Prostate cancer: diagnosis and treatment

NICE guideline
Draft for consultation, July 2007

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.
Introduction

Prostate cancer is one of the commonest cancers in men. Each year there are about 27,773 new cases in England and Wales and 9161 deaths. Prostate cancer is predominantly a disease of older men but around 20% of cases occur in men under the age of 65. Over the past 10 to 15 years there have been a number of significant advances in its management but also a number of major controversies, especially about the clinical management of patients with early, non-metastatic disease. These uncertainties clearly cause anxieties for patients and their families. There is evidence of practice variation around the country and of patchy availability of certain treatments and procedures. A clinical guideline will help to address these issues and offer guidance on best practice.

The guideline will assume that prescribers will use a drug’s summary of product characteristics to inform their decisions for individual patients.
Patient-centred care

This guideline offers best practice advice on the care of men with prostate cancer.

Treatment and care should take into account patients' 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 patients 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). Since April 2007 healthcare professionals need to follow a code of practice accompanying the Mental Capacity Act (summary available from www.dca.gov.uk/menincap/bill-summary.htm).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient’s needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.
Key priorities for implementation

- Men should be adequately informed about the effects of prostate cancer and the treatment options on their sexual function, appearance, continence and aspects of self-image. Healthcare professionals should support men and their partners to make treatment decisions taking into account the effects on quality of life as well as survival. [1.1.10]

- The man’s decision whether or not to proceed to prostate biopsy should be informed by the prostate specific antigen (PSA) level, estimate of prostate size, digital rectal examination (DRE) findings, age, ethnicity, and comorbidities, together with any history of a previous negative prostate biopsy. The serum PSA level alone should not automatically lead to a prostate biopsy. [1.2.1]

- Men with localised low-risk prostate cancer should not routinely be offered immediate radical therapy. They should be offered watchful waiting or active surveillance, depending on their life expectancy and values. [1.3.3]

- Men undergoing radical external beam radiotherapy for prostate cancer should receive a minimum dose of 74Gy to the prostate at no more than 2Gy per fraction. [1.3.12]

- Men and their partners should have early and ongoing access to specialist erectile dysfunction services. [1.3.21]

- Men with bothersome urinary symptoms 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, bladder retraining and pharmacotherapy. Men with intractable stress incontinence should be referred to a specialist surgeon for consideration of an artificial urinary sphincter. [1.3.26]

- Biochemical relapse alone should not necessarily prompt an immediate change in treatment. [1.4.2]

- Hormonal therapy is not routinely recommended for men with biochemical relapse unless they have:
  - symptomatic local disease progression; or
  - any proven metastases; or
• PSA doubling time <3months. [1.4.10]

• When men develop biochemical evidence of hormone refractory disease their management options should be discussed by the urology multidisciplinary team (MDT) with a view to seeking an oncological and/or specialist palliative care opinion as appropriate. [1.6.14]

• Palliative care should be 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. [1.6.30]
1 Guidance

The following guidance is based on the best available evidence. The full guideline [add hyperlink] gives details of the methods and the evidence used to develop the guidance.

1.1 Communication and patient centred care

1.1.1 Recommendations on communication and patient centred care made in the two service guidance documents: “Improving Outcomes in Urological Cancers service guidance (NICE 2002)” and “Improving Supportive and Palliative Care for Adults with Cancer (NICE 2004)” should be followed throughout the patient journey.

1.1.2 Men with prostate cancer should receive individualised information tailored to their own needs. This information should be given by a clinician (consultant or specialist nurse) and may be supported by written and visual media.

1.1.3 Men should be offered advice about how to access information and support from the internet (including “UK Prostate Cancer Link”) and other media, local and national cancer information services, and from cancer support groups.

1.1.4 When choosing or recommending information resources, healthcare professionals should ensure that their content is clear, reliable and up to date.

1.1.5 Healthcare professionals should seek and act on feedback from men with prostate cancer and their carers who use these resources.

1.1.6 Clinical staff caring for men with prostate cancer should ascertain the extent to which the man wishes to be involved in decision
making and ensure that they have sufficient information to enable them to be so.

1.1.7 A validated, up-to-date decision aid is recommended for use in all urology cancer teams. It should be offered to men with localised prostate cancer when making treatment decisions, by healthcare professionals trained in its use.

