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# **Prostate cancer**

## **Diagnosis and treatment**

**NICE clinical guideline 58**  
**Prostate cancer: diagnosis and treatment**

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- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- ‘Understanding NICE guidance’ – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

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This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer and informed by the summary of product characteristics of any drugs they are considering.

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## Introduction

Prostate cancer is one of the most common cancers in men. Every year there are 34,986 new cases in England and Wales and 10,000 deaths<sup>1</sup>. Prostate cancer is predominantly a disease of older men but around 20% of cases occur in men under the age of 65 years. Over the past 10 to 15 years there have been a number of significant advances in prostate cancer management but also a number of major controversies, especially about the clinical management of men with early, non-metastatic disease. These uncertainties clearly cause anxieties for men with prostate cancer 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 assumes that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

Definitions used in this guideline are provided in appendix D on page 38 and can be viewed individually by clicking on [hyperlinked](#) words in the text.

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<sup>1</sup> Cancer Research UK (2007). Available from [www.cancerresearchuk.org](http://www.cancerresearchuk.org)

## **Patient-centred care**

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

Treatment and care should take into account the man'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](http://www.dh.gov.uk)). Healthcare professionals should also follow a code of practice accompanying the Mental Capacity Act (summary available from [www.publicguardian.gov.uk](http://www.publicguardian.gov.uk)).

Good communication between healthcare professionals and men with prostate cancer is essential. It should be supported by evidence-based written information tailored to the man's needs. Treatment and care, and the information men with prostate cancer 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 man agrees, his partner, family 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

- 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.
- To help men decide whether to have a prostate biopsy, healthcare professionals should discuss with them their prostate specific antigen (PSA) level, digital rectal examination (DRE) findings (including an estimate of prostate size) and comorbidities, together with their risk factors (including increasing age and black African or black Caribbean ethnicity) and any history of a previous negative prostate biopsy. The serum PSA level alone should not automatically lead to a prostate biopsy.
- Men with low-risk localised prostate cancer who are considered suitable for radical treatment should first be offered active surveillance.
- Men undergoing radical external beam radiotherapy for localised prostate cancer<sup>2</sup> should receive a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction.
- Healthcare professionals should ensure that men and their partners have early and ongoing access to specialist erectile dysfunction services.
- Healthcare professionals should ensure that men with troublesome urinary symptoms after treatment have access to specialist continence services for assessment, diagnosis and conservative treatment. This may include coping strategies, along with pelvic floor muscle re-education, bladder retraining and pharmacotherapy.
- Healthcare professionals should refer men with intractable stress incontinence to a specialist surgeon for consideration of an artificial urinary sphincter.

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<sup>2</sup> This may also apply to some men with locally advanced prostate cancer.

- Biochemical relapse (a rising PSA) alone should not necessarily prompt an immediate change in treatment.
- Hormonal therapy is not routinely recommended for men with prostate cancer who have a biochemical relapse unless they have:
  - symptomatic local disease progression, or
  - any proven metastases, or
  - a PSA doubling time < 3 months.
- When men with prostate cancer develop biochemical evidence of hormone-refractory disease, their treatment options should be discussed by the urological cancer multidisciplinary team (MDT) with a view to seeking an oncologist and/or specialist palliative care opinion, as appropriate.
- Healthcare professionals should ensure that palliative care is available when needed and is not limited to the end of life. It should not be restricted to being associated with hospice care.

# 1 Guidance

The following guidance is based on the best available evidence. The full guideline [www.nice.org.uk/CG058fullguideline](http://www.nice.org.uk/CG058fullguideline) gives details of the methods and the evidence used to develop the guidance.

## 1.1 *Communication and support*

- 1.1.1 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.
- 1.1.2 Men with prostate cancer should be offered individualised information tailored to their own needs. This information should be given by a healthcare professional (for example, a consultant or specialist nurse) and may be supported by written and visual media (for example, slide sets or DVDs).
- 1.1.3 Men with prostate cancer should be offered advice on how to access information and support from websites (for example, UK Prostate Link – [www.prostate-link.org.uk](http://www.prostate-link.org.uk)), local and national cancer information services, and from cancer support groups.
- 1.1.4 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.
- 1.1.5 Healthcare professionals should seek feedback from men with prostate cancer and their carers to identify the highest quality information resources.
- 1.1.6 Healthcare professionals caring for men with prostate cancer should ascertain the extent to which the man wishes to be involved

in decision making and ensure that he has sufficient information to do so.

- 1.1.7 A validated, up-to-date decision aid is recommended for use in all urological cancer multidisciplinary teams (MDTs). It should be offered to men with localised prostate cancer when making treatment decisions, by healthcare professionals trained in its use<sup>3</sup>.
- 1.1.8 Healthcare professionals should discuss all relevant management options recommended in this guideline with men with prostate cancer and their partners or carers, irrespective of whether they are available through local services.
- 1.1.9 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.
- 1.1.10 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.
- 1.1.11 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.

## **1.2 *Diagnosis and staging of prostate cancer***

Men who are diagnosed with prostate cancer usually present in primary care with no clear symptoms of the disease. This section assumes that men have

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<sup>3</sup> A decision aid for men with localised prostate cancer is in development in the UK by the Urology Informed Decision Making Steering Group (publication expected 2008).

had a digital rectal examination (DRE) and usually a prostate specific antigen (PSA) test in the primary care setting, as set out in 'Referral guidelines for suspected cancer' (NICE clinical guideline 27).

## **Biopsy**

The aim of prostate biopsy is to detect prostate cancers with the potential for causing harm rather than detecting each and every cancer. Men with clinically insignificant prostate cancers that are unlikely to cause symptoms or affect life expectancy may not benefit from knowing that they have the disease. Indeed, the detection of clinically insignificant prostate cancer should be regarded as an under-recognised adverse effect of biopsy.

