NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Prostate cancer: diagnosis and management (update)

Draft for consultation, December 2018

This guideline covers diagnosing and managing prostate cancer in secondary care. It offers information on the best way to diagnose and identify different stages of the disease, and how to manage adverse effects of treatment. It includes recommendations on follow-up in primary care for people with a diagnosis of prostate cancer.

Who is it for?

- Healthcare professionals.
- Commissioners and providers of prostate cancer services.
- People with prostate cancer, their families and carers.

This guideline will update NICE guideline CG175 (published January 2014).

We have reviewed the evidence on the assessment, diagnosis and staging, treatment and follow-up of prostate cancer. You are invited to comment on the new and updated recommendations. These are marked as **[2019]**

You are also invited to comment on recommendations that NICE proposes to delete from the 2014 guideline.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See update information for a full explanation of what is being updated.

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2019 recommendations and how they might affect practice
- the guideline context.

Full details of the evidence and the committee's discussion on the 2019 recommendations are in the evidence reviews. Evidence for the 2014 recommendations is in the full version of the 2014 guideline.

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Contents

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Information and decision support for people with prostate cancer, their partners and carers

Information

1.1.1 For advice on communication and patient-centred care throughout the patient journey, follow the recommendations in the NICE service guidelines on improving outcomes in urological cancers and improving supportive and palliative care for adults with cancer. **[2008]**

1.1.2 Offer people with prostate cancer 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 **[2008]**

1.1.3 Offer people with prostate cancer advice on how to get information and support from websites, local and national cancer information services, and from cancer support groups. **[2008]**

1.1.4 Choose or recommend information resources for people with prostate cancer that are clear, reliable and up-to-date. Ask for feedback from people with prostate cancer and their carers to identify the highest quality information resources. **[2008]**

Decision support

1.1.5 Find out the extent to which the person wishes to be involved in their decision making, and ensure that they have sufficient information to do so. **[2008]**

1.1.6 Use a validated, up-to-date decision aid[1] in all urological cancer multidisciplinary teams (MDTs). Healthcare professionals trained in its use should offer it to people with localised prostate cancer when making treatment decisions. **[2008]**

1.1.7 Use nomograms together with people with prostate cancer to help:

- with decision making
- predict biopsy results
- predict pathological stage
- predict risk of treatment failure. **[2008]**

1.1.8 Explain the reliability, validity and limitations of any predictions made using nomograms. **[2008]**

1.1.9 Discuss all relevant management options in this guideline with people with prostate cancer and their partners or carers, even if they are not available through their local services. **[2008]**

1.1.10 Tell people with prostate cancer:

- about treatment options and their risks and benefits[1] in an objective, unbiased manner **and**
- that there is limited evidence for some treatment options. **[2014]**

1.1.11 Ensure that mechanisms are in place so people with prostate cancer and their primary care providers have access to specialist services throughout the course of their disease. **[2008]**

[1] A decision aid for people with localised prostate cancer is available from NHS Shared decision making.

1.1.12 Tell people 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
- other aspects of masculinity.

Support people and their partners or carers in making treatment decisions, taking into account the effects on quality of life as well as survival. **[2008]**

1.1.13 Offer people 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 condition and its treatment. **[2008]**

1.2 Assessment and diagnosis

Magnetic resonance imaging and biopsy

1.2.1 Do not routinely offer imaging to people with prostate cancer who are not going to be able to have radical treatment. **[2019]**

1.2.2 Offer multiparametric MRI as the first-line investigation for people with suspected clinically localised prostate cancer. Report the results using a 5-point Likert scale. **[2019]**

1.2.3 Offer multiparametric MRI-influenced prostate biopsy to people whose Likert score is 3 or more. **[2019]**

1.2.4 Consider omitting a prostate biopsy for people whose multiparametric MRI Likert score is 1 or 2, but only after discussing the risks and benefits with the person and reaching a shared decision (Table 1). Offer systematic prostate biopsy to people who opt for biopsy. **[2019]**

Table 1 Factors to consider when discussing the options for people whose multiparametric MRI Likert score is 1 or 2

Advantages of undergoing transrectal ultrasound (TRUS) biopsy	Disadvantages of undergoing TRUS biopsy
You may have prostate cancer that the MRI scan missed: • 28 out of 100 people with a low-risk MRI actually have clinically significant cancer. • There are many effective treatments for clinically significant cancer, which work best for disease that is caught early. This means that, if you actually do have clinically significant cancer that the MRI missed, you will have a better chance of long-term survival if the biopsy finds it. • However, you should be aware that TRUS biopsy is not perfect at detecting disease, if it is there (see disadvantages).	If you actually have clinically significant prostate cancer that the MRI scan missed, there is no guarantee that a TRUS biopsy will find it. This means that, if you have a TRUS biopsy and it is negative, you might still have clinically significant prostate cancer that both the MRI scan and the biopsy missed. • 14 out of 100 people with a low-risk MRI and a negative TRUS biopsy actually have clinically significant prostate cancer. • 52 out of 100 people with a low-risk MRI and a TRUS biopsy showing clinically insignificant prostate cancer actually have clinically significant prostate cancer.
	You may be diagnosed with clinically insignificant prostate cancer: • 18 out of 100 people with a low-risk MRI get a diagnosis of clinically insignificant prostate cancer if they have a TRUS biopsy (although 9 of these people actually have clinically significant disease; see above). • Clinically insignificant prostate cancer is disease that is unlikely to develop to be life-threatening, but will need monitoring and may lead to treatment. Therefore, if someone has prostate cancer that truly is clinically insignificant, it is better not to find it. However, because some people who are diagnosed with clinically insignificant disease actually have more serious prostate cancer (see above), there may be benefit in being followed up in case the disease progresses more quickly than expected.
	Some people find it unpleasant to undergo TRUS biopsy: • 3 out of 100 people feel light-headed or dizzy after the biopsy. • 7 out of 100 people pass blood in their urine immediately after biopsy. • 3 out of 100 people pass blood clots in their urine immediately after biopsy. • However, 85 out of 100 people describe no pain or mild pain associated with the biopsy procedure itself.

	It can take a while to recover from a TRUS biopsy. In the 5 weeks after a TRUS biopsy: • 44 out of 100 people report pain; in 15 of them, it will last for at least 2 weeks; 7 will consider it a moderate or serious problem. • 20 out of 100 people develop a fever; in 3 of them, it will last for at least 2 weeks; 5 will consider it a moderate or serious problem. • 66 out of 100 people have blood in their urine; in 20 of them, it will last for at least 2 weeks; 6 will consider it a moderate or serious problem. • 37 out of 100 people had blood in their bowel movements; in 5 of them, it will last for at least 2 weeks; 2 will consider it a moderate or serious problem. • 90 out of 100 people had blood in their semen; in 60 of them, it will last for at least 2 weeks; 25 will consider it a moderate or serious problem.

1.2.5 Do not offer mapping transperineal template biopsy as part of an initial assessment, unless as part of a clinical trial. **[2019]**

To find out why the committee made the 2019 recommendations on magnetic resonance imaging and how they might affect practice, see rationale and impact.

1.2.6 Help people decide whether to have an MRI or prostate biopsy by discussing:

- their prostate-specific antigen (PSA) level
- their digital rectal examination (DRE) findings (including an estimate of prostate size)
- any comorbidities, together with their risk factors (including increasing age and black African-Caribbean family origin)
- any history of a previous negative prostate biopsy.

