

# Prostate cancer: diagnosis and management

NICE guideline

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[www.nice.org.uk/guidance/ng131](https://www.nice.org.uk/guidance/ng131)

## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline replaces CG175 and DG17.

This guideline is the basis of QS91.

## Overview

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

### *Who is it for?*

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

## 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 an up-to-date decision aid 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 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]
- 1.1.12 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 multiparametric MRI 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 (see table 1). If a person opts to have a biopsy, offer systematic prostate 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 prostate biopsy	Disadvantages of undergoing prostate biopsy
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<p>You may have prostate cancer that the MRI scan missed:</p> <ul style="list-style-type: none"> <li>• between 11 and 28 out of 100 people with a low-risk MRI actually have clinically significant cancer</li> <li>• 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.</li> </ul>	<p>There is no guarantee that a prostate biopsy will find any disease that is there. Prostate biopsies find less than half of the clinically significant prostate cancers that MRI scans miss.</p>
	<p>You may be diagnosed with clinically insignificant prostate cancer. This is disease that is unlikely 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. Between 18 and 23 out of 100 people with a low-risk MRI get a diagnosis of clinically insignificant prostate cancer if they have a prostate biopsy.</p>
	<p>The most common type of biopsy, transrectal ultrasound-guided (TRUS), has some rare but important complications. The most serious is sepsis, which develops in a bit less than 1 out of 100 people. Other serious complications, including acute urinary retention, severe haematuria and severe rectal bleeding may need hospitalisation.</p>



	<p>TRUS biopsy has less serious complications that make it unpleasant to undergo for some people. On average:</p> <ul style="list-style-type: none"> <li>• 3 out of 100 people feel light-headed or dizzy immediately after the biopsy</li> <li>• 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</li> <li>• 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</li> <li>• 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</li> <li>• 37 out of 100 people have 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</li> <li>• 90 out of 100 people have 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.</li> </ul>
<p>There is more than 1 type of <a href="#">prostate biopsy</a>. The most common approach is <a href="#">TRUS biopsy</a>. The data in this table come from the PROMIS and ProtecT studies, which used TRUS. There are no equivalent data for other types of biopsy.</p> <p>The ranges given in the figures above reflect different definitions of <a href="#">clinically significant prostate cancer</a> (UCL1 and UCL2; see PROMIS publications).</p>	

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 MRI and biopsy 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 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

1.2.10 For people with a negative biopsy who have an MRI Likert score of 3 or more,

discuss the possibility of significant disease in an MDT meeting with a view to repeating the prostate biopsy. [2019]

1.2.11 For people who have a raised PSA and MRI Likert score of 1 or 2, and who have not had a prostate biopsy, repeat PSA test at 3 to 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]

1.2.12 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 to 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]

1.2.13 The PROGENSA PCA3 assay and the Prostate Health Index is not recommended in people having investigations for suspected prostate cancer who have had a negative or inconclusive prostate biopsy. [2019]

To find out why the committee made the 2019 recommendations on the MRI or biopsy being negative and how they might affect practice, see [rationale and impact](#).

## 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 to T2a
Intermediate risk	10–20 ng/ml	or	7	or	T2b
High risk <sup>1</sup>	>20 ng/ml	or	8–10	or	≥T2c

Abbreviation: PSA, prostate-specific antigen.

<sup>1</sup> 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**

<p>What are the treatment options for people with localised prostate cancer?</p>	<p>There are 3 options for treatment:</p> <ul style="list-style-type: none"> <li>• active surveillance<sup>a</sup></li> <li>• radical prostatectomy</li> <li>• radical radiotherapy.</li> </ul>
<p><b>Effects on survival and disease progression at 10 years</b></p>	
<p>What effect does each treatment option have on survival?</p>	<p>The evidence does not show a difference in the number of deaths from prostate cancer among people offered active surveillance, prostatectomy or radical radiotherapy.</p> <p>People who had not died of prostate cancer were:</p> <ul style="list-style-type: none"> <li>• 98 out of 100 patients offered active surveillance</li> <li>• 99 out of 100 patients offered radical prostatectomy</li> <li>• 99 out of 100 patients offered radical radiotherapy.</li> </ul>

