

Prostate Cancer Information Booklet

Contents

Facts, Tests and Diagnosis

1. The Prostate and Prostate Cancer	2
2. Your GP Consultation and the PSA Blood Test	4
3. Further Tests for Prostate Cancer	7
4. The Gleason Score	9
5. Staging of Prostate Cancer	10
6. Dealing with your Diagnosis	11
7. Questions You May Wish to Ask	13

Treatment Options

1. Summary of Treatment Options	15
2. Active Surveillance	17
3. Watchful Waiting	18
4. Surgery	19
5. External Beam Radiotherapy	22
6. Brachytherapy	25
7. High Intensity Focused Ultrasound (HIFU)	28
8. Cryotherapy	29
9. Hormonal Therapies	30
10. When Hormones Fail	32
11. Chemotherapy	33
12. A Treatment Path for Advanced Prostate Cancer	35

Side Effects

1. Sexual Problems	36
2. Problems with Continence	37
3. Long-term Severe Incontinence	38
4. Bone Health	39

Additional Information

1. The Clinical Nurse Specialist	40
2. Diet and Lifestyle	41
3. Clinical Trials	44
4. Some New Developments	46
6. Glossary of Terms and Abbreviations	48

The information contained in this booklet should not be taken as medical advice, which should always be obtained from qualified medical practitioners.

1. The Prostate and Prostate Cancer

What is the prostate?

The prostate is a sex gland found only in men. It lies at the base of the bladder, surrounding the tube called the urethra which carries urine and semen to the end of the penis. It is normally about the size of a walnut. A healthy prostate is essential to full sexual function. As men age, the gland becomes enlarged and can squeeze the urethra, giving a reduced urine flow. This can lead to problems with the prostate, more common in older men.

In a recent survey of 3,500 men, 54% of men didn't know where the prostate was; 92% were clueless about its role, and 17% didn't even know they had a prostate.



Prostate cancer: who is at risk?

By the age of 60 many men will have developed some evidence of cancer in the prostate. Once regarded as the curse of older men, younger men are being diagnosed in their 50s, and occasionally in their 40s and even late 30s.

Men of **African-Caribbean origin** and those with a **family history** of the disease are especially at risk. A rare variant of prostate cancer is caused by a faulty BRCA gene, so a strong family history of **breast** or **prostate cancer**, particularly at a young age, may therefore be a warning signal.

'Pussycats and tigers'

Evidence of cancer in the prostate need not necessarily be a cause for immediate concern, as many cancers grow so slowly that they may never develop to be life-threatening.

Prostate cancer has now been shown to have several variants. Research is progressing to predict more accurately the different types, and to identify which cancers are slow-growing and which are aggressive.

Most prostate cancers are found in the outer part of the prostate, called the **peripheral zone**. The slow-growing cancers, the ‘pussy-cats’, may stay here, unnoticed and indolent, for many years. These may only require careful monitoring, without necessarily needing any radical treatment at all. The more aggressive ‘tigers’, however, have the potential to spread outside the prostate, sometimes quite rapidly, when symptoms may become noticeable. These will need active treatment, ideally before the cancer starts to spread outside the prostate and invade other areas of the body.

Some facts

- Prostate Cancer is the most common cancer in men
- Each year in the UK over 47,000 men are diagnosed with prostate cancer and about 11,000 die of it
- If the cancer is confined within the prostate, it is generally curable, so early detection may prevent death from prostate cancer
- Urinary symptoms (e.g. difficulty in passing urine or frequent night-time visits) may indicate cancer, but could also be caused by an enlarged prostate or an infection
- Prostate cancer in its early stages does not normally have any symptoms
- Early stage disease offers a much wider choice of treatment options – more than for any other cancer
- Once the cancer begins to spread outside the prostate, there are fewer options for treatment, though there may still be possibilities for a cure
- If the cancer has spread to other organs or the bones, the disease can only be controlled.

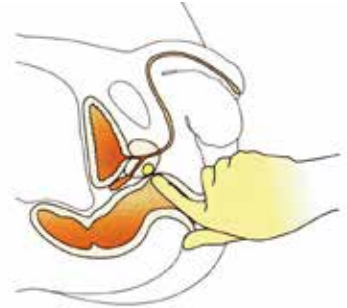
What causes prostate cancer?