- 1.2.1 To help men decide whether to have a prostate biopsy, healthcare professionals should discuss with them their PSA level, DRE findings (including an estimate of prostate size) and comorbidities, together with their risk factors (including increasing age and black African or black Caribbean ethnicity) and 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 or carers 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 increased chance of having to live with the diagnosis of clinically insignificant prostate cancer) and 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 bone metastases (identified by a positive isotope bone scan or sclerotic metastases on plain radiographs), prostate biopsy for histological confirmation should not be performed, unless this is required as part of a clinical trial.

- 1.2.4 Healthcare professionals should carry out prostate biopsy following the procedure recommended in ‘Undertaking a transrectal ultrasound guided biopsy of the prostate’ (PCRMP 2006)<sup>4</sup>.
- 1.2.5 The results of all prostate biopsies should be reviewed by a urological cancer MDT. Men should only be re-biopsied following a negative biopsy after an MDT review of the risk characteristics including life expectancy, PSA, DRE and prostate volume.
- 1.2.6 Men should decide whether or not to have a re-biopsy following a negative biopsy, having had the risks and benefits explained to them.

### Imaging

The clinical presentation and the treatment intent influence the decision about when and how to image an individual. Men with localised prostate cancer are stratified into risk groups according to their risk of recurrence (see table 1).

**Table 1 Risk stratification for men with localised prostate cancer.**

	PSA		Gleason score		Clinical stage
<b>Low risk</b>	< 10 ng/ml	<b>and</b>	≤ 6	<b>and</b>	T1-T2a
<b>Intermediate risk</b>	10–20 ng/ml	<b>or</b>	7	<b>or</b>	T2b-T2c
<b>High risk</b>	> 20 ng/ml	<b>or</b>	8-10	<b>or</b>	T3-T4 <sup>5</sup>

- 1.2.7 Healthcare professionals should determine the provisional treatment intent (radical or non-radical) before decisions on imaging are made.
- 1.2.8 Imaging is not routinely recommended for men in whom no radical treatment is intended.

<sup>4</sup> ‘Undertaking a transrectal ultrasound guided biopsy of the prostate’ (Prostate Cancer Risk Management Programme 2006). Available from: [www.cancerscreening.nhs.uk/prostate/pcrmp01.pdf](http://www.cancerscreening.nhs.uk/prostate/pcrmp01.pdf)

<sup>5</sup> Clinical stage T3-T4 represents locally advanced disease.

- 1.2.9 Computerised tomography (CT) of the pelvis is not recommended for men with low- or intermediate-risk localised prostate cancer (see table 1).
- 1.2.10 Men with high-risk localised (see table 1) and locally advanced prostate cancer who are being considered for radical treatment should have pelvic imaging with either magnetic resonance imaging (MRI), or CT if MRI is contraindicated.
- 1.2.11 Magnetic resonance spectroscopy is not recommended for men with prostate cancer except in the context of a clinical trial.
- 1.2.12 Isotope bone scans are not routinely recommended for men with low-risk localised prostate cancer.
- 1.2.13 Isotope bone scans should be performed when hormonal therapy is being deferred through [watchful waiting](#) in asymptomatic men who are at high risk of developing bone complications.
- 1.2.14 Positron emission tomography imaging for prostate cancer is not recommended in routine clinical practice.

### **Nomograms**

- 1.2.15 Nomograms may be used by healthcare professionals in partnership with men with prostate cancer to:
- aid decision making
  - help predict biopsy results
  - help predict pathological stage
  - help predict risk of treatment failure.
- 1.2.16 When nomograms are used, healthcare professionals should clearly explain the reliability, validity and limitations of the prediction.

### **1.3 Localised prostate cancer**

Men with high-risk localised prostate cancer (see table 1) may be managed as set out in section 1.6 (locally advanced prostate cancer).

#### **Watchful waiting and active surveillance**

- 1.3.1 Urological cancer MDTs should assign a risk category (see table 1) to all newly diagnosed men with localised prostate cancer.
- 1.3.2 Men with localised prostate cancer who have chosen a watchful waiting regimen and who have evidence of significant disease progression (that is, rapidly rising PSA level or bone pain) should be reviewed by a member of the urological cancer MDT.
- 1.3.3 Men with low-risk localised prostate cancer (see table 1) who are considered suitable for radical treatment should first be offered [active surveillance](#).
- 1.3.4 Active surveillance is particularly suitable for a subgroup of men with low-risk localised prostate cancer who have clinical stage T1c, a Gleason score of 3+3, a PSA density of < 0.15 ng/ml/ml and who have cancer in less than 50% of their total number of biopsy cores with < 10 mm of any core involved.
- 1.3.5 Active surveillance should be discussed as an option with men who have intermediate-risk localised prostate cancer (see table 1).
- 1.3.6 Active surveillance is not recommended for men with high-risk localised prostate cancer.
- 1.3.7 To reduce the sampling error associated with prostate biopsy, men who are candidates for active surveillance should have at least 10 biopsy cores taken.

- 1.3.8 Active surveillance should include at least one re-biopsy and may be performed in accordance with the ProSTART<sup>6</sup> protocol.
- 1.3.9 Men with localised prostate cancer who have chosen an active surveillance regimen and who have evidence of disease progression (that is, a rise in PSA level or adverse findings on biopsy) should be offered radical treatment.
- 1.3.10 The decision to proceed from an active surveillance regimen to radical treatment should be made in the light of the individual man's personal preferences, comorbidities and life expectancy.

### **Radical treatment**

- 1.3.11 Healthcare professionals should offer radical prostatectomy or radical radiotherapy (conformal) to men with intermediate-risk localised prostate cancer.
- 1.3.12 Healthcare professionals should offer radical prostatectomy or radical radiotherapy (conformal) to men with high-risk localised prostate cancer when there is a realistic prospect of long-term disease control.
- 1.3.13 Brachytherapy is not recommended for men with high-risk localised prostate cancer.
- 1.3.14 Clinical oncologists should use conformal radiotherapy for men with localised prostate cancer<sup>7</sup> receiving radical external beam radiotherapy.
- 1.3.15 Men undergoing radical external beam radiotherapy for localised prostate cancer<sup>7</sup> should receive a minimum dose of 74 Gy to the prostate at no more than 2 Gy per fraction.