<p>What effect does each treatment option have on disease progression<sup>b</sup>?</p>	<p>There is good evidence that both prostatectomy and radiotherapy reduce disease progression compared with active surveillance.</p> <p>Signs of disease progression were reported in:</p> <ul style="list-style-type: none"> <li>• 21 out of 100 patients offered active surveillance</li> <li>• 8 out of 100 patients offered radical prostatectomy</li> <li>• 8 out of 100 patients offered radical radiotherapy.</li> </ul>
<p>What effect does each treatment option have on the rate of development of distant metastases?</p>	<p>There is good evidence that both prostatectomy and radiotherapy reduce the rate of development of distant metastases compared with active surveillance.</p> <p>Distant metastases were developed in:</p> <ul style="list-style-type: none"> <li>• 8 out of 100 patients offered active surveillance</li> <li>• 3 out of 100 patients offered radical prostatectomy</li> <li>• 3 out of 100 patients offered radical radiotherapy.</li> </ul>
<p><b>Potential side effects of treatment</b></p>	
<p>What effect does each treatment option have on urinary function?</p>	<p>There is some evidence that urinary function is better for people offered active surveillance or radiotherapy than those offered prostatectomy.</p>

	<p>Problems with urinary continence:</p> <p>At 6 months, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 39 out of 100 patients offered active surveillance</li> <li>• 71 out of 100 patients offered radical prostatectomy</li> <li>• 38 out of 100 patients offered radical radiotherapy.</li> </ul> <p>At 6 years, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 50 out of 100 patients offered active surveillance</li> <li>• 69 out of 100 patients offered radical prostatectomy</li> <li>• 49 out of 100 patients offered radical radiotherapy.</li> </ul>
	<p>Moderate to severe urinary incontinence problems:</p> <p>At 6 months, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 4 out of 100 patients offered active surveillance</li> <li>• 19 out of 100 patients offered radical prostatectomy</li> <li>• 6 out of 100 patients offered radical radiotherapy.</li> </ul> <p>At 6 years, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 8 out of 100 patients offered active surveillance</li> <li>• 13 out of 100 patients offered radical prostatectomy</li> <li>• 5 out of 100 patients offered radical radiotherapy.</li> </ul>
<p>What effect does each treatment option have on erectile dysfunction?</p>	<p>There is some limited evidence that sexual function is better for people offered active surveillance or radiotherapy than those offered prostatectomy.</p>

	<p>Erectile dysfunction, moderate or severe problems:</p> <p>At 6 months, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 29 out of 100 patients offered active surveillance</li> <li>• 66 out of 100 patients offered radical prostatectomy</li> <li>• 48 out of 100 patients offered radical radiotherapy.</li> </ul> <p>At 6 years, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 40 out of 100 patients offered active surveillance</li> <li>• 50 out of 100 patients offered radical prostatectomy</li> <li>• 36 out of 100 patients offered radical radiotherapy.</li> </ul>
<p>What effect does each treatment option have on bowel function?</p>	<p>There is some evidence that bowel function is better for people offered active surveillance or prostatectomy than those offered radiotherapy in the short term.</p> <hr/> <p>Problems with faecal incontinence more than once per week:</p> <p>At 6 months, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 2 out of 100 patients offered active surveillance</li> <li>• 1 out of 100 patients offered radical prostatectomy</li> <li>• 5 out of 100 patients offered radical radiotherapy.</li> </ul> <p>At 6 years, problems were reported in:</p> <ul style="list-style-type: none"> <li>• 3 out of 100 patients offered active surveillance</li> <li>• 2 out of 100 patients offered radical prostatectomy</li> <li>• 4 out of 100 patients offered radical radiotherapy.</li> </ul>