Although the causes are not yet fully known, there is clear evidence of links to diet and lifestyle. Lack of exercise, obesity, and low exposure to sunlight can also be contributory factors. There are also genetic links, so it is important for every man to be aware of the disease, and to see his GP if he has concerns.

2. Your GP consultation and the PSA Test

If you have concerns

You should visit your GP. At your appointment the doctor may give you a **Digital Rectal Examination** (or DRE). Although not a completely reliable test for prostate cancer, it is a simple way that a doctor can check your prostate. It is done by feeling it using a gloved finger in the back passage. This only takes a few seconds and generally may cause only a little discomfort. If any abnormalities are felt, it may be a sign of a problem. A simple blood test called a PSA test may also be suggested.



The DRE examination

What is the PSA test?

This is a blood test that will give you and your GP an indication of a possible problem with the prostate. The PSA blood test is not primarily a test for prostate cancer but is simply a measure of the health of your prostate. At present it is the best simple test we have.

PSA measures the level of **Prostate Specific Antigen**, a protein found in the prostate secreted mainly in the blood. The blood sample is normally taken at the GP surgery and is then sent away for analysis and comes back within a week.

Most men (typically two out of three) who have raised PSA levels may turn out not to have prostate cancer. However, about one sixth of men with a 'normal' PSA result may actually have some evidence of prostate cancer.

Pros and Cons of knowing your PSA level

Your GP should also tell you the benefits and limitations of the test. If, after considering these, you wish to have the test and you decide to go ahead, it is your right to have the test. This is laid down in The Prostate Cancer Risk Management Programme (2016). It states:

“The PSA test is available free to any well man aged 50 and over who requests it”.

It also says:

“The man’s personal preferences are an important factor in the decision”.

If you decide to have a PSA test, you must ask your GP for it; you are entitled to it. Here are some simple facts to help you decide:

- It may reassure you
- It can be an early indication of prostate problems
- It can find cancers earlier than is possible by a DRE alone
- It may lead to treatment at an early stage and provide a cure.

But:

- A raised PSA level may lead to invasive tests when you have no cancer
- A mildly elevated PSA could lead to a diagnosis of prostate cancer which may be harmless and never need treatment.

Note: Be aware that PSA readings may be raised if the blood sample is taken after vigorous exercise, if ejaculation has occurred in the previous 48 hours, or shortly after a DRE.

What does it tell me about my prostate?

Sometimes a raised PSA level can be a sign of prostate cancer. It can also often point to something less serious, such as an inflamed or infected prostate (prostatitis), or an enlargement of the prostate that often comes as men age. This is called **Benign Prostatic Hyperplasia**, or BPH (sometimes now called BPE, standing for benign prostate enlargement).

What is a normal reading?

The older you are, the higher your PSA level is likely to be (whether or not you have prostate cancer), as PSA naturally seeps into the bloodstream with age. It is measured in nanograms per millilitre (ng/mL)*, and can range from less than 1ng/mL to readings in the 1000s. Readings from 1 to 4 (depending on age) are generally normal. A single reading is of little value, unless it is high (say over 10ng/mL).

What if my PSA is higher than normal?

If the reading is marginal (say between 3 and 5 ng/mL), a repeat test should be requested, normally after a few weeks. This is because the rate at which the PSA level may be increasing (called **PSA velocity** and **PSA doubling time**) can be a more reliable indicator of the presence of prostate cancer than a one-off test result. Most leading urologists recommend that all men over 50 or at special risk know and monitor their PSA regularly, and action should be taken when any substantial increase is noted. Any increase above 0.5 – 0.75ng/mL in one year should be a warning signal. The chart overleaf gives the generally accepted guidelines.

* Note: PSA levels are sometimes reported as µg/L (microgrammes per litre), but the resulting number is exactly the same.

