referrals with renal status will ensure that patients can undergo contrast imaging at the time of initial appointment.
  - Referral can be submitted without the results of the creatinine test as long as the test has been requested at the time of referral and is provided upon request from secondary care.

Appendix 2: LCA Key Worker Policy

Definition

A key worker is a person who, with the patient's consent and agreement, takes a key role in coordinating the patient's care and promoting continuity, ensuring that the patient knows who to access for information and advice in relation to their cancer diagnosis. In addition, the key worker will facilitate patients making informed decisions about their treatment.

The implementation of the key worker role is a requirement of the National Cancer Peer Review programme and is detailed in the *Manual for Cancer Services*, originally published by the National Cancer Action Team (NCAT), and related site-specific *Improving Outcomes Guidance*, issued by the National Institute for Health and Care Excellence.

Principles and responsibilities

Designation

1. The key worker is a named clinical member of the site-specific multidisciplinary team (MDT) and acts as the point of contact between the patient and MDT.
2. The key worker is a healthcare professional.
3. The key worker is assigned by the core Clinical Nurse Specialist (CNS) of an MDT, agreed by the MDT and recorded within the patient record and multidisciplinary meeting proforma.
4. The name of the key worker, designation and contact details will also be recorded in the patient handheld record (PHR), if used, and included in all correspondence and in the patient medical records. All entries in the medical notes will comply with the NHS Litigation Authority standards.

Access

5. All cancer patients will be made aware of their allocated key worker, but have the right to ask for an alternative if they prefer. This will usually happen at diagnosis.
6. The key worker will provide a contact number to all the patients for whom they act as the key worker.

Multi-professional communication

7. If a more appropriate person is identified as a key worker at a point in the patient's pathway, this will be discussed and agreed by the patient and the key worker, and recorded in the patient's notes.This situation is most likely to arise with referral to the palliative care team. In such cases the palliative care CNS will then negotiate and document care responsibilities in the patient's notes.
8. The key worker may change as patients pass through various stages of the care trajectory or when care is transferred to a different Trust. It is the responsibility of the key worker to hand over to the next one, to document this in the patient's notes and to keep the patient informed.
9. The key worker will lead on patient communication issues and coordination of the pathway for patients referred to the team.

10. The key worker will ensure that the patient pathway is coordinated and all relevant information is transferred to the appropriate professionals as the patient moves across care boundaries, e.g. on admission to and discharge from institutions, when care is transferred between teams.

11. The key worker has responsibility for ensuring holistic needs assessments (HNAs) are recorded/documented in patient records.

Patient communication and support

12. Where possible, the key worker will be available to support the patient on diagnosis to signpost and provide them with information and contacts for the MDT, national information and support services, self-help groups and associated site-specific support.

13. If the key worker is not available at the time of diagnosis, the person who is providing support at the time will ensure that the patient is aware of the key worker role and provide the relevant contact details.

14. The key worker will be accessible to the patient as a constant point of contact, handing over to colleagues when unavailable and making sure that the patient has clear information about alternative contacts and cover arrangements.

15. The key worker will provide information, care and support throughout the patient journey **regardless of the patient's condition**, liaising between health professionals to ensure continuity of care and a seamless service.

Data/audit

16. The key worker will contribute to the audit of key worker role in their organisation

Annex: NCAT peer review standard

There should be an operational policy whereby a single named key worker for the patient's care at a given time is identified by the MDT members for each individual patient and the name and contact number of the current key worker is recorded in the patient's case notes. The responsibility for ensuring that the key worker is identified should be that of the nurse MDT member(s).

The above policy should have been implemented for patients who came under the MDT's care after publication of these measures and who are under their care at the time of the peer review visit.

Notes

- According to the NICE supportive and palliative care guidance, a key worker is a person who, with the patient's consent and agreement, takes a key role in coordinating the patient's care and promoting continuity, e.g. ensuring that the patient knows who to access for information and advice. This is not intended to have the same connotation as the key worker in social work.
- It may be necessary to agree a single key worker across both a cancer site-specific MDT and the specialist palliative care MDT for certain patients.