	<p>Moderate to severe impact of bowel habits on quality of life:</p> <p>At 6 months, it was reported in:</p> <ul style="list-style-type: none"> <li>• 3 out of 100 patients offered active surveillance</li> <li>• 3 out of 100 patients offered radical prostatectomy</li> <li>• 10 out of 100 patients offered radical radiotherapy.</li> </ul> <p>At 6 years, it was reported in:</p> <ul style="list-style-type: none"> <li>• 4 out of 100 patients offered active surveillance</li> <li>• 3 out of 100 patients offered radical prostatectomy</li> <li>• 2 out of 100 patients offered radical radiotherapy.</li> </ul>
<p><sup>a</sup> 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.</p> <p><sup>b</sup> The trial defined disease progression as:</p> <ul style="list-style-type: none"> <li>• evidence of metastases or</li> <li>• diagnosis of clinical T3 or T4 disease or</li> <li>• need for long-term androgen deprivation therapy or</li> <li>• rectal fistula or the need for a urinary catheter owing to local tumour growth.</li> </ul> <p>Disease progression was suspected if there was:</p> <ul style="list-style-type: none"> <li>• any rise in prostate-specific antigen (PSA) &gt;20% between consecutive measures at any time during follow-up or</li> <li>• any rise in PSA level of 50% or greater in any 12-month period confirmed by repeat tests or</li> <li>• any indication of the appearance of symptomatic systemic disease.</li> </ul>	

To find out why the committee made the 2019 recommendations on active surveillance and how they might affect practice, see [rationale and impact](#).

## Multiparametric MRI and protocol for active surveillance

- 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 <sup>a</sup>
Year 1 of active surveillance	Every 3 to 4 months: measure prostate-specific antigen (PSA) <sup>b</sup> Throughout active surveillance: monitor PSA kinetics <sup>c</sup> At 12 months: digital rectal examination (DRE) <sup>d</sup> At 12 to 18 months: multiparametric MRI
Year 2 and every year thereafter until active surveillance ends	Every 6 months: measure PSA <sup>b</sup> Throughout active surveillance: monitor PSA kinetics <sup>c</sup> Every 12 months: DRE <sup>d</sup>
<p><sup>a</sup> If there is concern about clinical or PSA changes at any time during active surveillance, reassess with multiparametric MRI and/or re-biopsy.</p> <p><sup>b</sup> Could be carried out in primary care if there are agreed shared-care protocols and recall systems.</p> <p><sup>c</sup> Could include PSA density and velocity.</p> <p><sup>d</sup> Should be performed by a healthcare professional with expertise and confidence in performing DRE. In a large UK trial that informed this protocol, DREs were carried out by a urologist or a nurse specialist.</p>	

To find out why the committee made the 2019 recommendations on multiparametric MRI and the protocol for active surveillance and how they might affect practice, see [rationale and impact](#).

- 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]

### 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 1.3.9) for people who choose not to have immediate radical treatment.

Use [table 3](#) to discuss the benefits and harms of each option. [2019]

### 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]

To find out why the committee made the 2019 recommendations on active surveillance and how they might affect practice, see [rationale and impact](#).

### 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<sup>[1]</sup> who:

- 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 to 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<sup>2</sup> (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<sup>[2]</sup>. [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.
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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<sup>a</sup>, 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.
- 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 to 84 out of 100 people who did. However, this difference could be because of chance.

<p>What are the risks associated with docetaxel treatment?</p>	<p>A large UK randomised trial found that:</p> <ul style="list-style-type: none"> <li>• 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).</li> <li>• 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.</li> <li>• 8 out of 100 people who took docetaxel felt unusually weak or tired.</li> <li>• 8 out of 100 people who took docetaxel experienced gastrointestinal symptoms (including diarrhoea, abdominal pain, constipation and/or vomiting).</li> <li>• 5 out of 100 people who took docetaxel experienced respiratory symptoms (including breathlessness and/or chest infections).</li> <li>• 4 out of 100 people who took docetaxel experienced problems with their nervous systems (for example, numbness or weakness).</li> <li>• 1 out of 100 people who took docetaxel experienced problems with their nails that were serious enough to interfere with their daily lives.</li> </ul>
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<sup>a</sup> James ND, Sydes MR, Clarke NW et al. (2016) Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet* 387(10024): 1163–77.