Age	Normal	Marginal	High
Under 50	less than 2.0	2.0 - 3.0	over 3.0
Under 60	less than 3.0	3.0 - 4.0	over 4.0
Under 70	less than 4.0	4.0 - 5.0	over 5.0
70 and over	less than 5.0	5.0 - 6.0	over 6.0

You may wish to visit www.cancerscreening.nhs.uk/prostate/prostate-booklet-text.pdf, which gives further information on the benefits and disadvantages of the PSA test.

A particularly high reading (i.e. above 10ng/mL) is more likely to be an indication of the presence of cancer in the prostate rather than other causes, such as prostate enlargement or prostate infection.

If the PSA reading is high, if doubling time is abnormal or there are other indications, your GP should refer you to a urologist for further tests in order to determine if cancer is present. These tests are outlined in the next section.

Other tests your GP could arrange

Free-to-Total PSA (or Free and Bound PSA Ratio, or fPSA)

PSA may be free (not bound to a protein), or bound. Research indicates that if *more than* 18% (i.e. 1.8) of PSA is free, there is *less* chance of having a high grade prostate cancer. So the lower the percentage, the higher the risk. Currently it is not widely used, but knowing this PSA ratio may help avoid further unnecessary invasive tests.

PCA3

This is a urine test that is obtained from a sample, taken immediately after the doctor has massaged your prostate, which releases prostate cells into the urine. It claims higher accuracy at diagnosing the disease and its degree of aggressiveness. The higher the score, the greater likelihood of prostate cancer. Currently this test is only available privately, as NICE has concluded that it is insufficiently accurate.

Research is continuing to find other protein or genetic markers that can give a more precise diagnosis of prostate cancer and its aggressiveness. These need to be rigorously tested on a large number of men before they become nationally available. Details of some may be found in the Trials section on page 44.

3. Further tests for Prostate Cancer

MRI scan

Following referral for suspected prostate cancer, you will be recommended for various tests, the first of which should now be a non-invasive MRI scan. A **magnetic resonance imaging** scan creates a cross-section of the soft tissues around the selected part of the body by using magnetic fields. The machines for these scans use a tunnel in which the body is located. Some may find this a little claustrophobic, but the head usually remains clear of the tunnel, so that the patient can see some daylight. The machine can seem rather noisy and the patient is asked to keep as still as possible during the process. It is often possible to speak to the radiographer through a microphone/headphone system. The procedure is quite harmless.

In the past the test has normally been done after a biopsy as a further check to see whether there is any spread outside the prostate. Currently clinicians use a **multi-parametric MRI** scan of the prostate area before a biopsy is considered. Significant tumours can be detected more accurately, therefore allowing any subsequent biopsy to be guided more precisely. If no significant tumour is found on the MRI, then there may be no need for an immediate biopsy.

Special 3-Tesla MRI machines (with a more powerful magnetic field) are now in use in several hospitals, which can detect a tumour in much greater detail. These will become the gold standard in the future, though it will be some while before they come into use in many hospitals.

Recent advances in MRI scanning techniques and the introduction of advanced software has led to greater accuracy in identifying the position of any tumour and its potential aggressiveness.

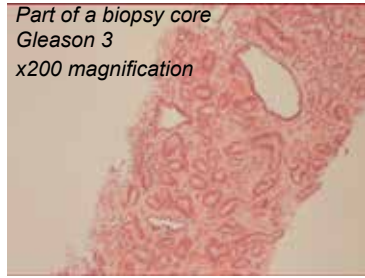
TRUS Biopsy

Biopsy is a procedure in which a number of small samples of an organ are extracted and examined under a microscope to identify the presence or not of cancer. A **trans-rectal ultrasound** (TRUS) and biopsy of the prostate is done at the hospital as an out-patient. The test itself normally takes no longer than about ten minutes, although it may be necessary to remain in hospital for a little longer. A local anaesthetic is given, but some men can still find the procedure uncomfortable.