Appendix 3: LCA Specialist Palliative Care Referral Form

LONDON CANCER ALLIANCE West and South LCA

Specialist Palliative Care (SPC) Community and SPC Inpatient Unit Referral Form (1/3)

Specialist Palliative Care Community Teams & Inpatient Units across South & West London

Greenwich & Bexley Community Hospice Bostall Hill, Abbey Wood **SE2 0GB** Home care: Tel: 020 83205837 Fax: 020 83205839 Admissions: Tel. 020 83122244 Fax: 020 83124344	**Lewisham Macmillan Community Team:** Lewisham High Street **SE13 6LH** Tel: 020 8333 3017 Fax: 020 8333 3270	**St Christopher's Hospice** Lawrie Park Rd, London **SE26 6DZ** Home care: Tel: 020 8776 5656 Fax: 020 87765798 Admissions: Tel. 020 87684582 Fax: 02086595051 St Christopher's Bromley Tel: 01689 825755 Fax: 01689 892999
Guy's & St Thomas' Community Team: Guy's Hospital, Great Maze Pond **SE1 9RT** Tel: 020 71884754 Fax: 020 71884748	**Meadow House Hospice** Southall **UB1 3HW** Tel: 020 89675179 Fax 020 89675756	**St John's Hospice** Grove End Road, St John's Wood **NW8 9NH** Tel:020 78064040 Fax: 020 78064041
Harlington Hospice St Peter's Way, Harlington **UB3 5AB** Tel: 020 87590453 Fax: 020 87590600	**Michael Sobell House** Northwood, Middlesex **HA6 2RN** Tel:01923 844531 Fax: 01923 844565	**St Luke's Hospice** Kenton Road, Harrow **HA3 0YG** Tel: 020 83828001 Fax: 020 83828080
Harrow Community Team Kenton Road, Harrow **HA3 0YG** Tel: 020 83828084 Fax: 020 83828085	**Pembridge Palliative Care Centre** Exmoor Street, **W10 6DZ** Tel: 020 8962 4410 Inpatient Fax: 020 89624422 Community Services Fax: 020 89624413	**St Raphael's Hospice** London Road, North Cheam **SM3 9DX** Tel: 020 80997777 Fax: 020 8099 1724
Hillingdon Community Team Pield Heath Road, Uxbridge **UB8 3NN** Tel:01895 279412 Fax: 01895 279452	**Princess Alice Hospice** West End Lane, Esher **KT10 8NA** Tel: 01372 461804 Fax: 01372 470937	**Trinity Hospice** Clapham Common **SW4 0RN** Tel: 020 7787 1000 Ref & Admissions Nurse: 020 77871065 Fax: 020 7787 1067

For further information and advice on these services, please visit the Help the Hospices service directory at:
http://www.helpthehospices.org.uk/about-hospice-care/find-a-hospice/uk-hospice-and-palliative-care-services/
and enter the postcode provided above.

Every LCA hospital has a Specialist Palliative Care team;
if your patient is a *hospital inpatient,* please contact the team, via the relevant hospital switchboard.

FAX MESSAGE	
From:	**To:**
Fax No:	**Date:**
No. of pages (incl cover sheet):	
Additional information	

Confidentiality: The content of this fax and attached documents are confidential and intended for the use of the addressee designated above. If you are not the addressee, you are hereby notified that you may not disclose, reproduce or otherwise disseminate or make use of this information for yourself or any third party. If you have received this in error, please notify us on the telephone number given above.

PLEASE SEND COPIES OF RECENT CLINICAL CORRESPONDENCE WITH THIS FORM – including recent clinic letters, blood tests and most recent imaging
NB. INSUFFICIENT INFORMATION MAY DELAY PATIENT ASSESSMENT

PATIENT NAME ..... **NHS No:**.....