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<sup>[3]</sup> 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<sup>[2]</sup>. [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]
- 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 for people with localised or locally advanced prostate cancer having radical treatment or on watchful waiting**

- 1.3.42 A urologist or specialist nurse should 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 A urologist or specialist nurse should 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 remote 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 only 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<sup>[4]</sup> (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*

- 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<sup>[5]</sup>. [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]
- 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<sup>[1]</sup> who do not have significant comorbidities as follows:
- start treatment within 12 weeks of starting androgen deprivation therapy and
  - use six 3-weekly cycles at a dose of 75 mg/m<sup>2</sup> (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]
- 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<sup>[6]</sup> (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 the NICE technology appraisal guidance on [docetaxel for the treatment of hormone-refractory metastatic prostate cancer](#).

- 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]\*
- 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]
- 1.5.18 For advice on treatments for metastatic hormone-relapsed prostate cancer previously treated with docetaxel, see the NICE technology appraisal guidance on:
- [abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen](#)
  - [enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen](#). [2019]

### Bone-targeted therapies

- 1.5.19 For people with hormone-relapsed metastatic prostate cancer, consider zoledronic acid to prevent or reduce skeletal-related events. [2019]
- 1.5.20 Consider oral or intravenous bisphosphonates for pain relief for people with hormone-relapsed metastatic prostate cancer when other treatments, including analgesics and palliative radiotherapy, have not given satisfactory pain relief. [2019]
- 1.5.21 For guidance on treatments for people with bone metastases from prostate



cancer, see the NICE technology appraisal guidance 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

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

## *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 prostate cancer

For the purpose of this guideline, this included any prostate cancer of Gleason score 7 and above.

### 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) prostate cancer

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 over 20 ng/ml, or Gleason score 8 to 10, or clinical stage T2c or more); T3b and T4, N0 prostate cancer; and any T, N1 prostate cancer.

## Localised prostate cancer

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

## Multiparametric MRI (mpMRI) of the prostate

An MRI study that incorporates anatomical and functional information about the prostate. The minimum functional information includes T2-weighted, diffusion-weighted imaging and dynamic contrast-enhanced imaging.

## Multiparametric MRI-influenced prostate biopsy

The information from the mpMRI scan taken before prostate biopsy is used to determine the best needle placement. In rare cases, the biopsy may be MRI-guided (the needle is inserted within the MRI machine). In most cases, the biopsy that follows the mpMRI will be ultrasound-guided, but the specific area(s) targeted will be predetermined by the mpMRI data.

## 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 biopsy

### *Template biopsy and mapping template biopsy*

A template biopsy is normally performed under a general anaesthetic, and involves taking transperineal core biopsies using a grid system. This might involve taking multiple cores from multiple sites, but usually 2 to 3 cores from 8 sites. A mapping template biopsy is where 20 sites are systematically sampled, with 2 or 3 cores per site, sometimes meaning over 50 core biopsies are taken.

### ***Local anaesthetic transperineal biopsy***

This is sampling 6 or 8 sites from the prostate using a transperineal route under local anaesthetic.

### ***Transrectal ultrasound guided biopsy (TRUS)***

This is where core biopsies of the prostate are taken via the rectum under local anaesthetic.

### ***Systematic versus MRI-influenced (targeted) biopsy***

The site for biopsy can be targeted based on mpMRI findings, or systematically but not guided by MRI. Most often there is a combination of both targeted and systematic MRI. The method used for the biopsy can be either transperineal or TRUS.

### **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.

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<sup>[1]</sup> At the time of publication (May 2019), 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.