A lubricated ultrasound probe is first inserted into the back passage in order to provide a 'map' of the prostate. The doctor will then pass a fine needle through the rectal wall into the prostate to extract 8–12 samples of tissue cores. These are sent for examination to a pathologist, who will then determine whether any cancerous tissue



is present. Antibiotics are given prior to and immediately following the procedure. However, with any biopsies taken through the rectum, there is a risk of infection. There may be a little blood in the urine and/or the back passage for up to three weeks after a biopsy, and blood in the semen for 4–6 weeks. This is not a cause for concern and is normal, but any other symptoms should be referred immediately to your GP or hospital.



As a biopsy takes tiny sample cores from the prostate, it is possible that the needle may miss the cancer. The greater the number of samples taken, the more likelihood of detecting cancer. Greater sampling, however, can lead to increased risk of complications. However, new techniques (see Fusion Guided Biopsy below) mean that better accuracy is now possible.

Template (or Perineal) Biopsy

Because a standard biopsy may miss finding smaller cancers, there is a growing shift towards using a **template biopsy**, a more precise test which can sample the whole prostate. This should be done when suspicions are high but normal biopsy results are inconclusive. Many urologists now prefer to recommend this method to their patients. The procedure is performed under a general anaesthetic. A grid will be placed over the perineal area (between the anus and scrotum) through which many more needles can be inserted to take samples. As well as being more accurate, a template biopsy is considered safer, as there is less risk of infections from untreatable bacteria than from a standard TRUS biopsy.

Fusion Guided Biopsy

Recently new software has been devised that ‘fuses’ the MRI images with the real-time ultra-sound probe. The MRI images are overlaid onto the ultrasound image which enables the urologist doing the procedure to pinpoint the suspicious areas with much greater accuracy. Although currently under development, it may lead to less samples being taken and, for those who may need further biopsies, less occasions where a repeat biopsy may be needed.

Bone Scan

This test is to show whether the disease has spread to the bones. A small amount of low dose radio-active material is injected into the arm about three hours before the scan. The scan takes about 45 minutes, and images of any bones showing the disease will show up on the scan. A bone scan will not usually be done unless the PSA score is greater than 10 and MRI and biopsy samples indicate a high-grade cancer. It is painless and quite harmless.

These tests are not normally part of the standard diagnosis for prostate cancer, but may sometimes be recommended

Bone density test

A **bone mineral density** test (BMD), sometimes called a **DEXA** scan (dual energy X-ray absorptiometry) measures bone mass, helps determine bone strength, and can predict the risk of future fracture. It may be requested through the GP before long-term hormone treatment in order to establish a baseline value, and repeated during the treatment course.

Cystoscopy

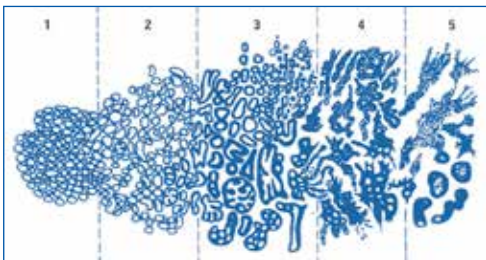
This is an examination of the bladder by passing a thin flexible tube through the urethra. It is occasionally recommended to eliminate any possibility of bladder disease.

4. The Gleason Score

The Gleason Score

A **Gleason score** is given after a pathologist has examined under a microscope cancerous tissue obtained from the needle biopsy. The cells identified are given a grade number from 1 to 5, depending on the abnormality of the cells, 1 being the lowest, 5 the highest. The grades of the two most common patterns are added together to give a *score* from 2 to 10. The higher the score, the more aggressive and fast-growing the cancer.

- A Gleason score of 2 – 5 is now rarely reported
- A Gleason score of 6 (cells are well differentiated) is ‘favourable’
- A Gleason score of 7 (cells are moderately differentiated) is ‘average’
- A Gleason score of 8 – 10 (cells are poorly differentiated) is ‘adverse’.



*Diagram of Gleason patterns grades 1-5.
Grade 5 is the most aggressive.*

The consultant will give you a total score out of 10, which should be split down as two numbers out of 5: for example, 4+3. The first number is the predominant grade, so a score of 4+3=7, for example, is likely to prove slightly more aggressive than a score of 3+4=7.