1.1.8 All relevant management options recommended in this guideline should be discussed whether or not they are available through local services.

1.1.9 Mechanisms should be put in place to ensure that, over prolonged periods of time, men and their primary care providers can gain access to specialist services.

1.1.10 Men should be adequately informed about the effects of prostate cancer and the treatment options on their sexual function, appearance, continence and aspects of self-image. Healthcare professionals should support men and their partners to make treatment decisions taking into account the effects on quality of life as well as survival.

1.1.11 Men and their partners should have the opportunity to discuss psychosexual issues with an appropriately skilled healthcare professional at any stage of the illness and its treatment.

1.2 Diagnosis and staging of prostate cancer

1.2.1 The man’s decision whether or not to proceed to prostate biopsy should be informed by the prostate specific antigen (PSA) level, estimate of prostate size, digital rectal examination (DRE) findings, age, ethnicity, and comorbidities, together with any history of a previous negative prostate biopsy. The serum PSA level alone should not automatically lead to a prostate biopsy.
1.2.2 Men (and their partners) should be given information, support and adequate time to decide whether or not they wish to undergo prostate biopsy. 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 potential benefits of prostate biopsy.

1.2.3 If the clinical suspicion of prostate cancer is high, because of a high PSA value and evidence of multiple bone metastases (positive isotope bone scan or sclerotic metastases on plain radiographs), prostate biopsy for histological confirmation should be omitted, unless this is required as part of a clinical trial.

1.2.4 Prostate biopsy should be carried out following the procedure recommended by the Prostate Cancer Risk Management Programme Document (PCRMP 2006).

1.2.5 The results of all prostate biopsies should be reviewed by a urological cancer multidisciplinary team (MDT). Men should only be re-biopsied after an MDT review of the risk characteristics including life expectancy, PSA, DRE, and prostate volume.

1.2.6 The provisional treatment intent (radical or not) should be determined before decisions on imaging are made.

1.2.7 Imaging is not routinely recommended for men in whom no radical treatment is intended.

1.2.8 Pelvic imaging is not recommended for men with low-risk disease (T1c or T2a, PSA≤10ng/ml, Gleason score ≤6).

1.2.9 Computerised Tomography (CT) imaging of the pelvis is not recommended for men with intermediate-risk disease (PSA 10-20ng/ml, or Gleason score 7, or clinical stage T2b or T2c).

1.2.10 Men with high-risk disease (T3, PSA>20ng/ml, or Gleason score 8-10) being considered for radical treatment should have pelvic
imaging with either Magnetic Resonance Imaging (MRI), or CT if contraindicated.

1.2.11 Magnetic Resonance Spectroscopy (MRS) is not recommended except in the context of a clinical trial.

1.2.12 Isotope bone scintigraphy is not routinely recommended for men with low-risk disease.

1.2.13 Bone scanning should be performed when hormonal therapy is being deferred in high-risk, asymptomatic men.

1.2.14 Positron emission tomography (PET) imaging for prostate cancer is not recommended in routine clinical practice.

1.2.15 Nomograms should be used by doctors and patients in partnership to:

- aid decision making
- predict biopsy results
- predict pathological stage
- predict risk of treatment failure.

1.2.16 Where nomograms are used the reliability, validity and limitations of the prediction should be clearly explained, with appropriate support.

1.3 **Localised prostate cancer**

1.3.1 Urological cancer MDTs should assign a risk category to all newly diagnosed men with localised prostate cancer.

1.3.2 Men who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care. Investigations should not be performed unless symptoms occur and treatment is appropriate.

1.3.3 Men with localised low-risk prostate cancer should not routinely be offered immediate radical therapy. They should be offered watchful...
waiting or active surveillance, depending on their life expectancy and values.

1.3.4 Active surveillance is strongly recommended for men with a clinical stage T1c, a Gleason score 3+3, and with a PSA density <0.15ng/ml and less than 50% of biopsy cores involved (<10mm of any 1 core involved).