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<sup>6</sup> Phase III randomized study of active surveillance versus radical treatment in patients with favorable-risk prostate cancer. ([www.cancer.gov/clinicaltrials/CAN-NCIC-CTG-PR11](http://www.cancer.gov/clinicaltrials/CAN-NCIC-CTG-PR11))

<sup>7</sup> This may also apply to some men with locally advanced prostate cancer.

- 1.3.16 Adjuvant hormonal therapy is recommended for a minimum of 2 years in men receiving radical radiotherapy for localised prostate cancer who have a Gleason score of  $\geq 8$ .
- 1.3.17 High-intensity focused ultrasound and cryotherapy are not recommended for men with localised prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions<sup>8</sup>.

### **Follow-up**

- 1.3.18 Healthcare professionals should discuss the purpose, duration, frequency and location of follow-up with each man with localised prostate cancer<sup>9</sup>, and if he wishes, his partner or carers.
- 1.3.19 Men with prostate cancer should be clearly advised about potential longer term adverse effects of treatment and when and how to report them.
- 1.3.20 Men with prostate cancer who have chosen a watchful waiting regimen with no curative intent should normally be followed up in primary care in accordance with protocols agreed by the local urological cancer MDT and the relevant primary care organisation(s). Their PSA should be measured at least once a year.
- 1.3.21 PSA levels for all men with prostate cancer who are having radical treatment should be checked at the earliest 6 weeks following treatment, at least every 6 months for the first 2 years and then at least once a year thereafter.
- 1.3.22 Routine DRE is not recommended in men with localised prostate cancer while the PSA remains at baseline levels.

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<sup>8</sup> NICE interventional procedures guidance 118,119 and 145 evaluated the safety and efficacy of cryotherapy and high-intensity focused ultrasound for the treatment of prostate cancer. NICE clinical guidelines provide guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS. As there was a lack of evidence on quality of life benefits and long-term survival these interventions are not recommended in this guideline.

<sup>9</sup> This may also apply to some men with locally advanced prostate cancer.

- 1.3.23 After at least 2 years, men with a stable PSA who have had no significant treatment complications, should be offered follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications, unless they are taking part in a clinical trial that requires formal clinic-based follow-up. Direct access to the urological cancer MDT should be offered and explained.

#### **1.4 *Managing adverse effects of treatment***

- 1.4.1 Given the range of treatment modalities and their serious side effects, men with prostate cancer who are candidates for radical treatment should have the opportunity to discuss their treatment options with a specialist surgical oncologist and a specialist clinical oncologist.
- 1.4.2 Men presenting with symptoms consistent with radiation-induced enteropathy should be fully investigated (including using flexible sigmoidoscopy) 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.
- 1.4.3 Men treated with radical radiotherapy for prostate cancer should be offered flexible sigmoidoscopy every 5 years.
- 1.4.4 Steroid enemas should not be used for treating men with radiation proctopathy.
- 1.4.5 The nature and treatment of radiation-induced injury to the gastrointestinal tract should be included in the training programmes for oncologists and gastroenterologists.
- 1.4.6 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.

- 1.4.7 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.
- 1.4.8 Healthcare professionals should ensure that men and their partners have early and ongoing access to specialist erectile dysfunction services.
- 1.4.9 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.
- 1.4.10 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.
- 1.4.11 Men experiencing troublesome urinary symptoms before treatment should be offered a urological assessment.
- 1.4.12 Men undergoing treatment for prostate cancer should be warned of the likely effects of the treatment on their urinary function.
- 1.4.13 Healthcare professionals should ensure that men with troublesome urinary symptoms after treatment have access to specialist continence services for assessment, diagnosis and conservative treatment. This may include coping strategies, along with pelvic floor muscle re-education, bladder retraining and pharmacotherapy.
- 1.4.14 Healthcare professionals should refer men with intractable stress incontinence to a specialist surgeon for consideration of an artificial urinary sphincter.
- 1.4.15 The injection of bulking agents into the distal urinary sphincter is not recommended to treat stress incontinence.

## **1.5 *Managing relapse after radical treatment***

- 1.5.1 Analyse serial PSA levels after radical treatment using the same assay technique.
- 1.5.2 Biopsy of the prostatic bed should not be performed in men with prostate cancer who have had a radical prostatectomy.
- 1.5.3 Biopsy of the prostate after radiotherapy should only be performed in men with prostate cancer who are being considered for local [salvage therapy](#) in the context of a clinical trial.
- 1.5.4 For men with evidence of biochemical relapse following radical treatment and who are considering radical salvage therapy:
- routine MRI scanning should not be performed prior to salvage radiotherapy in men with prostate cancer
  - an isotope bone scan should be performed if symptoms or PSA trends are suggestive of metastases.
- 1.5.5 Biochemical relapse (a rising PSA) alone should not necessarily prompt an immediate change in treatment.
- 1.5.6 Biochemical relapse should trigger an estimate of PSA doubling time, based on a minimum of 3 measurements over at least a 6 month period.
- 1.5.7 Men with biochemical relapse after radical prostatectomy, with no known metastases, should be offered radical radiotherapy to the prostatic bed.
- 1.5.8 Men with biochemical relapse should be considered for entry to appropriate clinical trials<sup>10</sup>.
- 1.5.9 Hormonal therapy is not routinely recommended for men with prostate cancer who have a biochemical relapse unless they have:

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<sup>10</sup> For example, RADICALS (Radiotherapy and androgen deprivation in combination after local surgery; [www.ctu.mrc.ac.uk/studies/PR10.asp](http://www.ctu.mrc.ac.uk/studies/PR10.asp))

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

## **1.6 Locally advanced prostate cancer**

There is no universally accepted definition of locally advanced prostate cancer. It covers a spectrum of disease from a tumour that has spread through the capsule of the prostate (T3a) to large T4 cancers that may be invading the bladder or rectum or have spread to pelvic lymph nodes.