LCA Palliative Care Group Revised April 2014

LONDON CANCER ALLIANCE West and South LCA

Referral Form for SPC Community and Inpatient Units (2/3)

Essential Patient Details		
Surname	Male/Female Age:	Patient consent to palliative care involvement? Yes ☐ No ☐
First Name	DoB	Is GP aware of referral? Yes ☐ No ☐
Address		
Postcode	Marital Status	Ethnicity
Tel	Mob	
NHS number	**Hospital No.**	

Primary diagnosis(es)

Communication	Other barriers to communication / registered disabilities:
Fluent in English? Yes ☐ No ☐ (If 'no' proceed with remaining questions)	
First Language, if not English:	
Would interpreter be helpful to patient and Palliative Care staff? Yes ☐ No ☐	

Next of Kin/Patient Representatives	**District Nurse** Yes ☐ No ☐	**General Practitioner**
Name	Name	Name
Address	Based at	Address
	Telephone	
Telephone	Fax	
Relationship to patient		Postcode
Main Carer (if different from above)	**Social Services** Yes ☐ No ☐	Telephone
Name	Name	
Telephone	Based at	Fax/email
Relationship to patient	Tel Fax	
	Continuing care assessment completed: Yes/No	CCG:
	Continuing care funding agreed: Yes/No	

Reason for Referral	**Service requested**	**The patient is currently**
Pain/symptom control ☐	Home assessment and support ☐	At Home ☐
Emotional/psychological support ☐	Hospital assessment ☐	In Hospital (see over) ☐
Social/financial ☐	Day Care ☐	Other e.g. Nursing Home ☐
Assessment for hospice admission ☐	Outpatient service ☐	Please specify.....
Carer support ☐	Admission (circle) ☐	
Other reason *(please give details below)* ☐	Respite / symptom control / terminal care	Does patient live alone? Yes ☐ No ☐
.....	Hospice at Home ☐	

Any access issues (e.g. key safe):	
MRSA Status Positive ☐ Negative ☐ Not known ☐	**Any other communicable infection:** .....
Special device in situ? Yes ☐ No ☐ If yes, give details (e.g. trache / PEG / ICD / NIPPV):.....	
Referrer's Name: (please print)	**Contact number:** **Bleep no:**
Hospital/Surgery:	**This information required on both pages if faxing**

IS REFERRAL URGENT (assess within 2 working days)? Yes ☐ No ☐

IF URGENT, PLEASE PHONE US FOR IMMEDIATE ADVICE

LCA Palliative Care Group Revised April 2014

LONDON CANCER ALLIANCE West and South LCA

Referral Form for SPC Community and Inpatient Units (3/3)

In-Patient details	**Patient Name:**
Hospital	NHS No:
Ward Direct Ward Ext.	Telephone
Key worker	Date of discharge (if known)
Consultant	Is Palliative Care team involved? Yes ☐ No ☐

Brief History of diagnosis(es) and Key treatments

Date	Progression of disease and investigations/treatment	Consultant and hospital

Current palliative care problems	
1.	4.
2.	5.
3.	6.
Patient Mobility:	**Bariatric Nursing required?** Yes ☐ No ☐

Any other comments/information (including preferences expressed about care or other psychosocial or spiritual issues)

Referrer's expectation of current treatment *(please circle)* symptom control / life prolonging / curative

Prognosis: In your opinion, is the patient

Stable? Yes ☐ No ☐ **Unstable?** Yes ☐ No ☐ **Deteriorating?** Yes ☐ No ☐ **Dying?** Yes ☐ No ☐

Is death anticipated within: Months ☐ Weeks ☐ Days ☐

Patient on Coordinate My Care? Yes ☐ No ☐ Unknown ☐ If not please give reason.....

On the GSF register? Yes ☐ No ☐ Unknown ☐ **DNACPR in place?** Yes ☐ No ☐

Past Medical and Psychiatric History	**Current Medication**	
		Known Drug Sensitivities/Allergies:
		Yes ☐ No ☐
		Details:

Insight: Has patient been told diagnosis? Yes ☐ No ☐ **Is the carer aware of patient's diagnosis?** Yes ☐ No ☐

Does patient discuss the illness freely Yes ☐ No ☐

Please ensure patients are aware information will be held on computer according to the Data Protection Act.

Referrer's signature:	**Name:** (please print)
Job title:	**Contact number:** **Bleep no:**
Surgery or Hospital:	**Date:**

Appendix 4: LCA Holistic Needs Assessment Tool

The tool can be downloaded from the LCA website.