1.3.5 Active surveillance can be recommended for other men with low-risk disease.

1.3.6 Active surveillance should be discussed as an option with men who have intermediate-risk disease.

1.3.7 Active surveillance is not recommended for men with high-risk localized disease.

1.3.8 For men on active surveillance the following regimen is recommended:

- To reduce the sampling error associated with prostate biopsy, men who are candidates for active surveillance should have had at least 10 biopsy cores.
- Repeat prostate biopsy should be performed at 1, 4 and 7 years, in accordance with the ProSTART trial protocol.
- PSA should be tested every 3 months during the first 2 years and 6 monthly thereafter.
- PSA velocity should be estimated by linear regression of PSA against time, using at least 5 PSA values over at least one year, and preferably over 2 or more years. A tool such as the Prostagram (http://www.mskcc.org/mskcc/html/10088.cfm) should be used.
- Indications for considering radical treatment include any of a PSA velocity >1ng/ml/year, higher-grade or more extensive disease on repeat biopsy, or evidence of locally advanced disease on DRE.
- The decision to proceed to radical treatment should be made in the light of the individual man’s values, comorbidities and life expectancy.

1.3.9 Radical prostatectomy or radical radiotherapy (conformal or brachytherapy) should be considered for men with intermediate-risk localised prostate cancer.

1.3.10 Radical prostatectomy or radical radiotherapy (conformal) is recommended for men with high-risk localised prostate cancer.

1.3.11 For men receiving radical external beam radiotherapy for localised prostate cancer, 3D conformal radiotherapy should be used.

1.3.12 Men undergoing radical external beam radiotherapy for prostate cancer should receive a minimum dose of 74Gy to the prostate at no more than 2Gy per fraction.

1.3.13 Given the range of treatment modalities and their serious side effects, men with prostate cancer who are candidates for radical therapies should have the opportunity to discuss their treatment options with both a specialist surgical oncologist and a specialist clinical oncologist.

1.3.14 Other radical therapies such as cryotherapy and high intensity focussed ultrasound (HIFU) are not recommended for men with localised or locally advanced prostate cancer other than in the context of controlled clinical trials.

1.3.15 Men 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.
1.3.16 Men treated with radical radiotherapy for prostate cancer should be offered follow-up with flexible sigmoidoscopy every 5 years.

1.3.17 Steroid enemas should not be used for treating men with radiation proctopathy.

1.3.18 The nature and treatment of radiation-induced injury to the gastrointestinal (GI) tract should be included in the training programmes for oncologists and gastroenterologists.

1.3.19 Prior to treatment, men and their partners should be warned that treatment for prostate cancer will result in an alteration of sexual experience, and may result in loss of sexual function.

1.3.20 Men and their partners should be warned about the potential loss of ejaculation and fertility associated with treatment for prostate cancer. Sperm storage should be offered if fertility is important to the man and/or his partner.

1.3.21 Men and their partners should have early and ongoing access to specialist erectile dysfunction services.

1.3.22 Men with prostate cancer who experience loss of erectile function should be offered PDE5 (phosphodiesterase type 5) inhibitors to improve the chance of spontaneous erections.

1.3.23 If PDE5 inhibitors fail to restore erectile function or are contraindicated, vacuum devices, intraurethral inserts or penile injections, or penile prostheses should be considered as an alternative.

1.3.24 Men experiencing bothersome urinary symptoms before treatment should undergo urological assessment.

1.3.25 Men undergoing treatment for prostate cancer should be warned of the likely effects of the treatment on their urinary function.
1.3.26 Men with bothersome urinary symptoms 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, bladder retraining and pharmacotherapy. Men with intractable stress incontinence should be referred to a specialist surgeon for consideration of an artificial urinary sphincter.

1.3.27 The injection of bulking agents into the distal urinary sphincter is not recommended to treat stress incontinence.

1.3.28 The purpose, duration, frequency and location of follow-up should be discussed with each man, and where he wishes, his partner.

1.3.29 Men should be clearly advised about potential longer term adverse effects and when and how to report them.

1.3.30 PSA levels should be checked at the earliest 6 weeks following treatment, at least 6 monthly for the first 2 years and then at least yearly thereafter.

1.3.31 Routine DRE is not recommended while the PSA remains at baseline levels.

1.3.32 After 2 years at the earliest, men with a stable PSA and no significant treatment complications, should be offered follow-up outside hospital, for example in primary care, by telephone or e-mail, or a combination, unless they are participating in a clinical trial which requires more formal clinic-based follow-up. The opportunity of direct access to the specialist team should be offered and explained.