5. Staging of Prostate Cancer

The current system of staging prostate cancer is known as the TNM system (standing for 'Tumour/Nodes/Metastasis'). The T stage of the disease refers to the form of the primary tumour in the prostate. This is the most relevant; it is described in full below.

Right shows stages T1 to T4, where the tumour (in yellow) develops from a small size to one where it has spread outside the prostate (in grey) to other structures.

T Stage disease

T1: The doctor is unable to feel the tumour or see it with imaging

T1a: Cancer is found incidentally during an operation for benign prostate enlargement (called a transurethral resection of the prostate, or TURP) and is present in less than 5% of the tissue removed.

T1b: Cancer is found after a TURP and is present in more than 5%.

T1c: Cancer is found by needle biopsy.

T2: Can feel that the tumour seems to be confined to the prostate

T2a: Cancer is found in one half or less of only one side of the prostate.

T2b: Cancer is found in more than half of one side of the prostate.

T2c: Cancer is found in both sides of the prostate.

T3: Cancer has begun to spread outside the prostate

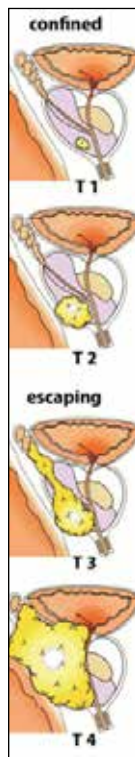
T3a: Cancer extends outside the prostate but not to the seminal vesicles.

T3b: Cancer has spread to the seminal vesicles.

T4: Cancer has spread to other tissues next to the prostate

T4a: Cancer invades bladder neck, sphincter, or rectum.

T4b: Tumour has invaded the levator muscles and/or fixed to the pelvic wall.



N and M Stages

N Stage disease refers to the **pelvic lymph Nodes** near the prostate. It is rated from 0 to 3, depending on the presence and extent of the spread, N1 being up to 2cm, to N3 being greater than 5 cm.

M Stage disease refers to the **Metastasis**, i.e. the degree to which the prostate cancer has travelled out of the immediate area of the prostate to other organs of the body. It is rated 0, M1a, M1b or M1c, depending on whether the disease has spread to the bones or other distant sites.

Your Risk Category

The NICE Guidelines for Prostate Cancer (2014) give three categories of risk: low risk, intermediate risk and high risk, depending on a combination of PSA, Gleason score and T stage.

Knowing your risk category will help decide the most appropriate treatment for you. The table below will help.

Risk	PSA		Gleason		T stage
Low	<10	AND	<6	AND	T1 - T2a
Intermediate	10 - 20	OR	7	OR	T2b - T2c
High	>20	OR	8 - 10	OR	T3 - T4

6. Dealing with Your Diagnosis

When you are told you have cancer, very often it becomes a life-changing experience for you, your family and close friends. There is a lot to come to terms with and the news can be a great shock and throw you into confusion. It is not uncommon to have feelings of anger, sadness, guilt, feeling alone, loss of confidence and control, but this usually gets easier as the shock wears off and the situation becomes more real to you. There is no ‘right’ way of reacting to the diagnosis; everyone reacts in their own way.

Fear of the future

Uncertainty about the future is one of the hardest feelings to deal with, and you could feel irritable, angry and frightened. It is normal to worry about dying if you’ve been given a cancer diagnosis. Many people find it helps to find out as much as possible about prostate cancer and the ‘stage’ that you have been diagnosed with and what is likely to happen. Not everyone feels this way, but it is worth discussing this with your doctors or nurse specialist, as they know your situation and treatment options. You could write down some questions listed in the next pages before you next see your consultant.

Remember that not all prostate cancers need be treated. Many are so slow growing that they may never cause a problem in your lifetime. Only the more aggressive types need active treatment.

Helping yourself

Think positively. Look at your treatment options, along with the side effects, so you know what to expect. They are all detailed in this booklet. Be as active as you can; the fitter you are the better your body will be able to cope with treatment. Think more about your diet; this is a way that you can make a difference in fighting the disease. Find someone to talk to about prostate cancer. It could be someone close to you, a counsellor, someone on your medical team or someone you may meet at a support group meeting. It is always useful to offload what is going on in your head and find answers. Try to manage stress by learning techniques to relax.