### **Systemic treatment**

- 1.6.1 Neoadjuvant and concurrent luteinising hormone-releasing hormone agonist (LHRHa) therapy is recommended for 3 to 6 months in men receiving radical radiotherapy for locally advanced prostate cancer.
- 1.6.2 Adjuvant hormonal therapy in addition to radical prostatectomy is not recommended, even in men with margin-positive disease, other than in the context of a clinical trial.
- 1.6.3 Adjuvant hormonal therapy is recommended for a minimum of 2 years in men receiving radical radiotherapy for locally advanced prostate cancer who have a Gleason score of  $\geq 8$ .
- 1.6.4 Bisphosphonates should not be used for the prevention of bone metastases in men with prostate cancer.

### **Radiotherapy**

- 1.6.5 Clinical oncologists should consider pelvic radiotherapy in men with locally advanced prostate cancer who have a > 15% risk of pelvic lymph node involvement<sup>11</sup> and who are to receive neoadjuvant hormonal therapy and radical radiotherapy.

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<sup>11</sup> Estimated using the Roach formula: %LN risk = 2/3 PSA + (10 x [Gleason score - 6])

- 1.6.6 Immediate post-operative radiotherapy after radical prostatectomy is not routinely recommended, even in men with margin-positive disease, other than in the context of a clinical trial<sup>12</sup>.
- 1.6.7 High-intensity focused ultrasound and cryotherapy are not recommended for men with locally advanced prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions<sup>13</sup>.

## **1.7 *Metastatic prostate cancer***

### **Hormonal therapy**

- 1.7.1 Healthcare professionals should offer bilateral orchidectomy to all men with metastatic prostate cancer as an alternative to continuous LHRHa therapy.
- 1.7.2 Combined [androgen blockade](#) is not recommended as a first-line treatment for men with metastatic prostate cancer.
- 1.7.3 For 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, anti-androgen monotherapy with bicalutamide (150 mg)<sup>14</sup> should be offered.
- 1.7.4 Healthcare professionals should begin [androgen withdrawal](#) and stop bicalutamide treatment in men with metastatic prostate cancer who are taking bicalutamide monotherapy and who do not maintain satisfactory sexual function.

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<sup>12</sup> For example, RADICALS; [www.ctu.mrc.ac.uk/studies/PR10.asp](http://www.ctu.mrc.ac.uk/studies/PR10.asp)

<sup>13</sup> NICE interventional procedures guidance 118,119 and 145 evaluated the safety and efficacy of cryotherapy and high-intensity focused ultrasound for the treatment of prostate cancer. NICE clinical guidelines provide guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS. As there was a lack of evidence on quality of life benefits and long-term survival these interventions are not recommended in this guideline.

<sup>14</sup> At the time of publication (February 2008) bicalutamide did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented.

- 1.7.5 Intermittent androgen withdrawal may be offered to men with metastatic prostate cancer providing they are informed that there is no long-term evidence of its effectiveness.

### **Managing the complications of hormonal therapy**

- 1.7.6 Synthetic progestogens (administered orally or parenterally) 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.
- 1.7.7 Men starting long-term bicalutamide monotherapy (> 6 months) should receive prophylactic radiotherapy to both breast buds within the first month of treatment. A single fraction of 8 Gy using orthovoltage or electron beam radiotherapy is recommended.
- 1.7.8 If radiotherapy is unsuccessful in preventing gynaecomastia, weekly tamoxifen should be considered.
- 1.7.9 Inform men starting androgen withdrawal therapy that regular resistance exercise reduces fatigue and improves quality of life.

### **Hormone-refractory prostate cancer**

- 1.7.10 When men with prostate cancer develop biochemical evidence of hormone-refractory disease, their treatment options should be discussed by the urological cancer MDT with a view to seeking an oncologist and/or specialist palliative care opinion, as appropriate.
- 1.7.11 Docetaxel is recommended, within its licensed indications, as a treatment option for men with hormone-refractory prostate cancer only if their Karnofsky performance-status score is 60% or more<sup>15</sup>.
- 1.7.12 It is recommended that treatment with docetaxel should be stopped:
- at the completion of planned treatment of up to 10 cycles, or

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<sup>15</sup> These recommendations are from 'Docetaxel for the treatment of hormone-refractory metastatic prostate cancer' (NICE technology appraisal guidance 101).

- if severe adverse events occur, or
  - in the presence of progression of disease as evidenced by clinical or laboratory criteria, or by imaging studies<sup>15</sup>.
- 1.7.13 Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy<sup>15</sup>.
- 1.7.14 A corticosteroid such as dexamethasone (0.5 mg daily) is recommended as third-line hormonal therapy after androgen withdrawal and anti-androgen therapy for men with hormone-refractory prostate cancer.
- 1.7.15 Men with hormone-refractory prostate cancer shown to have extensive metastases in the spine (for example, on a bone scan), should have spinal MRI if they develop any spinal-related symptoms.
- 1.7.16 The routine use of spinal MRI for all men with hormone-refractory prostate cancer and known bone metastases is not recommended.
- 1.7.17 The use of bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-refractory prostate cancer is not recommended.
- 1.7.18 Bisphosphonates for pain relief may be considered for men with hormone-refractory prostate cancer when other treatments (including analgesics and palliative radiotherapy) have failed. The oral or intravenous route of administration should be chosen according to convenience, tolerability and cost.
- 1.7.19 Bisphosphonates should not be used routinely to prevent osteoporosis in men with prostate cancer receiving androgen withdrawal therapy.
- 1.7.20 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.

- 1.7.21 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.
- 1.7.22 The option of no intervention should also be discussed with men with obstructive uropathy secondary to hormone-refractory prostate cancer and remains a choice for some.