1.3.33 Men who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care.

1.4 The management of relapse after radical treatment

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1.4.1 Serial PSA levels after radical treatment should be analysed using the same assay technique.

1.4.2 Biopsy of the prostatic bed should not be performed in men who have had a radical prostatectomy.

1.4.3 Biopsy of the prostate after radiotherapy should only be done in men being considered for salvage local therapy in the context of clinical research.

1.4.4 Routine MRI scanning should not be performed prior to salvage radiotherapy.

1.4.5 An isotope bone scan should be performed if symptoms or PSA trends are suggestive of metastases.

1.4.6 Biochemical relapse alone should not necessarily prompt an immediate change in treatment.

1.4.7 Biochemical relapse should trigger an estimate of PSA doubling time, based on a minimum of 3 measurements over at least a 6 month period.

1.4.8 Men with biochemical relapse after radical prostatectomy, with no known metastases, should be offered early radical radiotherapy to the prostate bed.

1.4.9 Men with biochemical relapse should be considered for entry to appropriate clinical trials, for example RADICALS.

1.4.10 Hormonal therapy is not routinely recommended for men with biochemical relapse unless they have:

- symptomatic local disease progression; or
- any proven metastases; or
- a PSA doubling time <3months.
1.5 *Locally advanced prostate cancer*

1.5.1 Neoadjuvant and concurrent luteinising hormone-releasing hormone agonist (LHRHa) therapy for 3 to 6 months is recommended for men receiving radical radiotherapy for high-risk localised or locally advanced prostate cancer.

1.5.2 Adjuvant hormonal therapy in addition to radical prostatectomy is not recommended, even in margin positive disease, other than in the context of a clinical trial, for example RADICALS.

1.5.3 Adjuvant hormonal therapy for up to 3 years is recommended for men receiving neoadjuvant hormonal therapy and radical radiotherapy for high-risk localised or locally advanced prostate cancer who have a Gleason score of ≥8.

1.5.4 Adjuvant hormonal therapy is not recommended for men with a Gleason score of ≤7.

1.5.5 Bisphosphonates should not be used for the prevention of bone metastases in men with prostate cancer.

1.5.6 Pelvic radiotherapy should be considered in men with >15% risk (estimated using the Roach formula (%LN risk = 2/3 PSA + [10x (Gleason score - 6)]) of pelvic lymph node involvement who are to receive neoadjuvant hormonal therapy and radical radiotherapy to the prostate.

1.5.7 Immediate post-operative radiotherapy after radical prostatectomy is not recommended, even in margin positive disease, other than in the context of a clinical trial, for example RADICALS.

1.6 *Metastatic prostate cancer*

1.6.1 Bilateral orchidectomy should be recommended as an alternative to continuous LHRHa therapy.
1.6.2 Combined androgen blockade is not recommended as first-line treatment.

1.6.3 For men who are willing to accept the adverse impact on overall survival and gynaecomastia in the hope of retaining sexual function, anti-androgen monotherapy with bicalutamide\(^1\) is appropriate.

1.6.4 Men taking bicalutamide who do not maintain satisfactory sexual function, should stop bicalutamide and be treated with androgen withdrawal.

1.6.5 Intermittent androgen withdrawal may be offered as an alternative to continuous androgen withdrawal, especially to men with severe side effects.

1.6.6 Synthetic progestogens are recommended as first-line therapy for the management of troublesome hot flushes. If oral therapy is used it should be given for 2 weeks, and re-started, if effective, on recurrence of symptoms.

1.6.7 Men starting long-term (>6 months) bicalutamide monotherapy daily should receive prophylactic radiotherapy to both breast buds within the first month of treatment. A single fraction of 8 Gy using orthovoltage radiotherapy is recommended.

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

1.6.9 Men starting androgen withdrawal therapy should be informed that regular resistance exercise reduces fatigue and improves quality of life.

1.6.10 Docetaxel is recommended, within its licensed indications, as a treatment option for men with hormone refractory metastatic prostate cancer.

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\(^1\) BNF states that bicalutamide monotherapy should be at a dose of 150 mg daily. A lower dose (50 mg) is used for combined androgen blockade.
prostate cancer only if their Karnofsky performance status score is 60% or more.