LONDON CANCER ALLIANCE West and South | LONDON CANCER NORTH AND EAST

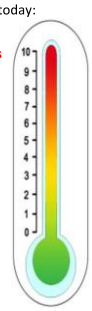
London Holistic Needs Assessment

For each item below, please tick **yes** or **no** if they have been a concern for you during the last week, including today. Please also tick **discuss** if you wish to speak about it with your health professional.
Choose not to complete the assessment today by ticking this box ☐

Date:	
Name:	
Hospital/NHS number:	

Please **tick the number** that best describes the overall level of distress you have been feeling during the last week, including today:

10 ☐ **Extreme distress**
9 ☐
8 ☐
7 ☐
6 ☐
5 ☐
4 ☐
3 ☐
2 ☐
1 ☐
0 ☐ **No distress**



For health professional use

Date of diagnosis:	
Diagnosis:	
Pathway point:	

Practical concerns	**Yes**	**No**	**Discuss**
Caring responsibilities	☐	☐	☐
Housing or finances	☐	☐	☐
Transport or parking	☐	☐	☐
Work or education	☐	☐	☐
Information needs	☐	☐	☐
Difficulty making plans	☐	☐	☐
Grocery shopping	☐	☐	☐
Preparing food	☐	☐	☐
Bathing or dressing	☐	☐	☐
Laundry or housework	☐	☐	☐
Family concerns			
Relationship with children	☐	☐	☐
Relationship with partner	☐	☐	☐
Relationship with others	☐	☐	☐
Emotional concerns			
Loneliness or isolation	☐	☐	☐
Sadness or depression	☐	☐	☐
Worry, fear or anxiety	☐	☐	☐
Anger, frustration or guilt	☐	☐	☐
Memory or concentration	☐	☐	☐
Hopelessness	☐	☐	☐
Sexual concerns	☐	☐	☐
Spiritual concerns			
Regret about the past	☐	☐	☐
Loss of faith or other spiritual concern	☐	☐	☐
Loss of meaning or purpose in life	☐	☐	☐

Physical concerns	**Yes**	**No**	**Discuss**
High temperature	☐	☐	☐
Wound care	☐	☐	☐
Passing urine	☐	☐	☐
Constipation or diarrhoea	☐	☐	☐
Indigestion	☐	☐	☐
Nausea and/or vomiting	☐	☐	☐
Cough	☐	☐	☐
Changes in weight	☐	☐	☐
Eating or appetite	☐	☐	☐
Changes in taste	☐	☐	☐
Sore or dry mouth	☐	☐	☐
Feeling swollen	☐	☐	☐
Breathlessness	☐	☐	☐
Pain	☐	☐	☐
Dry, itchy or sore skin	☐	☐	☐
Tingling in hands or feet	☐	☐	☐
Hot flushes	☐	☐	☐
Moving around or walking	☐	☐	☐
Fatigue	☐	☐	☐
Sleep problems	☐	☐	☐
Communication	☐	☐	☐
Personal appearance	☐	☐	☐
Other medical condition	☐	☐	☐

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Care Plan

During my holistic needs assessment, these issues were identified and discussed:

Preferred name: **Hospital/NHS number:**

Number	**Issue**	**Summary of discussion**	**Actions required/by (name and date)**
Example	Breathlessness	Possible causes identified Coping strategies discussed Printed information provided	Referral to anxiety management programme; CNS to complete by 24th Dec
1			
2			
3			
4			

Other actions/outcomes e.g. additional information given, health promotion, smoking cessation, 'My actions':

Signed (patient):	Date:
Signed (healthcare professional):	Date:

For health professional use		
Date of diagnosis:	Diagnosis:	Pathway point:

Appendix 5: Treatment of Children

Children below the age of 16 years with a diagnosis of cancer or suspected cancer must be referred to the paediatric oncology team at the principal treatment centre (PTC) and must not be managed exclusively by adult site-specific teams.

- The joint PTC for children aged 1 to 16 years for South Thames is The Royal Marsden Hospital (Sutton site)/St George's Hospital.
- The PTC for North Thames (including North West London) is Great Ormond Street Hospital/University College London Hospital.
- **All** patients aged <1 year from both North and South Thames should be referred to Great Ormond Street Hospital.

For certain tumour types that are uncommon in children (e.g. skin, melanoma, head and neck, thyroid, gastrointestinal, hepatobiliary) the paediatric oncology team should liaise with the appropriate site-specific multidisciplinary team for advice about management and to agree surgical interventions, but overall responsibility for managing the patient remains with the paediatric oncology team.