### **Palliative care**

- 1.7.23 Men with metastatic prostate cancer should be offered tailored information and access to specialist urology and palliative care teams to address the specific needs of men with metastatic prostate cancer. They should have the opportunity to discuss any significant changes in their disease status or symptoms as these occur.
- 1.7.24 The regular assessment of needs should be applied systematically to men with metastatic prostate cancer<sup>16</sup>.
- 1.7.25 Palliative interventions at any stage should be integrated into coordinated care, and any transitions between care settings should be facilitated as smoothly as possible.
- 1.7.26 Healthcare professionals should discuss personal preferences for palliative care as early as possible with men with metastatic prostate cancer, their partners and carers. Treatment/care plans should be tailored accordingly and the preferred place of care should be identified.

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<sup>16</sup> 'Improving supportive and palliative care for adults with cancer' (NICE cancer service guidance 2004).

1.7.27 Healthcare professionals should ensure that palliative care is available when needed and is not limited to the 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](http://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 'Referral guidelines for 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 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](http://www.nice.org.uk/guidelinesprocess) or from NICE publications (phone 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) and 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', (available from [www.doh.gov.uk](http://www.doh.gov.uk)).

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/CG058](http://www.nice.org.uk/CG058)).

- 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 support for monitoring 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 *Prognostic factors***

Further research is required into the identification of prognostic indicators in order to differentiate effectively between men who may die with prostate cancer and those who might die from prostate cancer.

#### **Why this is important**

The greatest uncertainties in managing prostate cancer are around the identification of which cancers are of clinical significance and over the choice of radical treatment, and in which settings they are appropriate.

With the diagnosis of prostate cancer being made more frequently in asymptomatic men, it is of growing importance to know which of these men are likely to benefit from aggressive treatment.

### **4.2 *Treatments aimed at elimination of disease***

Research is required into the clinical and cost effectiveness of treatments aimed at the elimination of disease in men with localised prostate cancer, with locally advanced disease and with locally recurrent disease. This research should include a rigorous examination of the value of procedures such as brachytherapy (localised disease only), cryotherapy and high-intensity focused ultrasound, as well as combinations of surgery and radiotherapy with hormonal therapy and chemotherapy. The endpoints should include survival, local recurrence, toxicity and quality of life outcomes.

#### **Why this is important**

A wide and growing range of radical therapies aimed at the eradication of disease are available. Although long-term follow-up data are available for

some of these in the localised disease setting, there have been no randomised trials comparing these treatments and there is little evidence to support their use in locally advanced disease or localised recurrent disease.

## **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 the National Collaborating Centre for Cancer, and is available from [www.wales.nhs.uk/sites3/home.cfm?orgid=432](http://www.wales.nhs.uk/sites3/home.cfm?orgid=432), our website ([www.nice.org.uk/CG058fullguideline](http://www.nice.org.uk/CG058fullguideline)) and the National Library for Health ([www.nlh.nhs.uk](http://www.nlh.nhs.uk)).

### **5.2 Quick reference guide**

A quick reference guide for healthcare professionals is available from [www.nice.org.uk/CG058quickrefguide](http://www.nice.org.uk/CG058quickrefguide)

For printed copies, phone NICE publications on 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) (quote reference number N1457).

### **5.3 'Understanding NICE guidance'**

Information for patients and carers ('Understanding NICE guidance') is available from [www.nice.org.uk/CG058publicinfo](http://www.nice.org.uk/CG058publicinfo)

For printed copies, phone NICE publications on 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) (quote reference number N1458).

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about prostate cancer.

## **6 Related NICE guidance**

### **Published**

Improving outcomes in urological cancers. NICE cancer service guidance (2002). Available from <http://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/cs/gsp](http://www.nice.org.uk/cs/gsp)

Referral guidelines for suspected cancer. NICE clinical guideline CG27 (2005). Available from [www.nice.org.uk/CG027](http://www.nice.org.uk/CG027)

Docetaxel for the treatment of hormone-refractory metastatic prostate cancer. NICE technology appraisal guidance 101 (2006). Available from [www.nice.org.uk/TA101](http://www.nice.org.uk/TA101)

Cryotherapy for recurrent prostate cancer. NICE interventional procedure guidance 119 (2005). Available from [www.nice.org.uk/IPG119](http://www.nice.org.uk/IPG119)

Cryotherapy as a primary treatment for prostate cancer. NICE interventional procedure guidance 145 (2005). Available from [www.nice.org.uk/IPG145](http://www.nice.org.uk/IPG145)

High-intensity focused ultrasound for prostate cancer. NICE interventional procedure guidance 118 (2005). Available from [www.nice.org.uk/IPG118](http://www.nice.org.uk/IPG118)

Low dose rate brachytherapy for localised prostate cancer. NICE interventional procedure guidance 132 (2005). Available from [www.nice.org.uk/IPG132](http://www.nice.org.uk/IPG132)

High dose rate brachytherapy in combination with external-beam radiotherapy for localised prostate cancer. NICE interventional procedure guidance 174 (2006). Available from [www.nice.org.uk/IPG174](http://www.nice.org.uk/IPG174)

### **Under development**

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

- Metastatic spinal cord compression: Diagnosis and management of adults at risk of and with metastatic spinal cord compression. NICE clinical guideline (publication expected November 2008).