Do not automatically offer a prostate biopsy on the basis of serum PSA level alone. **[2008]**

1.2.7 Give people and their partners or carers information, support and adequate time to decide whether or not they wish to have an MRI or prostate biopsy. Explain the risks (including the increased chance of having to live with the diagnosis of clinically insignificant prostate cancer) and benefits. **[2008]**

1.2.8 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), do not offer prostate biopsy for histological confirmation unless this is needed as part of a clinical trial. **[2008]**

1.2.9 Carry out prostate biopsy following the procedure recommended by the Prostate Cancer Risk Management Programme in Undertaking a transrectal ultrasound guided biopsy of the prostate. **[2008]**

1.2.10 Have a core member of the urological cancer MDT review the risk factors of all people who have had a negative first prostate biopsy. Discuss with the person that:

- there is still a risk that prostate cancer is present **and**
- the risk is slightly higher if any of the following risk factors are present:
  - the biopsy showed high-grade prostatic intra-epithelial neoplasia (HGPIN)
  - the biopsy showed atypical small acinar proliferation (ASAP)
  - abnormal digital rectal examination. **[2014]**

If the MRI or biopsy is negative

1.2.11 For people with a negative biopsy who have an MRI Likert score of 3 or more, discuss the possibility of significant disease in a multidisciplinary team meeting with a view to repeating the prostate biopsy. **[2019]**

1.2.12 For people who have a raised PSA, and MRI Likert score of 1 or 2 and have not had a prostate biopsy, repeat PSA test at 3–6 months and:

- offer prostate biopsy if there is a strong suspicion of prostate cancer (for example, PSA density greater than 0.15 ng/ml/ml or PSA velocity greater than 0.75 ng/year, or strong family history), taking into account their life expectancy and comorbidities
- discharge the person to primary care if the level of suspicion is low: advise PSA follow-up at 6 months and then every year, and set a PSA

level for primary care at which to re-refer based on PSA density (0.15 ng/ml/ml) or velocity (0.75 ng/year). **[2019]**

1.2.13 For people who have a raised PSA, an MRI Likert score of 1 or 2 (or a contraindication to MRI), and negative biopsy, repeat PSA at 3–6 months and:

- offer prostate biopsy if there is a strong suspicion of prostate cancer (for example, PSA density greater than 0.15 ng/ml/ml or PSA velocity greater than 0.75 ng/year, or strong family history), taking into account their life expectancy and comorbidities
- discharge the person to primary care if the level of suspicion is low: advise PSA follow-up every 2 years, and set a PSA level for primary care at which to re-refer, based on PSA density (0.15 ng/ml/ml) or velocity (0.75 ng/year). **[2019]**

Staging

1.2.14 Offer isotope bone scans when hormonal therapy is being deferred as part of watchful waiting to asymptomatic people who are at high risk of developing bone complications. **[2008]**

1.2.15 Consider CT for people with histologically proven prostate cancer for whom MRI is contraindicated if knowledge of the T or N stage could affect management. **[2014]**

1.2.16 Urological cancer MDTs should assign a risk category (see Table 2) to all newly diagnosed people with localised prostate cancer. [2008]

Table 2 Risk stratification for people with localised prostate cancer

Level of risk	PSA		Gleason score		Clinical stage
Low risk	<10 ng/ml	and	≤6	and	T1–T2a
Intermediate risk	10–20 ng/ml	or	7	or	T2b
High risk[1]	>20 ng/ml	or	8–10	or	≥T2c
[1] High-risk localised prostate cancer is also included in the definition of locally advanced prostate cancer.					

1.2.17 Do not routinely offer isotope bone scans to people with low-risk localised prostate cancer. **[2008]**

1.3 Localised and locally advanced prostate cancer

1.3.1 Before radical treatment, explain to people and, if they wish, their partner, that radical treatment for prostate cancer will result in an alteration of sexual experience, and may result in loss of sexual function. **[2008, amended 2014]**

1.3.2 Explain to people and, if they wish, their partner, about the potential loss of ejaculation and fertility associated with radical treatment for prostate cancer. Offer sperm storage. **[2008, amended 2014]**

1.3.3 Warn people undergoing radical treatment for prostate cancer of the likely effects of the treatment on their urinary function. **[2008, amended 2014]**

1.3.4 Offer a urological assessment to people who have troublesome urinary symptoms before treatment. **[2008]**

1.3.5 People with prostate cancer who are candidates for radical treatment should have the opportunity to discuss the range of treatment modalities and their serious side effects in relation to their treatment options with a specialist surgical oncologist and a specialist clinical oncologist. **[2008]**

1.3.6 Explain to people that there is a small increase in the risk of colorectal cancer after radical external beam radiotherapy for prostate cancer. **[2014]**

Low-risk localised prostate cancer

1.3.7 Offer a choice between active surveillance, radical prostatectomy or radical radiotherapy to people with low-risk localised prostate cancer for whom radical treatment is suitable. Use Table 3 to discuss the benefits and harms with them. **[2019]**

Table 3 Factors to consider when discussing active surveillance, radical prostatectomy or radical radiotherapy as treatment options for people with

low–risk or intermediate–risk localised prostate cancer, using evidence from a large UK trial

What are the treatment options for people with localised prostate cancer?	There are 3 options for treatment: active surveillance[1] radical prostatectomy radical radiotherapy
Effects on survival and disease progression at 10 years	
What effect does each treatment option have on survival?	The evidence does not show a difference in the number of deaths from prostate cancer among people offered active surveillance, prostatectomy or radical radiotherapy. 98 out of 100 patients offered active surveillance had not died of prostate cancer 99 out of 100 patients offered radical prostatectomy had not died of prostate cancer 99 out of 100 patients offered radical radiotherapy had not died of prostate cancer
What effect does each treatment option have on disease progression[2]?	There is good evidence that both prostatectomy and radiotherapy reduce disease progression compared with active surveillance. 21 out of 100 patients offered active surveillance had signs of disease progression 8 out of 100 patients offered radical prostatectomy had signs of disease progression 8 out of 100 patients offered radical radiotherapy had signs of disease progression
What effect does each treatment option have on the rate of development of distant metastases?	There is good evidence that both prostatectomy and radiotherapy reduce the rate of development of distant metastases compared with active surveillance. 8 out of 100 patients offered active surveillance had developed distant metastases 3 out of 100 patients offered radical prostatectomy had developed distant metastases 3 out of 100 patients offered radical radiotherapy had developed distant metastases
Potential side effects of treatment	
What effect does each treatment option have on urinary function?	There is some evidence that urinary function is better for people offered active surveillance or radiotherapy than those offered prostatectomy. At 6 months: 39 out of 100 patients offered active surveillance reported problems with urinary continence 71 out of 100 patients offered radical prostatectomy reported problems with urinary continence

	39 out of 100 patients offered radical radiotherapy reported problems with urinary continence At 6 years: 50 out of 100 patients offered active surveillance reported problems with urinary continence 69 out of 100 patients offered radical prostatectomy reported problems with urinary continence 49 out of 100 patients offered radical radiotherapy reported problems with urinary continence
What effect does each treatment option have on erectile dysfunction?	There is some limited evidence that sexual function is better for people offered active surveillance or radiotherapy than those offered prostatectomy. At 6 months: 29 out of 100 patients offered active surveillance reported moderate or severe problems with erectile dysfunction 67 out of 100 patients offered radical prostatectomy reported moderate or severe problems with erectile dysfunction 48 out of 100 patients offered radical radiotherapy reported moderate or severe problems with erectile dysfunction At 6 years: 40 out of 100 patients offered active surveillance reported a moderate or severe problem with erectile dysfunction 50 out of 100 patients offered radical prostatectomy reported a moderate or severe problem with erectile dysfunction 36 out of 100 patients offered radical radiotherapy reported a moderate or severe problem with erectile dysfunction
What effect does each treatment option have on bowel function?	At 6 months: 2 out of 100 patients offered active surveillance reported faecal incontinence more than once per week 1 out of 100 patients offered radical prostatectomy reported faecal incontinence more than once per week 5 out of 100 patients offered radical radiotherapy reported faecal incontinence more than once per week At 6 years: 3 out of 100 patients offered active surveillance reported faecal incontinence more than once per week 1 out of 100 patients offered radical prostatectomy reported faecal incontinence more than once per week 4 out of 100 patients offered radical radiotherapy reported faecal incontinence more than once per week

[1]The trial used the intention-to-treat method of analysis and some of the patients in the active surveillance arm may therefore have undergone prostatectomy or radiotherapy during the follow-up period.