1.6.11 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.

1.6.12 Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy.

1.6.13 When men develop biochemical evidence of hormone refractory disease their management options should be discussed by the urology MDT with a view to seeking an oncological and/or specialist palliative care opinion as appropriate.

1.6.14 Dexamethasone at a dose of 0.5mg daily\textsuperscript{2} is recommended as third line hormonal therapy after androgen withdrawal and anti-androgen therapy.

1.6.15 Men with hormone refractory prostate cancer shown to have extensive disease in the spine, for example on a bone scan, should have spinal MRI if they develop any spinal related symptoms.

1.6.16 The routine use of spinal MRI for all men with hormone refractory prostate cancer and known bone metastases is not recommended.

1.6.17 The use of bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone refractory prostate cancer (HRPC) is not recommended.

\textsuperscript{2} Often used at higher doses in other indications

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1.6.18 Bisphosphonates for pain relief may be considered when other treatments, including analgesics and palliative radiotherapy, have failed. The choice of drug should be based on the cost and either the oral or intravenous route of administration should be chosen according to convenience and tolerability.

1.6.19 Bisphosphonates should not be used routinely in men receiving androgen withdrawal therapy for prostate cancer.

1.6.20 The recommendations in the NICE Clinical Guideline on Osteoporosis should be followed once it is published.

1.6.21 Sr-89 should be considered for men with painful bone metastases from HRPC especially for men who are unlikely to receive myelosuppressive chemotherapy.

1.6.22 Upper urinary tract decompression 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.

1.6.23 The option of no intervention should also be discussed openly with men and remains a choice for some.

1.6.24 Men with metastatic prostate cancer should receive tailored information and access to specialist urology and palliative care teams to address their specific needs.

1.6.25 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.

1.6.26 Men with metastatic prostate cancer should be given the opportunity to discuss their therapy and information needs with members of both urology and specialist palliative care teams when there are significant changes in their disease status or symptoms.
1.6.27 Palliative interventions at any stage should be integrated into co-ordinated care, and any transitions of care settings should be facilitated as smoothly as possible.

1.6.28 Men with 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.

1.6.29 Palliative care should be 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.
2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from www.nice.org.uk/page.aspx?o=273125.

Groups that will be covered:

- Adults referred from primary care for investigation of possible prostate cancer, in line with the NICE clinical guidelines on referral suspected cancer (NICE clinical guideline 27).
- Adults with a biopsy-proven diagnosis of primary adenocarcinoma of the prostate or an agreed clinical diagnosis* when biopsy would be inappropriate. (*Agreed clinical diagnosis on the basis of, for example, digital rectal examination, high prostate-specific antigen [PSA] and known metastases.)
- No patient subgroups needing special consideration have been identified.

Groups that will not be covered:

- Asymptomatic adults with an abnormal, age-specific PSA level and no biopsy-proven diagnosis of prostate cancer.
- Patients with metastatic disease of different primary origin involving the prostate.
- Children and adults with rare malignant tumours of the prostate, such as small cell carcinoma and rhabdomyosarcoma.
How this guideline was developed

NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information in the booklet: ‘The guideline development process: an overview for stakeholders, the public and the NHS’ (third edition, published April 2007), which is available from www.nice.org.uk/guidelinesprocess or by telephoning 0870 1555 455 (quote reference N1233).

3 Implementation

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in ‘Standards for better health’, issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CGXXX).

[NICE to amend list as needed at time of publication]

- Slides highlighting key messages for local discussion.
- Costing tools:
  - costing report to estimate the national savings and costs associated with implementation
  - costing template to estimate the local costs and savings involved.
- Implementation advice on how to put the guidance into practice and national initiatives that support this locally.
- Audit criteria to monitor local practice.
4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group’s full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Radiation-induced enteropathy

Research into the causes, and clinical trials of prevention and management of radiation-induced enteropathy should be undertaken.

Why this is important
Radiotherapy remains the most common radical treatment for localised prostate cancer and is often associated with varying degrees of enteropathy. These effects may be early or late; short-lasting or long-lasting. The biological processes are poorly understood and the best way of preventing or managing the condition is unclear.