- Osteoporosis: Assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. NICE clinical guideline. (publication date to be confirmed).
- Lower urinary tract symptoms in men: Assessment, investigation, management and referral of men with lower urinary tract symptoms in primary care. 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**

### **Professor Mark Baker (Chair)**

The Lead Cancer Clinician, The Leeds Teaching Hospitals

### **Dr John Graham (Lead clinician)**

Consultant Lead Clinical Oncologist, Taunton and Somerset NHS Trust

### **Philip Barnard**

Patient/Carer Representative, Honorary Secretary, PSA Prostate Cancer Support Association

### **Angela Billington**

Specialist Nurse, Director of Continence Services, Bournemouth and Poole PCT

### **Dr Brendan Carey**

Consultant Radiologist, Cookridge Hospital, Leeds

### **Mr David Gillatt**

Consultant Urologist, Southmead Hospital, Bristol

### **Jane Gosling**

Consultant Nurse – Urology, Derriford Hospital, Plymouth

### **Dr Chris Hiley**

Patient/Carer Representative, Head of Policy and Research Management, The Prostate Cancer Charity

### **Margaret Jewitt**

Superintendent Radiographer, Weston Park Hospital, Sheffield

### **Mr John McLoughlin**

Consultant Urologist, West Suffolk Hospital Bury Edmunds and Honorary Consultant Urologist, Addenbrooke's Hospital Cambridge

### **Dr Chris Parker**

Consultant in Clinical Oncology, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton

**John Rawlinson**

Patient/Carer Representative, Senior Lecturer/Academic Lead in Mental Health, University of Plymouth

**Professor David Weller**

Head, General Practice, University of Edinburgh Primary Care

**Dr John Wiles**

Consultant in Palliative Medicine, Bromley Hospitals NHS Trust

## **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 NHS Trust

### **Ash Paul**

Deputy Medical Director, Health Commission Wales (Specialist Services)

### **Jon Seddon**

Lay Representative

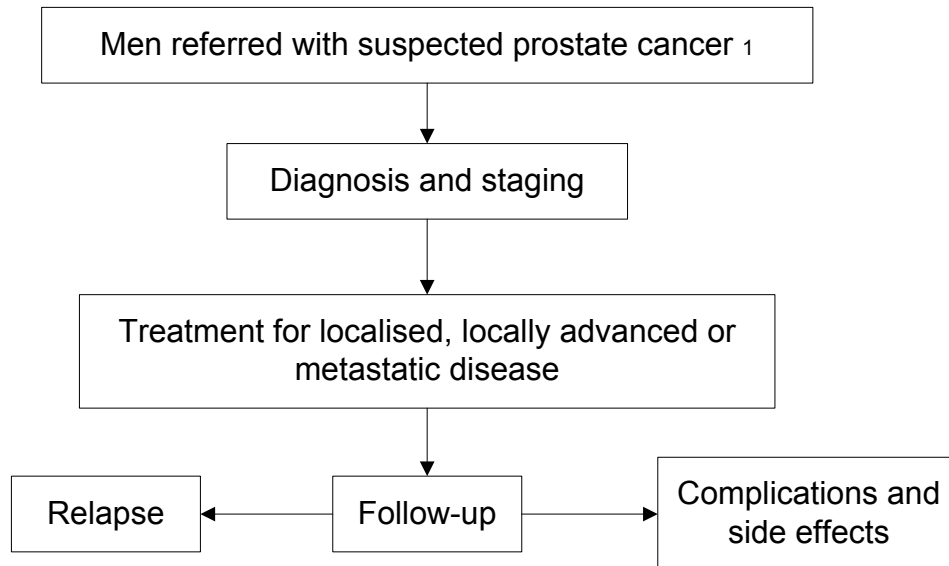
### **Jonathan Hopper**

Medical Director (UK and Ireland), Convatec

## Appendix C: The algorithms

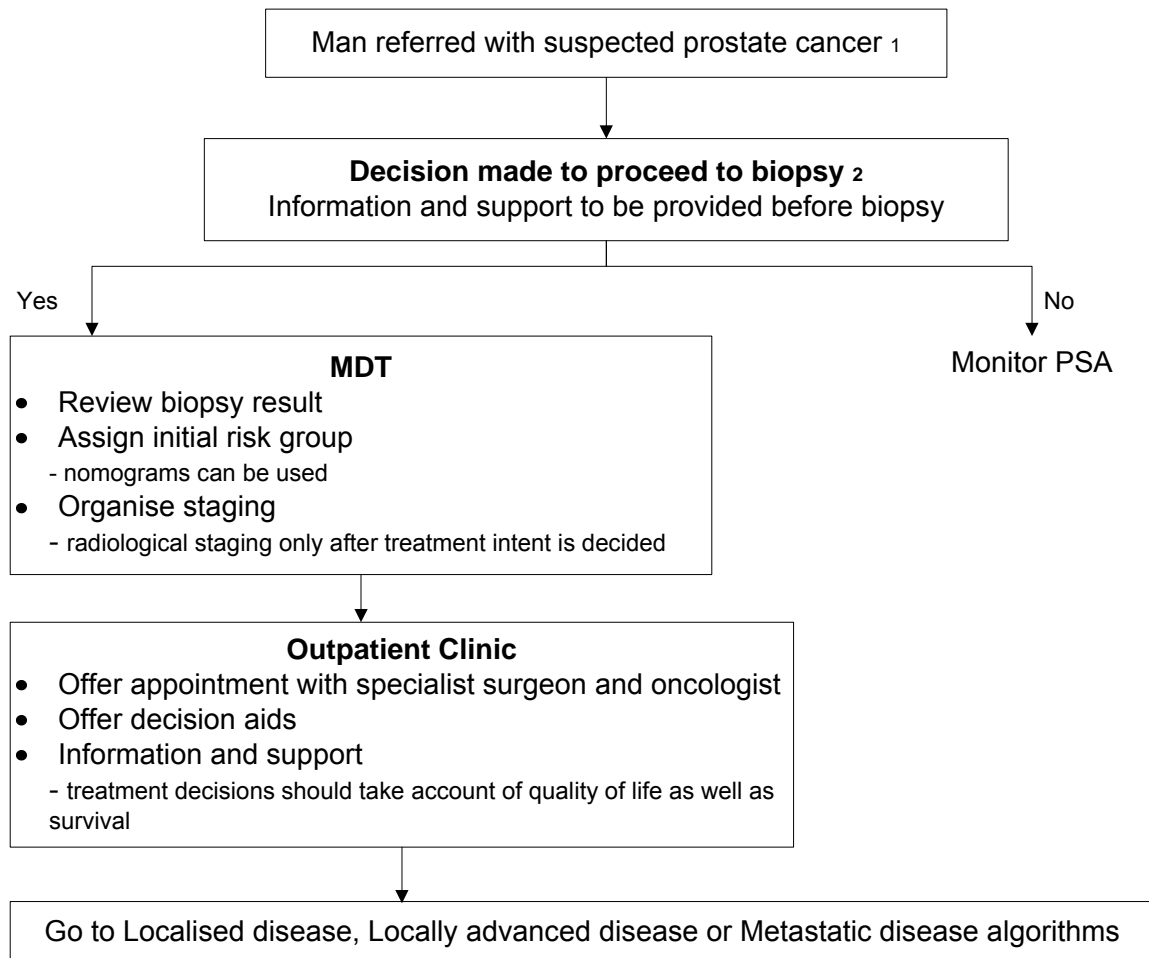
A pictorial guide to show how the guideline is structured.