[2]The trial defined disease progression as:

- any rise in prostate-specific antigen (PSA) >20% between consecutive measures at any time during follow-up or
- any rise in PSA level of 50% or greater in any 12 month period confirmed by repeat tests or
- any indication of the appearance of symptomatic systemic disease.

1.3.8 Offer multiparametric MRI to people having active surveillance who have not had an MRI previously. If the MRI results do not agree with the biopsy findings, offer a new MRI-influenced biopsy. **[2019]**

1.3.9 Consider using the protocol in Table 4 for people who have chosen active surveillance. **[2019]**

Table 4 Protocol for active surveillance

Timing	Tests[1]
Year 1 of active surveillance	Every 3–4 months: measure PSA[2] Throughout active surveillance: monitor PSA kinetics[3] At 12 months: digital rectal examination (DRE)[4] At 12–18 months: multiparametric MRI
Year 2 and every year thereafter until active surveillance ends	Every 6 months: measure PSA[2] Throughout active surveillance: monitor PSA kinetics[3] Every 12 months: DRE[4]
[1] If there is concern about clinical or PSA changes at any time during active surveillance, reassess with multiparametric MRI and/or re-biopsy. [2] Could be carried out in primary care if there are agreed shared-care protocols and recall systems. [3] Could include PSA density and velocity. [4] Should be performed by a healthcare professional with expertise and confidence in performing DRE.	

1.3.10 If a person wishes to move from active surveillance to radical treatment at any stage in their care, make a shared decision to do so based on the person's preferences, comorbidities and life expectancy. **[2019]**

1.3.11 Offer radical treatment to people with localised prostate cancer who had chosen an active surveillance regimen and who now have evidence of disease progression. **[2019]**

To find out why the committee made the 2019 recommendation on active surveillance and how they might affect practice, see rationale and impact.

Intermediate-risk localised prostate cancer

1.3.12 For people with intermediate-risk localised prostate cancer

- offer radical prostatectomy or radical radiotherapy **and**
- consider active surveillance (in line with recommendation 1.3.10) for people who choose not to have immediate radical treatment.

Use Table 3 to discuss the benefits and harms of each option. **[2019]**

To find out why the committee made the 2019 recommendation on active surveillance and how they might affect practice, see rationale and impact.

High-risk localised prostate cancer

1.3.13 Do not offer active surveillance to people with high-risk localised prostate cancer. **[2019]**

1.3.14 Offer radical prostatectomy or radical radiotherapy to people with high-risk localised prostate cancer when it is likely the person's cancer can be controlled in the long term**. [2019]**

Radical treatment

1.3.15 Commissioners of urology services should consider providing robotic surgery to treat localised prostate cancer. **[2014]**

1.3.16 Commissioners should base robotic systems for the surgical treatment of localised prostate cancer in centres that are expected to perform at least 150 robot-assisted laparoscopic radical prostatectomies per year to ensure they are cost effective. **[2014]**

1.3.17 For people having radical external beam radiotherapy for localised prostate cancer:

- offer hypofractionated radiotherapy (60 Gy in 20 fractions) using image-guided intensity modulated radiation therapy (IMRT), unless contraindicated **or**
- offer conventional radiotherapy (74 Gy in 37 fractions) to people who cannot have hypofractionated radiotherapy. **[2019]**

1.3.18 Offer people with localised and locally advanced prostate cancer receiving radical external beam radiotherapy with curative intent planned treatment techniques that optimise the dose to the tumour while minimising the risks of normal tissue damage. **[2008]**

1.3.19 Offer people with intermediate- and high-risk localised prostate cancer a combination of radical radiotherapy and androgen deprivation therapy, rather than radical radiotherapy or androgen deprivation therapy alone. **[2014]**

1.3.20 Offer people with intermediate- and high-risk localised prostate cancer 6 months of androgen deprivation therapy before, during or after radical external beam radiotherapy. **[2014]**

1.3.21 Consider continuing androgen deprivation therapy for up to 3 years for people with high-risk localised prostate cancer, and discuss the benefits and risks of this option with them. **[2014]**

1.3.22 Consider brachytherapy in combination with external beam radiotherapy for people with intermediate- and high-risk localised prostate cancer. **[2019]**

1.3.23 Do not offer brachytherapy alone to people with high-risk localised prostate cancer. **[2008]**

1.3.24 Discuss the option of docetaxel chemotherapy with people who have newly diagnosed non-metastatic prostate cancer[2] who:

[2] At the time of consultation (December 2018), docetaxel only has UK marketing authorisation for hormone-refractory metastatic prostate cancer. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and

- are starting long-term androgen deprivation therapy **and**
- have no significant comorbidities **and**
- have high-risk disease, as shown by:
  - T3/T4 staging or
  - Gleason score 8–10 or
  - PSA greater than 40 ng/ml.

Explain the benefits and harms (see Table 5) and make a shared decision about whether the person should have this treatment. **[2019]**

1.3.25 For people having docetaxel chemotherapy:

- start treatment within 12 weeks of starting androgen deprivation therapy
- use six 3-weekly cycles at a dose of 75 mg/m^2 (with or without daily prednisolone). **[2019]**

1.3.26 Do not offer high-intensity focused ultrasound and cryotherapy to people with localised prostate cancer, other than in the context of controlled clinical trials comparing their use with established interventions[3]. **[2008]**

Table 5 Factors to consider when discussing the option of docetaxel chemotherapy for people with high-risk, non-metastatic prostate cancer

What does treatment with docetaxel involve?	Docetaxel chemotherapy is given at 6 appointments, each 3 weeks apart. It is given as an intravenous infusion that takes about 1 hour.
What are the benefits of docetaxel treatment for people with high-risk, non-metastatic prostate cancer?	• There is clear, high-quality evidence that docetaxel chemotherapy delays disease progression in people with high-risk, non-metastatic disease. • In a large UK randomised trial, the average person who did not receive docetaxel experienced disease progression about 5 years after the start of the trial, whereas the average person receiving docetaxel experienced disease progression after about 6 years.

documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information

[3] NICE interventional procedure 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.

	• We do not yet know whether docetaxel improves survival in people with high-risk, non-metastatic disease and we will only be confident about whether it does when trials have been running for longer. • In a large UK randomised trial, 80 out of 100 people with high-risk disease who did not receive docetaxel were still alive after 5 years compared with 84 out of 100 people who did. However, this difference could be because of chance.
What are the risks associated with docetaxel treatment?	A large UK randomised trial found that: • 15 out of 100 people who took docetaxel developed febrile neutropenia (that is, they got a fever because the chemotherapy had reduced their white blood cells' ability to fight infection). • 1 out of 100 people who took docetaxel died because of infections that, in the opinion of the investigators, they might not have developed if they had not received docetaxel. • 8 out of 100 people who took docetaxel felt unusually weak or tired. • 8 out of 100 people who took docetaxel experienced gastrointestinal symptoms (including diarrhoea, abdominal pain, constipation and/or vomiting). • 5 out of 100 people who took docetaxel experienced respiratory symptoms (including breathlessness and/or chest infections). • 4 out of 100 people who took docetaxel experienced problems with their nervous systems (for example, numbness or weakness). • 1 out of 100 people who took docetaxel experienced problems with their nails that were serious enough to interfere with their daily lives.

To find out why the committee made the 2019 recommendations on radiotherapy and how they might affect practice, see rationale and impact.

To find out why the committee made the 2019 recommendations on docetaxel chemotherapy and how they might affect practice, see rationale and impact.