4.2 Erectile dysfunction

Further research should be conducted into the timing and effectiveness of treatments for erectile dysfunction after all treatments for prostate cancer.

Why this is important
Erectile dysfunction is especially common after radical treatment for prostate cancer and also in more advanced disease. While effective treatments are available, it is not known which are most effective in this setting or when it is best to commence treatment.

4.3 Complications of long term androgen withdrawal therapy

More research should be conducted into the prevention and management of osteoporosis in men receiving long-term androgen withdrawal therapy.
Why this is important
Androgen withdrawal therapy is sometimes used in men with advanced prostate cancer but it often causes loss of bone mineral and consequential bone fractures. The current evidence of commonly used interventions is insufficient to make conclusions about their clinical efficacy and cost effectiveness in this setting.

4.4 Radical surgery and extended lymphadenectomy
The role of radical surgery and extended lymphadenectomy as primary therapy for locally advanced prostate cancer should be studied in clinical trials.

Why this is important
Lymph node involvement is a risk factor for death from prostate cancer. Some patients undergoing radical surgical treatment have involved margins (locally advanced disease) at resection. Others have extracapsular disease diagnosed prior to treatment decisions being made. It is not known if a radical attempt at cure with surgery improves survival.

4.5 Role of bisphosphonates
Further clinical trials should be conducted to determine if there is a role for bisphosphonates in men with prostate cancer.

Why this is important
Many men with metastatic prostate cancer develop bone metastases. These are often painful and may result in serious spinal injury. In other cancer sites, e.g. breast, there is a demonstrable benefit from the use of bisphosphonates. However, there is insufficient evidence of a beneficial effect of their use in men with prostate cancer.

5 Other versions of this guideline

5.1 Full guideline
The full guideline, 'Prostate Cancer: diagnosis and treatment' contains details of the methods and evidence used to develop the guideline. It is published by Prostate Cancer: NICE guideline DRAFT (July 2007)
the National Collaborating Centre for Cancer, and is available from [NCC website details to be added], our website (www.nice.org.uk/CGXXXfullguideline) and the National Library for Health (www.nlh.nhs.uk). [Note: these details will apply to the published full guideline.]

5.2 Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/CGXXXquickrefguide

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

5.3 ‘Understanding NICE guidance’

Information for patients and carers (‘Understanding NICE guidance’) is available from www.nice.org.uk/CGXXXpublicinfo

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

6 Related NICE guidance

Published


Prostate Cancer: NICE guideline DRAFT (July 2007)


Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Osteoporosis: Assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. NICE clinical guideline. (publication date to be confirmed).

7 Updating the guideline

NICE clinical guidelines are updated as needed so that recommendations take into account important new information. We check for new evidence 2 and 4 years after publication, to decide whether all or part of the guideline should be updated. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.
Appendix A: The Guideline Development Group

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Margaret Jewitt
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Mr John McLoughlin
Consultant Urologist, West Suffolk Hospital Bury Edmunds and Honorary Consultant Urologist Addenbrooke’s Hospital Cambridge
Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

John Hyslop (Chair)
Consultant Radiologist, Royal Cornwall Hospital NHS Trust

Ash Paul
Deputy Medical Director, Health Commission Wales (Specialist Services)

Debra Collard
Lay representative

Jonathan Hopper
Medical Director (UK and Ireland), ConvaTec
Appendix C: The algorithms

A pictorial guide to show how the guideline is structured.

Prostate Cancer Pathway

Man referred with suspected prostate cancer*¹ →

Diagnosis & Staging

→

Treatment for localised, locally advanced or metastatic disease

→

Relapse

Follow Up

Complications & side effects

¹ NICE Guidance on Referral for Suspected Cancer
Diagnosis & staging

Man referred with suspected prostate cancer

Decision made to proceed to biopsy
- Information & support to be provided before biopsy

MDT:
- Review biopsy result
- Assign initial risk group
  - Use nomograms
- Organise staging
  - Radiological staging only after treatment intent is decided

Monitor PSA

Yes

Outpatient Clinic:
- Offer appointment with specialist surgeon & oncologist
- Offer decision aids
- Information & support
  - Treatment decisions should take account of quality of life as well as survival

Go to Localised Disease, Locally Advanced Disease or Metastatic Disease algorithms

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*PCRMP Guidance on Prostate Biopsy