### Prostate cancer pathway



<sup>1</sup> 'Referral guidelines for suspected cancer' (NICE clinical guideline 27)

## Diagnosis and staging



<sup>1</sup> 'Referral guidelines for suspected cancer' (NICE clinical guideline 27)

<sup>2</sup> 'Undertaking a transrectal ultrasound guided biopsy of the prostate' PCRMP (2006).

### **Localised disease**

(For the management of complications and side effects of treatment see algorithm on page 37)

- Should be treatment of choice in low-risk men who are suitable for radical treatment
- Include at least 1 re-biopsy
- If evidence of disease progression men should be offered radical treatment

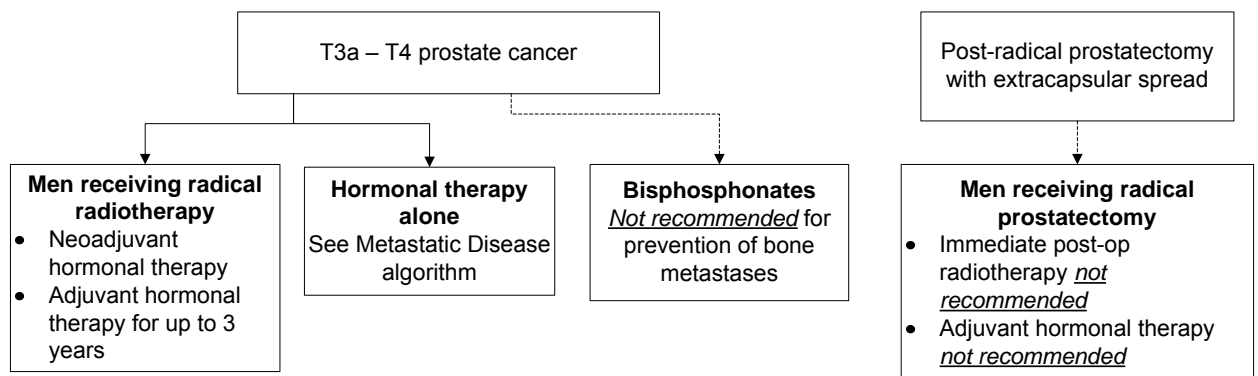
- Use 3D conformal radiotherapy
- Minimum dose 74 Gy (maximum 2 Gy per fraction)

	Low-risk men (PSA ≤ 10 ng/ml and Gleason score ≤ 6 and T1-T2a)	Intermediate risk men (PSA 10-20 ng/ml or Gleason score 7 or T2b-2c)	High-risk men (PSA ≥20 ng/ml or Gleason score ≥8 or T3-T4)
Watchful waiting	◇	◇	◇
Active surveillance	✓	◇	X
Brachytherapy	◇	◇	X
Prostatectomy	◇	✓	✓
Radiotherapy	◇	✓	✓
Cryotherapy	X*	X*	X*
HIFU	X*	X*	X*

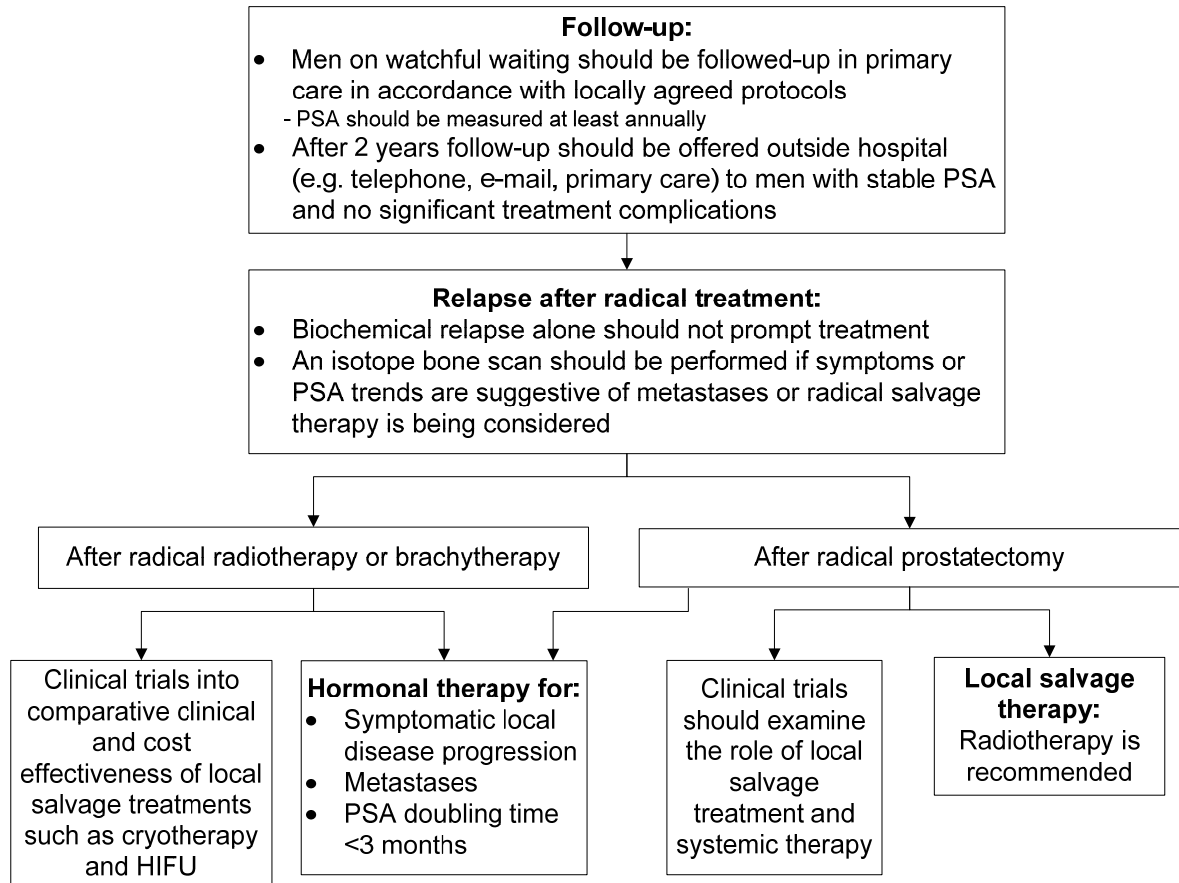
✓	Preferred treatment
◇	Treatment option
X	Not recommended
X*	Not recommended other than in the context of clinical trials