Watchful waiting

1.3.27 People with localised prostate cancer who have chosen watchful waiting and who have evidence of significant disease progression (that is, rapidly

rising PSA level or bone pain) should have their situation reviewed by a member of the urological cancer MDT. **[2008]**

Locally advanced prostate cancer

1.3.28 Consider pelvic radiotherapy for people with locally advanced prostate cancer who have a higher than 15% risk of pelvic lymph node involvement[4] and who are to receive neoadjuvant hormonal therapy and radical radiotherapy. **[2008]**

1.3.29 Do not offer immediate post-operative radiotherapy after radical prostatectomy, even to people with margin-positive disease, other than in the context of a clinical trial. **[2008]**

1.3.30 Do not offer adjuvant hormonal therapy in addition to radical prostatectomy, even to people with margin-positive disease, other than in the context of a clinical trial. **[2008]**

1.3.31 Do not offer high-intensity focused ultrasound and cryotherapy to people with locally advanced prostate cancer other than in the context of controlled clinical trials comparing their use with established interventions[5]. **[2008]**

1.3.32 Do not offer bisphosphonates for the prevention of bone metastases in people with prostate cancer. **[2008]**

Managing adverse effects of radical treatment

Sexual dysfunction

1.3.33 Offer people who have had radical treatment for prostate cancer access to specialist erectile dysfunction services. **[2008, amended 2014]**

[4] Estimated using the Roach formula; %LN risk = 2/3 PSA + (10x [Gleason score – 6])

[5] NICE interventional procedure 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.

1.3.34 Offer people with prostate cancer who experience loss of erectile function phosphodiesterase type 5 (PDE5) inhibitors to improve their chance of spontaneous erections. **[2008]**

1.3.35 If PDE5 inhibitors do not restore erectile function or are contraindicated, offer people vacuum devices, intraurethral inserts or penile injections, or penile prostheses as an alternative. **[2008]**

Urinary incontinence

1.3.36 Ensure that people with prostate cancer who have troublesome urinary symptoms after treatment have access to specialist continence services for assessment, diagnosis and conservative treatment. This could include coping strategies, pelvic floor muscle re-education, bladder retraining and pharmacotherapy. **[2008]**

1.3.37 Refer people with prostate cancer who have intractable stress incontinence to a specialist surgeon for consideration of an artificial urinary sphincter. **[2008]**

1.3.38 Do not offer injection of bulking agents into the distal urinary sphincter to treat stress incontinence in people with prostate cancer. **[2008]**

Radiation-induced enteropathy

1.3.39 Offer people with signs or symptoms of radiation-induced enteropathy care from a team of professionals with expertise in radiation-induced enteropathy (who may include oncologists, gastroenterologists, bowel surgeons, dietitians and specialist nurses). **[2014]**

1.3.40 Include the nature and treatment of radiation-induced enteropathy in training programmes for oncologists and gastroenterologists. **[2014]**

1.3.41 Carry out full investigations, including flexible sigmoidoscopy, in people who have symptoms of radiation-induced enteropathy to exclude inflammatory bowel disease or malignancy of the large bowel and to ascertain the nature of the radiation injury. Use caution when performing

anterior wall rectal biopsy after brachytherapy because of the risk of fistulation. **[2014]**

Follow-up

1.3.42 Discuss the purpose, duration, frequency and location of follow-up with each person with localised and locally advanced prostate cancer, and if they wish, their partner or carers. **[2019]**

1.3.43 Advise people with prostate cancer about potential longer-term adverse effects of treatment and when and how to report them. **[2019]**

1.3.44 Check PSA levels for all people with prostate cancer who are having radical treatment no earlier than 6 weeks after treatment, at least every 6 months for the first 2 years, and then at least once a year after that. **[2019]**

1.3.45 Do not routinely offer digital rectal examination to people with localised prostate cancer who are not on active surveillance while their PSA remains at baseline levels. **[2019]**

1.3.46 After at least 6 months' initial follow-up, consider a non-hospital based follow-up strategy for people with a stable PSA who have had no significant treatment complications, unless they are taking part in a clinical trial that needs formal clinic-based follow-up. **[2019]**

1.3.47 Follow up people with prostate cancer who have chosen a watchful waiting regimen with no curative intent in primary care if protocols for this have been agreed between the local urological cancer MDT and the relevant primary care organisation(s). Measure their PSA at least once a year. **[2019]**

To find out why the committee made the 2019 recommendations on follow-up and how they might affect practice, see rationale and impact.

Managing relapse after radical treatment

1.3.48 Analyse serial PSA levels after radical treatment using the same assay technique as used before. **[2008]**

1.3.49 Do not offer biopsy of the prostatic bed to people with prostate cancer who have had a radical prostatectomy. **[2008]**

1.3.50 Only offer biopsy of the prostate after radiotherapy to people with prostate cancer who might have local salvage therapy in the context of a clinical trial. **[2008]**

1.3.51 For people with evidence of biochemical relapse after radical treatment who are thinking about having radical salvage therapy:

- do not offer routine MRI scanning before salvage radiotherapy in people with prostate cancer
- offer an isotope bone scan if symptoms or PSA trends are suggestive of metastases. **[2008]**

1.3.52 Take into account that biochemical relapse (a rising PSA) alone should not mean an immediate change in treatment is needed. **[2008]**

1.3.53 Estimate PSA doubling time if biochemical relapse occurs. Base this on a minimum of 3 measurements over at least a 6-month period. **[2008]**

1.3.54 Offer people with biochemical relapse after radical prostatectomy, with no known metastases, radical radiotherapy to the prostatic bed. **[2008]**

1.3.55 Consider entry to appropriate clinical trials for people with biochemical relapse. **[2008]**

1.3.56 Do not routinely offer hormonal therapy to people with prostate cancer who have a biochemical relapse unless they have:

- symptomatic local disease progression, or
- any proven metastases, or
- a PSA doubling time of less than 3 months. **[2008]**

1.4 People having hormone therapy

1.4.1 Consider intermittent therapy for people having long-term androgen deprivation therapy (not in the adjuvant setting). Discuss with the person (and their partner, family or carers if they wish):

- the rationale for intermittent therapy
- the limited evidence for reduction in side effects from intermittent therapy
- the effect of intermittent therapy on progression of prostate cancer. **[2014]**

1.4.2 For people who are having intermittent androgen deprivation therapy:

- measure PSA every 3 months **and**
- restart androgen deprivation therapy if PSA is 10 ng/ml or above, or if there is symptomatic progression. **[2014]**

Managing adverse effects of hormone therapy

Hot flushes

1.4.3 Offer medroxyprogesterone[6] (20 mg per day), initially for 10 weeks, to manage troublesome hot flushes caused by long-term androgen suppression. Evaluate the effect at the end of the treatment period. **[2014]**

1.4.4 Consider cyproterone acetate (50 mg twice a day for 4 weeks) to treat troublesome hot flushes if medroxyprogesterone is not effective or not tolerated. **[2014]**

1.4.5 Tell people that there is no good-quality evidence for the use of complementary therapies to treat troublesome hot flushes**. [2014]**

Sexual dysfunction

[6] At the time of publication (April 2019), medroxyprogesterone did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

1.4.6 Before they start androgen deprivation therapy, tell people and, if they wish, their partner, that long-term androgen deprivation will cause a reduction in libido and possible loss of sexual function. **[2014]**

1.4.7 Advise people and, if they wish, their partner, about the potential loss of ejaculation and fertility associated with long-term androgen deprivation and offer sperm storage. **[2014]**

1.4.8 Ensure that people starting androgen deprivation therapy have access to specialist erectile dysfunction services. **[2014]**

1.4.9 Consider referring people who are having long-term androgen deprivation therapy, and their partners, for psychosexual counselling. **[2014]**

1.4.10 Offer PDE5 inhibitors to people having long-term androgen deprivation therapy who experience loss of erectile function. **[2014]**

1.4.11 If PDE5 inhibitors fail to restore erectile function or are contraindicated, offer a choice of:

- intraurethral inserts
- penile injections
- penile prostheses
- vacuum devices. **[2014]**

Osteoporosis

1.4.12 Do not routinely offer bisphosphonates to prevent osteoporosis in people with prostate cancer having androgen deprivation therapy. **[2008]**