Further support for yourself and/or your partner. If you or your partner find yourself badly effected by the stresses of your cancer, take action and seek further support from your GP, your local mental health line or Macmillan.

After treatment

Many men survive prostate cancer that has been diagnosed in the early stages, but for some the treatment can be hard on your body and it can take some time before you feel fit again. Some men have side effects that gradually improve, while for others these can be ongoing or delayed. Not everyone experiences side effects, but some may experience difficulty sleeping, feeling weaker and more tired, lost or gained weight, stiffness in muscles or joints.

If you are worried about erectile dysfunction or urinary problems following treatment, read the sections on pages 36-37. It may help to put your mind at ease. There are on-line communities or forums for prostate cancer, where men can share their treatment experience and ask questions of others. These can be an effective way dealing with prostate cancer together.

Local support groups also have meetings where men get together to share their experiences of treatment and living with the disease. Here you can often offload worries and know that someone within the group understands what you are going through, or just listening to other men talking about their treatment journey can help.

On-going treatment

Some men will be diagnosed with advanced prostate cancer and be put on hormone therapy. Other men, in the early stages of localised cancer, will be put on active surveillance. In both cases the treatment can be long-term and on-going. If you are on hormone therapy, in some hospitals there is a specialist nurse who can do an holistic assessment and help prescribe or refer you to other agencies that can help.

If you are on **Active Surveillance**, some men find this to be quite stressful and are so concerned at having cancer in the body without having radical treatment to remove it that they opt for surgery or radiotherapy with all the possible side effects those treatments carry. The best way of avoiding anxiety over whether you should have radical treatment or stay on active surveillance is to educate yourself fully on the facts about prostate cancer. You are then able to make a logical decision on what is right for you. Reading this booklet fully is one way of doing that.

Lifestyle changes

Living a healthy lifestyle can help your body recover more quickly. It can also reduce the risk of other illnesses such as heart disease or strokes. Some men will want to change entirely the way they were living before diagnosis. You may

have a stressful job that allows the options of working part-time or taking early retirement. You have control over what you eat and a well-balanced diet has been proven to help fight many diseases. Evidence is now emerging that shows exercise can reduce fatigue, improve mood, psychological wellbeing and body composition. Adopting lifestyle changes has been proven to reduce the rate of PSA progression in patients on active surveillance. See the section on ‘Diet and Lifestyle’.

REMEMBER: Take control of your cancer: don't let it control you.

7. Questions to Ask

Many men and their partners often find it difficult to know the kind of questions to ask their consultant or nurse specialist. We have listed some that we find are commonly in the minds of the newly diagnosed. We hope that the list overleaf will help you to realise the importance of asking for the information you want to know, and will give you the confidence to ask any that are important to you.

Work in partnership with your consultant

Let your consultant know if you want to work in partnership with him or her and be involved in the decision making; otherwise he or she may be unsure of how much involvement you want. The new NHS reforms clearly emphasise ‘**No decision about me without me**’ and strongly feature patient choice in where you want to be treated.

Your consultant should refer you to a **nurse specialist** (your keyworker), who should have more time to go into greater depth of detail about treatments and side effects. You should be given written material about the details of the most appropriate treatments for you before you leave. If you are not given any leaflets or booklets, you should ask for these. You cannot be expected to remember all you were told.

Try to list your questions before you go and take them with you, or you may wish to photocopy the page overleaf. Write down the answers, so that you can refer to them at a later date. Try to take your partner or a friend with you to the consultation. It often helps. You may want to record the consultation; this is often possible with the agreement of your consultant.

Hospitals now adopt a **multi-disciplinary team** (MDT) approach to managing your treatment. A team would typically consist of a urologist, an oncologist, a pathologist, a radiologist and a urology nurse (see Glossary on page 48). The team meets regularly to discuss all their patients. Each patient's treatment is considered and approved by a range of senior clinicians, not just the doctor who happens to be facing the patient.