## **Locally advanced disease**

(For the management of complications and side effects of treatment see algorithm on page 37)

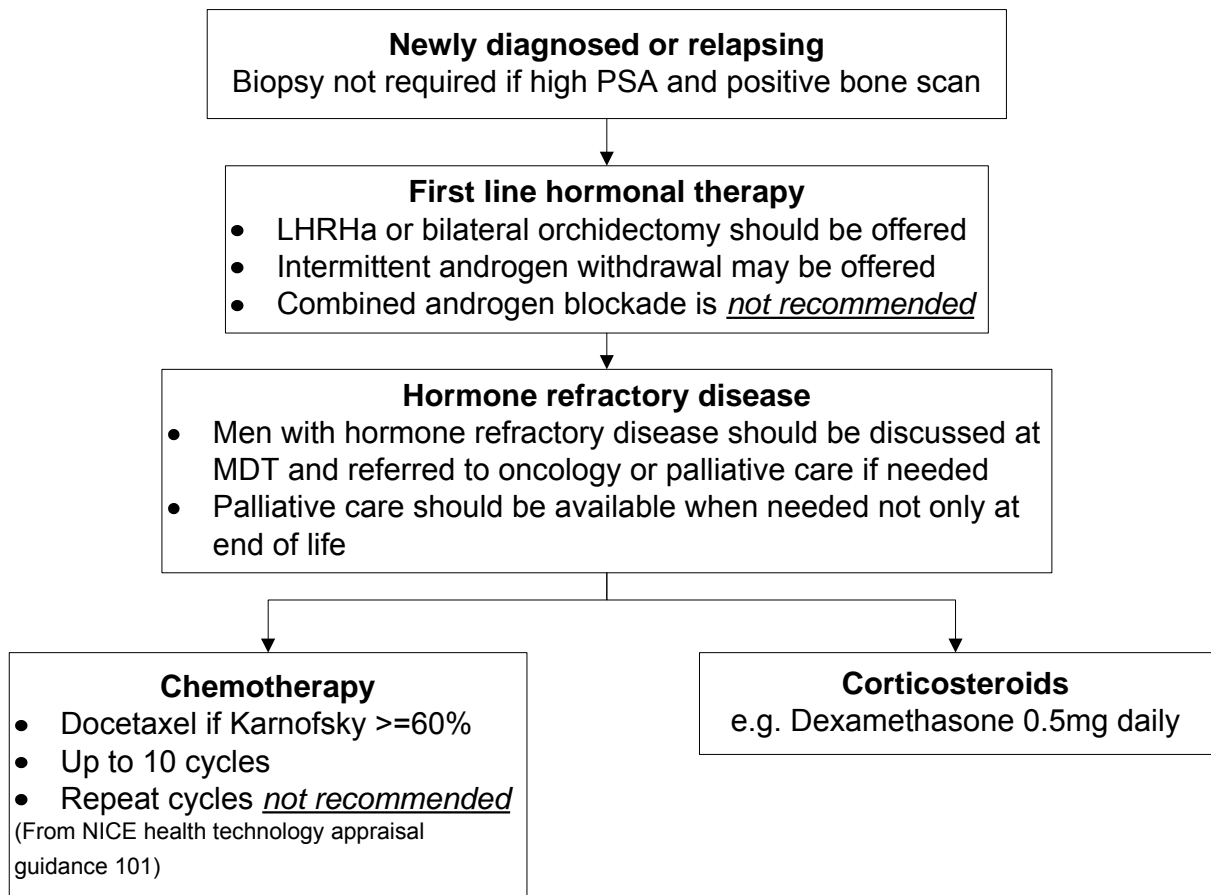


## Follow-up and relapse after radical treatment



## **Metastatic disease**

(For the management of complications and side effects of treatment see algorithm on page 37)





## **Appendix D: Definitions used in this guideline**

**Active surveillance:** a method of managing men with low or intermediate-risk localised prostate cancer that aims to target radical treatment only to those who would benefit most.

**Androgen blockade:** the use of drugs that bind to and block the hormone receptors of cancer cells, preventing androgens from stimulating cancer growth.

**Androgen withdrawal:** treatment that lowers testosterone levels, that is, bilateral orchidectomy or treatment with LHRH agonists.

**Salvage therapy:** treatment that is given after prostate cancer has progressed, following other treatments.

**Watchful waiting:** a method of managing men with prostate cancer who are not suitable for radical treatment, involving treatment only if and when they develop symptoms.