1.4.13 Consider assessing fracture risk in people with prostate cancer who are having androgen deprivation therapy, in line with the NICE guideline on osteoporosis: assessing the risk of fragility fracture). **[2014]**

1.4.14 Offer bisphosphonates to people who are having androgen deprivation therapy and have osteoporosis. **[2014]**

1.4.15 Consider denosumab for people who are having androgen deprivation therapy and have osteoporosis if bisphosphonates are contraindicated or not tolerated. **[2014]**

Gynaecomastia

1.4.16 For people starting long-term bicalutamide monotherapy (longer than 6 months), offer prophylactic radiotherapy to both breast buds within the first month of treatment. Use a single fraction of 8 Gy using orthovoltage, or electron beam radiotherapy. **[2008]**

1.4.17 If radiotherapy does not prevent gynaecomastia, consider weekly tamoxifen[7]. **[2008]**

Fatigue

1.4.18 Tell people who are starting androgen deprivation therapy that fatigue is a recognised side effect of this therapy, and might not be because of their prostate cancer. **[2014]**

1.4.19 Offer people who are starting or having androgen deprivation therapy supervised resistance and aerobic exercise at least twice a week for 12 weeks to reduce fatigue and improve quality of life. **[2014]**

1.5 Metastatic prostate cancer

Information and support

1.5.1 Offer people with metastatic prostate cancer tailored information and access to specialist urology and palliative care teams to address their specific needs. Give them the opportunity to discuss any significant changes in their disease status or symptoms as these occur. **[2008]**

[7] At the time of consultation (April 2019), tamoxifen did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

1.5.2 Integrate palliative interventions at any stage into coordinated care, and facilitate any transitions between care settings as smoothly as possible. **[2008]**

1.5.3 Discuss personal preferences for palliative care as early as possible with people with metastatic prostate cancer, their partners and carers. Tailor treatment/care plans accordingly, and identify the preferred place of care. **[2008]**

1.5.4 Ensure that palliative care is available when needed and is not limited to the end of life. Care should not be restricted to being associated with hospice care. **[2008]**

1.5.5 Offer a regular assessment of needs to people with metastatic prostate cancer. **[2008]**

Treatment

1.5.6 Offer docetaxel chemotherapy to people with newly diagnosed metastatic prostate cancer[8] who do not have significant comorbidities:

- start treatment within 12 weeks of starting androgen deprivation therapy, and
- use six 3-weekly cycles at a dose of 75 mg/m^2 (with or without daily prednisolone). **[2019]**

To find out why the committee made the 2019 recommendation on docetaxel chemotherapy and how they might affect practice, see rationale and impact.

1.5.7 Offer bilateral orchidectomy to all people with metastatic prostate cancer as an alternative to continuous luteinising hormone-releasing hormone agonist therapy. **[2008]**

[8] At the time of consultation (December 2018), docetaxel only has UK marketing authorisation for hormone-refractory metastatic prostate cancer. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information

1.5.8 Do not offer combined androgen blockade as a first-line treatment for people with metastatic prostate cancer. **[2008]**

1.5.9 For people with metastatic prostate cancer who are willing to accept the adverse impact on overall survival and gynaecomastia with the aim of retaining sexual function, offer anti-androgen monotherapy with bicalutamide[9] (150 mg). **[2008]**

1.5.10 Begin androgen deprivation therapy and stop bicalutamide treatment in people with metastatic prostate cancer who are taking bicalutamide monotherapy and who do not maintain satisfactory sexual function. **[2008]**

Hormone-relapsed metastatic prostate cancer

Recommendations in this section marked with an asterisk are from Docetaxel for the treatment of hormone-refractory metastatic prostate cancer (NICE technology appraisal guidance 101).

1.5.11 Discuss the treatment options for people with prostate cancer who develop biochemical evidence of hormone-relapsed disease at the urological cancer MDT. Seek an oncologist and/or specialist palliative care opinion, as appropriate. **[2008]**

1.5.12 Docetaxel is recommended, within its licensed indications, as a treatment option for people with hormone-refractory prostate cancer only if their Karnofsky performance-status score is 60% or more. **[2008]***

1.5.13 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. **[2008]***

[9] At the time of publication (April 2019), bicalutamide did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

1.5.14 Repeat cycles of treatment with docetaxel are not recommended if the disease recurs after completion of the planned course of chemotherapy. **[2008]***

1.5.15 Offer a corticosteroid such as dexamethasone (0.5 mg daily) as third-line hormonal therapy after androgen deprivation therapy and anti-androgen therapy to people with hormone-relapsed prostate cancer. **[2008]**

1.5.16 Offer spinal MRI to people with hormone-relapsed prostate cancer shown to have extensive metastases in the spine (for example, on a bone scan) if they develop any spinal-related symptoms. **[2008]**

1.5.17 Do not routinely offer spinal MRI to all people with hormone-relapsed prostate cancer and known bone metastases. **[2008]**

Bone-targeted therapies

1.5.18 For people with hormone-refractory metastatic prostate cancer, consider zoledronic acid to prevent or reduce skeletal-related events. **[2019]**

1.5.19 Consider oral or intravenous bisphosphonates for pain relief for people with hormone-refractory metastatic prostate cancer when other treatments, including analgesics and palliative radiotherapy, have not given satisfactory pain relief. **[2019]**

1.5.20 For guidance on treatments for people with bone metastases from prostate cancer, see the NICE technology appraisal on radium-223 dichloride. **[2019]**

> To find out why the committee made the 2019 recommendations on bone-targeted therapies and how they might affect practice, see rationale and impact.

Pelvic-targeted therapies

1.5.21 Offer decompression of the upper urinary tract by percutaneous nephrostomy or by insertion of a double J stent to people with obstructive uropathy secondary to hormone-relapsed prostate cancer. **[2008]**

1.5.22 Discuss the option of no intervention as a treatment choice with people with obstructive uropathy secondary to hormone-relapsed prostate cancer. **[2008]**

Recommendations for research

The guideline committee has made the following recommendations for research.

As part of the 2019 update, the guideline committee made additional research recommendations on the follow-up, diagnosis and progression of prostate cancer.

Key recommendations for research

1. Follow-up during active surveillance

What is the most suitable surveillance protocol for people for whom active surveillance is appropriate, as assessed by multiparametric MRI and biopsy, when there are no clinical concerns during follow-up?

To find out why the committee made the research recommendation on follow-up during active surveillance see rationale and impact.

2. Follow-up after radical treatment

What is the most clinically- and cost-effective follow-up protocol for people with prostate cancer who have had radical treatment, with specific regard to risk stratification, duration of follow-up, frequency of follow-up appointments, the type of examination or blood tests, and the roles of primary and secondary care in follow-up?

To find out why the committee made the research recommendation on follow-up after radical treatment see rationale and impact.

3. Diagnosis of clinically significant cancer

What is the most clinically- and cost-effective pathway for diagnosing clinically significant prostate cancer?

To find out why the committee made the research recommendation on diagnosing clinically significant cancer see rationale and impact.

4. Progression of cancer

What is the most clinically and cost-effective pathway for excluding the clinically significant progression of cancer in people with low to intermediate risk prostate cancer?

To find out why the committee made the research recommendation on the clinically significant progression of cancer see rationale and impact.

5. Natural history of prostate cancer

What is the natural history of people with a Likert score on MRI of less than 3 without biopsy at long-term follow-up?

To find out why the committee made the research recommendation on diagnosing clinically significant cancer see rationale and impact.

Other recommendations for research

Diagnosing prostate cancer

In patients with negative MRI (Likert score 1 or 2), what is the next best diagnostic investigation to rule out clinically significant prostate cancer?

What is the diagnostic accuracy of transperineal mapping biopsy compared with transperineal non-mapping biopsy in the diagnosis of clinically significant prostate cancer?

Risk stratification

What is the prognostic value of different risk stratification methods for people with locally advanced prostate cancer?