<sup>[2]</sup> NICE interventional procedures guidance [IPG118](#), [IPG119](#) and [IPG145](#) evaluated the safety and efficacy of cryotherapy and high-intensity focused ultrasound for the treatment of prostate cancer. NICE guidelines provide guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS. Because there was a lack of evidence on quality-of-life benefits and long-term survival, these interventions are not recommended in this guideline.

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

<sup>[4]</sup> At the time of publication (May 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.

<sup>[5]</sup> At the time of publication (May 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.

<sup>[6]</sup> At the time of publication (May 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.

## 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 (including the role of digital rectal examination [DRE] and prostate-specific antigen [PSA] measures) 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?

## 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.

### *MRI and biopsy*

Recommendations [1.2.1 to 1.2.5](#)

### Why the committee made the recommendations

The committee saw no new evidence to suggest that 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. The committee did not see any evidence that allowed them to clearly differentiate between transperineal (non-mapping) and transrectal biopsy, so it agreed to refer to 'prostate biopsy' throughout the recommendations.

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 need less 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](#).

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## *If the MRI or biopsy is negative*

Recommendations [1.2.10](#) 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 committee recommended that people with a Likert 3 score should be discussed at a multidisciplinary team (MDT) meeting. It made the recommendation because these cases can be difficult to deal with. Scoring of scans may fluctuate by 20% between raters and therefore a discussion in an MDT is warranted. The committee noted that this does not necessarily imply the full cancer MDT, but is subject to local arrangement.

The follow-up strategies recommended for primary care are based on standard prostate-specific antigen (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 previous guidance on PCA3 assay and the Prostate Health Index (DG17) are 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 (TRUS) prostate biopsy, and therefore the committee did not recommend use of these technologies.

The committee identified a gap in the evidence for the performance of transperineal route (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](#).

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## ***Active surveillance or radical treatment***

Recommendations [1.3.7](#) and [1.3.10 to 1.3.14](#)

### **Why the committee made the recommendations**

#### ***Low- to intermediate-risk localised prostate cancer***

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.

Because 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.

#### ***High-risk localised prostate cancer***

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](#).

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## *Multiparametric MRI for active surveillance*

Recommendations [1.3.8](#) and [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 PSA-derived measures to monitor, and the use of multiparametric MRI to identify, clinically significant prostate cancer. The committee kept the use of digital rectal examination in this population because they did not see any new evidence to not recommend it for this group. In addition, digital rectal examination was part of the protocol in one of the studies included in the evidence review.

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, including the use of digital rectal examination.

### **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, because 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: identifying prostate cancer clinical progression in people with low- to intermediate-risk cancer](#).

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## ***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. The committee also agreed that as most centres do not offer both types of brachytherapy, the new advice gives clinicians a choice of either high-dose or low-dose rate 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 (high-dose rate or low-dose rate), 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: radical radiotherapy](#).

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## *Docetaxel chemotherapy*

Recommendations [1.3.24](#) and [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 1.3.24 and 1.3.25](#)

[Return to recommendation 1.5.6](#)

## *Follow-up*

Recommendations [1.3.42 to 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. Because 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](#).

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## ***Bone-targeted therapies (bisphosphonates)***

Recommendations [1.5.19](#) to [1.5.21](#)

### **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](#).

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## 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 to 2014). Out of every 10 prostate cancer cases, 4 are only diagnosed at a late stage in England (2014) and Northern Ireland (2010 to 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 to 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 to 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

You can see everything NICE says on prostate cancer in our interactive flowchart on [prostate cancer](#).

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

For full details of the evidence and the guideline committee's discussions, see the [evidence reviews](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources](#) to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see [resources to help you put guidance into practice](#).

## Update information

**May 2019:** We have reviewed the evidence and made new recommendations on diagnosis, treatment and monitoring for people with prostate cancer. These recommendations are marked [2019].

Recommendations marked [2008] or [2014] last had an evidence review in 2008 or 2014, respectively. Changes made to recommendations at the last review that did not come from a new evidence review are marked [2008, amended 2014]. In some cases minor changes have been made to the wording to bring the language and style up to date, without changing the meaning.

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## Accreditation