Please see below for contact details for the children's PTCs.

South Thames principal treatment centre contacts

The Royal Marsden NHS Foundation Trust	Lead Clinician – Dr Julia Chisholm julia.chisholm@rmh.nhs.uk 020 8661 3549 **Paediatric oncology on-call registrar (new referrals)** **020 8915 6248 (24-hour line)**

North Thames principal treatment centre contacts

Great Ormond Street Hospital (patients aged <13 years)	Lead Clinician – Darren Hargrave darren.hargrave@nhs.net
University College London Hospitals (patients aged ≥13 years)	Lead Clinician – Dr Sara Stoneham sara.stoneham@uclh.nhs.uk 020 3447 9950

Appendix 6: Treatment of Teenagers and Young Adults

The *Improving Outcomes Guidance (IOG) for children and young people with cancer* (2005) and subsequent *Teenage and Young Adults Cancer Measures* (2012) recommend that patients aged 16–18 are managed at a principal treatment centre (PTC) for teenager and young adult (TYA) cancers and that those aged 19–24 are given the choice of being managed at a PTC or a TYA designated hospital.

- The PTC for TYA for South Thames is The Royal Marsden Hospital.
- The PTC for North Thames (including north west London) is University College London Hospital.

All patients within this age range, regardless of place of care, should be referred to the TYA MDT at the relevant PTC. Referral to the MDT should be made using the TYA referral form.

Discussion at the TYA multidisciplinary team (MDT) is in addition to the specialist MDT; key functions of the TYA MDT are to agree the treatment plan of the specialist MDT, ensure cancer registration and provide a psychosocial care plan. Members of the specialist MDT or TYA service at the PTC or TYA designated hospitals are invited to attend the TYA either remotely or in person.

South Thames principal treatment centre contacts

The Royal Marsden NHS Foundation Trust	Lead Clinician – Dr Julia Chisholm julia.chisholm@rmh.nhs.uk TCT Nurse Consultant for Adolescents and Young Adults Louise Soanes lsoanes@nhs.net

LCA TYA designated centres contacts allied to RMH PTC

Joint Centre (Guy's and St Thomas' NHS Foundation Trust/King's College Hospital NHS Foundation Trust)	Guy's and St Thomas'	Lead Clinician – Dr Robert Carr Robert.carr@gstt.nhs.uk Lead Nurse – Gavin Maynard-Wyatt Gavin.maynard-wyatt@gstt.nhs.uk
Joint Centre (Guy's and St Thomas' NHS Foundation Trust/King's College Hospital NHS Foundation Trust)	King's College Hospital	Lead Clinician – Dr Donal.Mclornan donal.mclornan@nhs.net Lead Nurse – Gavin Maynard-Wyatt Gavin.maynard-wyatt@gstt.nhs.uk
St George's Healthcare NHS Trust	St George's Hospital	Lead Clinician – Dr Jens Samol jens.samol@stgeorges.nhs.uk Lead Nurse – Linda Shephard Linda.shephard@stgeorges.nhs.uk

North Thames principal treatment centre contacts

University College London Hospitals	Lead Clinician – Dr Rachael Hough Rachael.hough@uclh.nhs.uk TCT Nurse Consultant for Teenagers and Young Adults – Wendy King wendy.king@uclh.nhs.uk

LCA TYA designated centres contacts allied to UCLH PTC

Chelsea and Westminster Hospital NHS Foundation Trust	Chelsea and Westminster (HIV and skin only)	Lead Clinician – Dr Mark Bower (interim) Mark.Bower@chelwest.nhs.uk Lead Nurse – Kate Shaw (interim) Kate.Shaw@chelwest.nhs.uk
Imperial College Healthcare NHS Trust	Charing Cross	Lead Clinician – Dr Josu de la Fuente (deputy) j.delafuente@imperial.ac.uk Lead Nurse – Sinead Cope sinead.cope@imperial.nhs.uk
East and North Hertfordshire NHS Trust	Mount Vernon Cancer Centre	Lead Clinician (MVCC) – Dr Gordon Rustin grustin@nhs.net Lead Nurse (MVCC) – Laura Miles laura.miles@nhs.net

Appendix 7: List of contributors

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