Zoledronic acid

What is the effectiveness and cost effectiveness of different scheduling of zoledronic acid in the prevention and reduction of skeletal events in people with hormone-refractory prostate cancer?

Terms used in this guideline

Active surveillance

This is part of a 'curative' strategy and is aimed at people with localised prostate cancer for whom radical treatments are suitable, keeping them within a 'window of curability' whereby only those whose tumours are showing signs of progressing, or those with a preference for intervention are considered for radical treatment. Active surveillance may thus avoid or delay the need for radiotherapy or surgery.

Clinically significant cancer

For the purpose of this guideline, this includes any prostate cancer with a Gleason score of 7 or more.

External beam radiotherapy (EBRT)

This is radiotherapy given by using ionising radiation (for example, high energy X-rays) produced in a machine and directed at the tumour from outside the patient.

Hormone relapsed (also known as hormone resistant, hormone refractory and castrate resistant)

Refers to prostate cancer after failure of primary androgen deprivation therapy.

Locally advanced prostate cancer

For the purposes of this guideline, this includes: high-risk localised prostate cancer (PSA > 20 ng/ml, or Gleason score 8-10, or clinical stage ≥T2c) T3b and T4, N0 prostate cancer; and any T, N1 prostate cancer.

Localised prostate cancer

Cancer which has been staged as T1 or T2 (confined to the prostate gland).

Multiparametric MRI

A magnetic resonance imaging study that incorporates anatomical and functional information about a body part. The functional information may include one or more sequences based on diffusion-weighted imaging, dynamic contrast enhanced imaging or magnetic resonance spectroscopy.

Prostatectomy

Surgery to remove part, or all of the prostate gland. Radical prostatectomy aims at the removal of the entire prostate gland and lymph nodes. This can be performed by an open approach or by keyhole technique (laparoscopic or robotically assisted laparoscopic prostatectomy).

Prostate-specific antigen (PSA)

A protein produced by the prostate gland and identified in the blood. People with prostate cancer tend to have higher levels of PSA in their blood (although most people with prostate cancer have normal PSA levels). PSA levels may also be increased by conditions other than cancer and levels tend to increase naturally with age.

PSA density

The PSA level in the blood relative to the volume of the prostate

Radical treatment

Treatment given with the aim of cure, rather than just improving symptoms.

Radiotherapy

The use of radiation, usually X-rays or gamma rays, to kill tumour cells. This can either be EBRT or brachytherapy.

Systematic prostate biopsy

For the purposes of this guideline, this included 12 core biopsy by transrectal or transperineal biopsy.

Watchful waiting

This is part of a strategy for ‘controlling’ rather than ‘curing’ prostate cancer and is aimed at people with localised prostate cancer who do not ever wish to have curative treatment, or it is not suitable for them. Instead, it involves the deferred use of hormone therapy. Watchful waiting avoids the use of surgery or radiation, but implies that curative treatment will not be attempted.

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice. They link to details of the evidence and a full description of the committee's discussion.

Magnetic resonance imaging

Recommendations 1.2.1 to 1.2.5

Why the committee made the recommendations

The committee saw no new evidence to suggest any changes were needed to the recommendations on imaging in people who are not going to have radical treatment.

There was good evidence that showed that multiparametric MRI is useful in identifying lesions before biopsy, and the combination of MRI with prostate biopsy leads to better identification of clinically significant prostate cancer than systematic prostate biopsy alone. The committee recommended using a 5-point Likert scale because this scale takes into account clinical factors and not just the lesion size, improving the diagnostic ability of multiparametric MRI.

The committee made a recommendation to consider omitting prostate biopsy for people whose multiparametric MRI Likert score is 1 or 2 because there was some evidence that this is safe to do. However, there is a small risk that in some cases significant cancers may be missed, so the committee recommended clinicians discuss the risk and benefits with the person.

Based on their expertise and economic evidence, the committee recommended not offering mapping transperineal template biopsy as an initial biopsy, because the technique is currently too resource intensive to be used as an initial assessment – it requires general anaesthetic and extensive histological analysis. The committee recognised that this technique could be allowed as part of a clinical trial because it is often used as the benchmark or gold standard test in those trials.

As there was limited evidence on the most effective pathway for excluding clinically significant progression of prostate cancer in people with low to intermediate risk, the committee made a research recommendation on this topic. They also identified that

there was a gap in the evidence on the most suitable surveillance protocol in this population group.

How the recommendations might affect practice

The recommendations should not have a significant resource impact as many centres already perform MRI-influenced biopsy. Since all people who have a biopsy will previously have had an MRI, using the MRI to target the biopsy will be more efficient and will need fewer biopsy cores to be taken. Health economic evidence shows that MRI-influenced prostate biopsy may be more cost effective than systematic prostate biopsy as it takes less time and is more efficient in identifying clinically significant cancer.

Full details of the evidence and the committee's discussion are in evidence review D: diagnosing and identifying clinically significant prostate cancer.

Return to recommendations

If the MRI or biopsy is negative

Recommendations 1.2.12 to 1.2.13

Why the committee made the recommendations

There was no clinical evidence in this area, therefore the committee used evidence from economic modelling that showed people with a negative diagnosis of prostate cancer can still be at substantial risk of having prostate cancer, so follow-up is important. The evidence showed that the prevalence of initially undetected, but clinically significant, prostate cancer varies based on a person's diagnostic history, so their diagnostic history should influence the frequency of follow-up.

The follow-up strategies recommended for primary care are based on standard PSA tests, with which primary care healthcare professionals are familiar. The committee agreed it was important that specialist healthcare professionals should calculate thresholds for re-referral and provide these when discharging people, rather than expecting the calculations to be made in primary care.

The recommendations in NICE's existing guidance on PCA3 assay and the prostate health index (DG17) will be updated by this guideline. The committee saw no

evidence that either technique represents an effective use of NHS resources in the follow-up of people who have had a negative transrectal ultrasound guided prostate biopsy, and therefore did not make any recommendations on these technologies.

The committee identified a gap in the evidence for the performance of transperineal non-mapping biopsy and therefore made a research recommendation in this area.

The committee also noted that there is limited long-term follow-up evidence on the natural history of people whose multiparametric MRI Likert score is 1 or 2. In addition, there is limited evidence on the number of people whose multiparametric MRI is Likert score 1 or 2, who have normal PSA density and kinetics and who are found to have clinically significant cancer. Further research recommendations were made in these areas to help provide evidence across the prostate cancer treatment pathway.

How the recommendations might affect practice

Currently, there is substantial variation in clinical practice in the follow-up of people with a negative prostate biopsy. The committee's recommendations should help to standardise practice.

Other recommendations made by the committee make it likely that more people will have a negative diagnosis on the basis of low-risk multiparametric MRI findings and no biopsy. This is a new population who will need effective follow-up strategies, and the recommendations give guidance on approaches that are likely to provide a good balance of benefits, harms and costs for this group.

The committee were confident that none of the recommendations would have a significant resource impact, as they are based on PSA measurements that are commonly used within primary care settings. In addition, if further multiparametric MRI is needed during follow-up, the evidence showed that MRI-influenced prostate biopsy may be more cost effective than systematic prostate biopsy, as it takes less time and is more efficient in identifying clinically significant cancer.

Full details of the evidence and the committee's discussion are in evidence review E: following-up people at increased risk of prostate cancer.

Return to recommendations

Active surveillance

Recommendations 1.3.7 and 1.3.10–-1.3.14

Why the committee made the recommendations

The committee agreed that the existing recommendations were in line with the available good body of evidence for the treatment of localised prostate cancer, and reflected the trade-off seen in the evidence between the clinical benefits of radical treatments and potential side effects in people with low to intermediate risk prostate cancer.