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*NICE Guidance on Referral for Suspected Cancer
## Localised Disease

<table>
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<th>High-risk PSA &gt;20ng/ml or Gleason score &gt;= 8</th>
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<td>Watchful Waiting</td>
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<td>?</td>
<td>?</td>
</tr>
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<td>Active Surveillance</td>
<td>✓</td>
<td>?</td>
<td>x</td>
</tr>
<tr>
<td>Brachytherapy</td>
<td>?</td>
<td>?</td>
<td>x</td>
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<tr>
<td>Radical Prostatectomy</td>
<td>?</td>
<td>?</td>
<td>✓</td>
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<tr>
<td>Radical Radiotherapy</td>
<td>?</td>
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<tr>
<td>Cryotherapy</td>
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<td>HIFU</td>
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- Preferred treatment
- Treatment option – to be discussed with specialist urologist & oncologist
- Not recommended

- should be treatment of choice in low-risk
- repeat biopsy at 1, 4 & 7 years
- Measure PSA velocity

- 3D conformal radiotherapy
- Minimum dose 74Gy

High-risk PSA >20ng/ml or Gleason score >= 8 should be treatment of choice in low-risk
- repeat biopsy at 1, 4 & 7 years
- Measure PSA velocity

- 3D conformal radiotherapy
- Minimum dose 74Gy
Locally Advanced Disease

**T3a – T4 prostate cancer:**
- Radiotherapy & Hormonal Therapy:
  - Neoadjuvant hormonal therapy
  - Adjuvant hormonal therapy for Gleason >=8
- Hormonal Therapy alone:
  - See Metastatic Disease
- Bisphosphonates:
  - Not recommended for prevention of bone metastases

**Post-Radical prostatectomy with extracapsular Spread:**
- Radiotherapy:
  - Immediate post-op radiotherapy not recommended
  - Adjuvant hormonal therapy not recommended

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Follow-Up & Relapse after Radical Treatment

**Follow-Up:**
- Men on Watchful Waiting should be followed-up in primary care
- After 2 years follow-up should be offered outside hospital e.g. telephone, e-mail, primary care

**Relapse after Radical treatment:**
- Biochemical relapse alone should not prompt treatment
- An isotope bone scan should be performed if symptoms or PSA trends are suggestive of metastases or radical salvage therapy is being considered

**After Radical Radiotherapy or Brachytherapy**
- Clinical Trial: Clinical trials should examine the role of local salvage treatment
- Hormonal Therapy for: symmetrical disease, Metastases, PSA doubling time <3 months

**After Radical Prostatectomy**
- Clinical Trial: Consider RADICALS trial
- Local Salvage Therapy: Radiotherapy is recommended
Metastatic Disease

**Newly diagnosed or Relapsing:**
- Biopsy not required if high PSA and positive bone scan

**First Line Hormonal Therapy:**
- LHRHa or bilateral orchidectomy should be offered
- Intermittent androgen withdrawal may be offered

**Hormone Refractory Disease:**
- Men with hormone refractory disease should be discussed at MDT and referred to oncology or palliative care
- Palliative Care should be available when needed not only at end of life

**Chemotherapy:**
- Docetaxel if Karnofsky >=60
- Up to 10 cycles
- Repeat cycles not recommended

**Steroids:**
- Dexamethasone 0.5mg daily recommended
Management of Complications & Side Effects of Treatment

Complications of Treatment

- **Radical Prostatectomy:**
  - Men with urinary dysfunction should have access to specialist continence services

- **Radical Radiotherapy:**
  - Men should be offered flexible sigmoidoscopy every 5 years after radiotherapy

- **Hormonal Therapy:**
  - Hot flushes should be treated with synthetic progestagens
  - Androgen withdrawal therapy is a risk factor for the development of osteoporosis

Complications of Disease

- **Pelvic Disease:**
  - Men with obstructive uropathy should be offered decompression

- **Bone Metastases:**
  - Bisphosphonates are not recommended for the complications of bone metastases except uncontrolled pain
  - Sr-89 should be considered
  - Spinal MRI should be considered in men with hormone refractory disease and extensive bone metastases

- **Sexual Dysfunction:**
  - Men and their partners should have early access to specialist erectile dysfunction services

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