The committee noted that active surveillance has often been offered as a non-preferred treatment rather than as an equal choice alongside prostatectomy and radiotherapy. It agreed that active surveillance was a safe option for people with low-risk localised prostate cancer because most people live with low risk cancer for many years with no disease progression. The lasting negative effects of radiotherapy or prostatectomy mean that many people may prefer active surveillance. It also agreed that active surveillance might be a safe option for some people with intermediate-risk localised prostate cancer, although for this group there was more risk that the cancer would have an impact on their lives and they are more likely to need radical treatment. Since the committee agreed that all 3 options may be suitable for different people, it included a preference decision table to assist both the clinician and the patient in making the right choice for them. The committee did not change the existing recommendations that active surveillance should not be offered to those people with high-risk localised prostate cancer, as there is no new evidence to suggest it is beneficial.

The committee saw no new evidence to suggest any changes were needed to the recommendation on radical prostatectomy and radical radiotherapy in people with high-risk prostate cancer.

How the recommendations might affect practice

The recommendations reflect current practice, so there will be minimal impact on resources.

Full details of the evidence and the committee's discussion are in evidence review G: active surveillance, radical prostatectomy or radical radiotherapy in people with localised prostate cancer.

Recommendations 1.3.8 to 1.3.9

Why the committee made the recommendations

The committee made recommendations based on a good body of evidence that multiparametric MRI can be used as part of an active surveillance protocol to identify clinically significant cancer, or restage prostate cancer after diagnosis. The committee took into account the benefits seen in using multiparametric MRI pre-biopsy in people who have not had a biopsy and who have suspected prostate cancer, and concluded that this benefit can be extended to people having active surveillance without having had an MRI to allow for confirmation or reclassification of the prostate cancer.

The committee amended the protocol for active surveillance based on their expertise and good evidence on which PSA kinetics to monitor and the use of multiparametric MRI to identify clinically significant prostate cancer.

Because of the limited evidence on the most effective pathway for excluding clinically significant progression of prostate cancer in people with low to intermediate risk, the committee made research recommendations in this area. They also identified that there was a gap in the evidence on the most suitable surveillance protocol for this population group.

How the recommendations might affect practice

The use of multiparametric MRI in people who are enrolled on active surveillance will influence active surveillance protocols across the country. Multiparametric MRI is clinically and cost effective, as clinically significant cancers are more likely to be identified, therefore decisions on treatment can be made earlier in the diagnosis pathway saving on future treatment costs.

Full details of the evidence and the committee's discussion are in evidence review F

Return to recommendations

Radical treatment

Recommendations 1.3.17 and 1.3.22

Why the committee made the recommendations

A large body of evidence showed that hypofractionated radiotherapy and conventional radiotherapy were equally effective. The committee noted that hypofractionated radiotherapy is associated with higher rates of acute gastrointestinal toxicity, but overall it could enable people to have a better quality of life because people would need to make fewer clinic visits. Fewer clinic visits for hypofractionated radiotherapy would also mean fewer resources were needed compared with conventional radiotherapy treatment. Therefore, hypofractionated radiotherapy was recommended as the first option.

The committee agreed that 60 Gy in 20 fractions was the optimal dose for people having hypofractionated radiotherapy. This was the dosage used in the large UK CHHiP trial that was associated with greater efficacy compared with a 57 Gy schedule, although the 60 Gy schedule did also show slightly greater toxicity.

The committee considered evidence from a large trial that showed a reduction in biochemical failure (for example, local recurrence or distant metastases) associated with the use of low-dose brachytherapy in combination with external beam radiation therapy for people with high-risk localised prostate cancer. As a result, the committee amended the previous recommendation so it was not limited to high-dose brachytherapy.

How the recommendations might affect practice

As hypofractionated radiotherapy is already routinely used in practice (alongside other non-radiotherapy treatment options) for people with localised prostate cancer, these recommendations are unlikely to have an impact on resources.

For brachytherapy, the committee agreed that only a small number of people (typically those with high-risk prostate cancer) would currently have brachytherapy, so the changes to the recommendations are unlikely to have a significant impact on current practice.

Full details of the evidence and the committee's discussion are in evidence review C: radiotherapy.

Return to recommendations

Docetaxel chemotherapy

Recommendations 1.3.24, 1.3.25 and 1.5.6

Why the committee made the recommendations

There was good evidence that showed docetaxel improves overall survival, prostate cancer-specific survival and clinical progression-free survival in people with newly diagnosed metastatic prostate cancer who are starting long-term hormone therapy. The committee agreed these benefits outweighed the potential harms of the treatment.

The evidence also showed docetaxel slows clinical progression in people with newly diagnosed high-risk non-metastatic cancer starting long-term hormone therapy. However, the evidence did not show any extension of overall survival. Because of the known toxicities associated with docetaxel treatment, the benefits and harms are more finely balanced in this population. As a result, the committee identified this decision as being preference sensitive, and the person's values and preferences are likely to be particularly important in their decision about the best course of action for them.

The committee also made a research recommendation as it identified a gap in the evidence related to there being no universal definition of locally advanced prostate cancer. A risk stratification study will help identify patients at various levels of risks, and help tailor treatment according to need.

How the recommendations might affect practice

Off-label use of docetaxel in people diagnosed with hormone-sensitive metastatic prostate cancer is current practice, therefore the recommendation for the metastatic prostate cancer population is likely to have no impact. However, this does not include high-risk non-metastatic prostate cancer. Therefore, the recommendation for this population could result in an increase in the number of people with high-risk non-

metastatic prostate cancer receiving docetaxel chemotherapy. Although this could result in an increase in some shorter term costs to the NHS, the economic evidence showed a reduction in longer-term management costs, with the net effect that docetaxel is likely to be cost-saving in the long term in this population and, once its benefits are also taken into account, almost certain to represent a good use of NHS resources.

Full details of the evidence and the committee's discussion are in evidence review B: docetaxel in people with hormone-sensitive prostate cancer.

Return to recommendations

Follow-up

Recommendations 1.3.42–1.3.47

Why the committee made the recommendations

The committee saw no new evidence to suggest any changes were needed to the recommendations on follow-up strategies after radical treatment. The committee did not change the existing recommendations that digital rectal examination should not be offered, as there was no new evidence to suggest it was beneficial for people who were not on active surveillance.

Based on their expertise, the committee amended the recommendations on the location of the follow-up. The committee discussed different strategies already in use across the country such as shared care, supported self-management and telephone based follow-up. Since it had not looked at the specific evidence for these, it was unable to recommend a specific programme. The committee agreed that the 2-year follow-up recommended in the previous guideline was conservative, and based on their expertise people with no complications and with a stable PSA could be cared for outside of the hospital environment. Complex cases might need longer contact with hospital-based services.

Given the lack of evidence, the committee also made a research recommendation in this area.

How the recommendations might affect practice

The committee noted that follow-up strategies are variable across the country and the recommendations will therefore have a varied resource impact across the country depending on the level of follow-up that is currently in place locally. Depending on the changes implemented there may be a large resource impact.

Full details of the evidence and the committee's discussion are in evidence review H: Follow-up protocols after radical treatment.

Return to recommendations

Bone-targeted therapies (bisphosphonates)

Recommendations 1.5.18-1.5.20

Why the committee made the recommendations

There was some evidence that showed zoledronic acid prolonged the time without skeletal-related events in people with hormone-refractory metastatic prostate cancer. However, the committee could not make a stronger recommendation because the evidence did not show whether zoledronic acid affects mortality in this population.

There was no new evidence that could affect the existing recommendation on the administration of bisphosphonates for pain relief for people with hormone-refractory metastatic prostate cancer.

How the recommendations might affect practice

There may be a small increase in the cost of hormone-refractory metastatic prostate cancer treatment, but as zoledronic acid is now out of patent this should limit the cost impact.

Full details of the evidence and the committee's discussion are in evidence review A: Bisphosphonates.

Return to recommendations

Context

Prostate cancer is the most common cancer in men, and the second most common cancer in the UK. In 2014 there were over 46,000 new diagnoses of prostate cancer, which accounts for 13% of all new cancers diagnosed. About 1 in 8 men will get prostate cancer at some point in their life.

Prostate cancer can also affect transgender women, as the prostate is usually conserved after gender-confirming surgery, but it is not clear how common it is in this population.

More than 50% of prostate cancer diagnoses in the UK each year are in men aged 70 years and over (2012), and the incidence rate is highest in men aged 90 years and over (2012–2014). Out of every 10 prostate cancer cases, 4 are only diagnosed at a late stage in England (2014) and Northern Ireland (2010–2014). Incidence rates are projected to rise by 12% between 2014 and 2035 in the UK to 233 cases per 100,000 in 2035.

A total of 84% of men aged 60–69 years at diagnosis in 2010–2011 are predicted to survive for 10 or more years after diagnosis. When diagnosed at the earliest stage, virtually all people with prostate cancer survive 5 years or more: this is compared with less than a third of people surviving 5 years or more when diagnosed at the latest stage.

There were approximately 11,000 deaths from prostate cancer in 2014. Mortality rates from prostate cancer are highest in men aged 90 years and over (2012–2014). Over the past decade, mortality rates have decreased by more than 13% in the UK. Mortality rates are projected to fall by 16% between 2014 and 2035 to 48 deaths per 100,000 men in 2035.

People of African family origin are at higher risk of prostate cancer (lifetime risk of approximately 1 in 4). Prostate cancer is inversely associated with deprivation, with a higher incidence of cases found in more affluent areas of the UK.

Costs for the inpatient treatment of prostate cancer are predicted to rise to £320.6 million per year in 2020 (from £276.9 million per year in 2010).

This guidance was updated in 2014 to include several treatments that have been licensed for the management of hormone-relapsed metastatic prostate cancer since the publication of the original NICE guideline in 2008.

Since the last update in 2014, there have been changes in the way that prostate cancer is diagnosed and treated. Advances in imaging technology, especially multiparametric MRI, have led to changes in practice, and new evidence about some prostate cancer treatments means that some recommendations needed to be updated.

Finding more information and resources

To find out what NICE has said on topics related to this guideline, see our web page on prostate cancer.

Update information

March 2019

We have reviewed the evidence on diagnosis, treatment and monitoring for people with prostate cancer.

Recommendations are marked **[2019]** if the evidence has been reviewed.

Recommendations that have been deleted or changed

We propose to delete some recommendations from the 2014 guideline. Table 1 sets out these recommendations and includes details of replacement recommendations. If there is no replacement recommendation, an explanation for the proposed deletion is given.

In recommendations shaded in grey and ending **[2008, amended 2019], or [2014, amended 2019]** we have made changes that could affect the intent without reviewing the evidence. Yellow shading is used to highlight these changes, and reasons for the changes are given in table 2.

In recommendations shaded in grey and ending **[2008] or [2014]**, we have not reviewed the evidence. In some cases minor changes have been made – for

example, to update links, or bring the language and style up to date – without changing the intent of the recommendation. Minor changes are listed in table 3.

See also the previous NICE guideline and supporting documents.

Table 1 Recommendations that have been deleted

Recommendation in 2014 guideline	Comment
Do not offer another biopsy if the multiparametric MRI (using T2- and diffusion-weighted imaging) is negative, unless any of the risk factors listed in recommendation 1.2.5 are present. (1.2.6) and Do not offer another biopsy if the multiparametric MRI (using T2- and diffusion-weighted imaging) is negative, unless any of the risk factors listed in recommendation 1.2.5 are present. (1.2.7)	Replaced by: 1.2.2 Offer multiparametric MRI as the first-line investigation to people with suspected clinically localised prostate cancer. Report the results using a 5-point Likert scale. 1.2.3 Offer multiparametric MRI-influenced prostate biopsy to people whose Likert score is 3 or more 1.2.4 Consider omitting a prostate biopsy for people whose multiparametric MRI Likert score is 1 or 2, but only after discussing the risks and benefits with the person and reaching a shared decision (Table 1). Offer systematic prostate biopsy to people who opt for biopsy. 1.2.5 Do not offer mapping transperineal template biopsy as initial assessment unless as part of a clinical trial.
Determine the provisional treatment intent (radical or non-radical) before decisions on imaging are made.(1.2.8) And Do not offer CT of the pelvis to men with low- or intermediate-risk localised prostate cancer (see table 1). (1.2.13) and Do not offer positron emission tomography imaging for prostate cancer in routine clinical practice. (1.2.15)	These recommendations have been deleted because the committee agreed they were incorrect in the context of the new recommendations on imaging
Offer active surveillance (in line with recommendation 1.3.10) as an option to men with low-risk localised prostate cancer for whom radical prostatectomy or radical radiotherapy is suitable. (1.3.8)	Replaced by: Offer a choice between active surveillance (in line with recommendation 1.3.10), radical prostatectomy or radical radiotherapy to people with low-risk localised prostate cancer for whom radical treatment is suitable. Use Table 3 to discuss the benefits and harms with them (1.3.7)

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 (1.3.9)	Replaced by: Make the decision to move from active surveillance to radical treatment based on the person's preferences, comorbidities and life expectancy. (1.3.11)
Consider using the protocol in table 2 for people who have chosen active surveillance. (1.3.10)	Consider using the protocol in table 3 for people who have chosen active surveillance. (1.3.7). The table associated with this recommendation has been updated.
Consider active surveillance (in line with recommendation 1.3.8) for men with intermediate-risk localised prostate cancer who do not wish to have immediate radical prostatectomy or radical radiotherapy. (1.3.12)	Replaced by: For people with intermediate-risk localised prostate cancer • offer radical prostatectomy or radical radiotherapy **and** • consider active surveillance (in line with recommendation 1.3.7) for people who choose not to have immediate radical treatment. Use Table 3 to discuss the benefits and harms of each option. (1.3.13)
Consider high-dose rate brachytherapy in combination with external beam radiotherapy for men with intermediate- and high-risk localised prostate cancer. (1.3.24)	Replaced by: Consider brachytherapy in combination with external beam radiotherapy for people with intermediate- and high-risk localised prostate cancer (1.3.23)
After at least 2 years, offer follow-up outside hospital (for example, in primary care) by telephone or secure electronic communications to men with a stable PSA who have had no significant treatment complications, 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. (1.3.46)	Replaced by : After at least 6 months initial follow-up, consider a non-hospital based follow-up strategy for people with a stable PSA who have had no significant treatment complications, unless they are taking part in a clinical trial that requires formal clinic-based follow-up. Strategies may include supported self-management, shared care, and telephone based follow-up (1.3.47)
Bisphosphonates for pain relief may be considered for men with hormone-relapsed prostate cancer when other treatments (including analgesics and palliative radiotherapy) have failed. Choose the oral or intravenous route of administration according to convenience, tolerability and cost. (1.5.19)	Replaced by: Consider oral or intravenous bisphosphonates for pain relief for people with hormone-refractory prostate cancer when other treatments, including analgesics and palliative radiotherapy, have not given satisfactory pain relief. (1.5.19)
Strontium-89 should be considered for people with hormone-relapsed prostate cancer and painful bone metastases, especially those people who are unlikely	Replaced by: For guidance on treatments for people with bone metastases from prostate cancer, see the NICE technology

to receive myelosuppressive chemotherapy. (1.5.20)	appraisal on radium-223 dichloride (1.5.20)
Do not offer bisphosphonates to prevent or reduce the complications of bone metastases in men with hormone-relapsed prostate cancer (1.5.18)	Replaced by : For people with hormone-refractory metastatic prostate cancer, consider zoledronic acid to prevent or reduce skeletal-related events (1.5.19)

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2 **Table 2 Minor changes to recommendation wording (no change to intent)**

Recommendation numbers in current guideline	**Comment**
All recommendations except those labelled [2019]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in guidelines) when possible. Yellow highlighting has not been applied to these changes.
All recommendations except those labelled [2019]	Wording has been changed from ‘men’ to ‘people’ to ensure that people who do not identify as men but who have a prostate are included in the guideline.

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