Some questions for your consultant

1. What is my Gleason score, and how is it split? (see p. 9)
2. What T stage is my cancer? (p. 10)
3. Is my PSA increasing abnormally? (p. 5)
4. Can you tell me whether the cancer is fast or slow growing? (p. 3)
5. As far as you know, is the cancer confined to my prostate?
6. What further tests do I need, and when will I have them? (pp. 8-9)
7. Is there a team and a Nurse Specialist managing my case? (p. 40)
8. What is the long-term situation for me? (You may prefer not to ask).

Treatment options and some general questions

1. What treatments are available for my type of cancer? (pp. 15-16)
2. What treatments would you recommend, and why?
3. What are the potential risks and benefits from these treatments?
4. Are any treatment options available elsewhere, which are not here?
5. If so, would this treatment be funded if I had to go elsewhere?
6. How quickly do I need to decide on treatment?
7. What are the possible side effects from the treatments? (pp. 36-39)
8. Can anything be done to ease the side effects?

Three important questions for surgery

1. What type of surgery will I have – open, keyhole or robotic? (p. 21)
2. How many operations like this have you done, and what are your results?
3. Is it possible to have nerve-sparing surgery? If not, why not? (p. 19)

Three important questions for radiotherapy

1. Will I be able to have IMRT or IGRT radiotherapy? (p. 23)
2. What dosage will I receive, and over how many weeks? (p. 24)
3. Do I have hormone therapy treatment as well? If not, why not? (p. 30)

Three important questions for hormone treatment

1. Do I need to have a bone density scan? (p. 39)
2. Will you recommend intermittent hormone therapy if necessary? (p. 31)
3. What drugs can I have to ease any side effects?

Clinical Trials

1. Are there any clinical trials or research being done for my stage?
2. Would I be a suitable candidate? (pp. 45-46)

Support

1. Can I see my oncologist/urologist and specialist nurse? (p. 40)
2. Can I do anything to help myself with diet and supplements? (p. 41)
3. Can you give me details of any local support groups? (see inside back cover)

1. Summary of Treatment Options

You will have been diagnosed with one of three categories of prostate cancer:

Localised (or early stage) cancer is where the cancer has been found to be enclosed within the prostate; this will be most likely be at Stage T1 or T2. Localised disease has the most options available for a possible cure.

Locally advanced cancer is where the cancer has been found to have begun to spread outside the prostate but not to other organs. The treatment options are more limited, but the disease may still be potentially curable.

Advanced cancer will have spread to other organs of the body (i.e. will be at an M1 stage – see p. 10). In this situation it is only possible to treat the cancer with drugs designed to delay the progression of the disease.

Where options are available, you may not always be informed of all the possible choices, nor will you necessarily be recommended a particular treatment. It is therefore not always easy to make a decision as to which treatment to choose. Some may not be available at your local hospital and you may have to travel to a centre of expertise. Others are not currently approved by NICE and may only be available privately. Some treatments may effectively be used in combination (e.g. hormone therapy before surgery or radiotherapy in order to shrink the prostate).

You should be aware that all treatments have consequences and side effects, which are listed under each treatment in this section, with more information on pages 36-39. After treatment, regular PSA readings are taken in order to check its success. Any possible cure may not be confirmed for several years.

In the summary below, treatments suitable for Localised prostate cancer are marked (L), Locally advanced (LA) and Advanced (A).

Active Surveillance (L): pro-active monitoring of early-stage cancer.

Watchful Waiting (L, LA, A): regular check-ups, leading to hormone treatments or palliative care where necessary.

Surgery (L): an operation to remove the whole prostate.

External Beam Radiotherapy (L, LA): using radiation to destroy the cancer.

Low-dose rate Brachytherapy (L): the implantation of radio-active seeds.

High-dose rate Brachytherapy (L, LA): the insertion of radiated plastic rods, removed after treatment.

HIFU (L): the cancer cells are heated and destroyed by ultrasound.

Cryotherapy (or cryosurgery) (LA): the freezing of cells in the prostate.

Hormone Treatments (L, LA, A): drugs used either where the cancer has spread outside the prostate (LA, A), or prior to curative treatments (L).

Chemotherapy (A): drugs used with or after hormone therapies have failed.

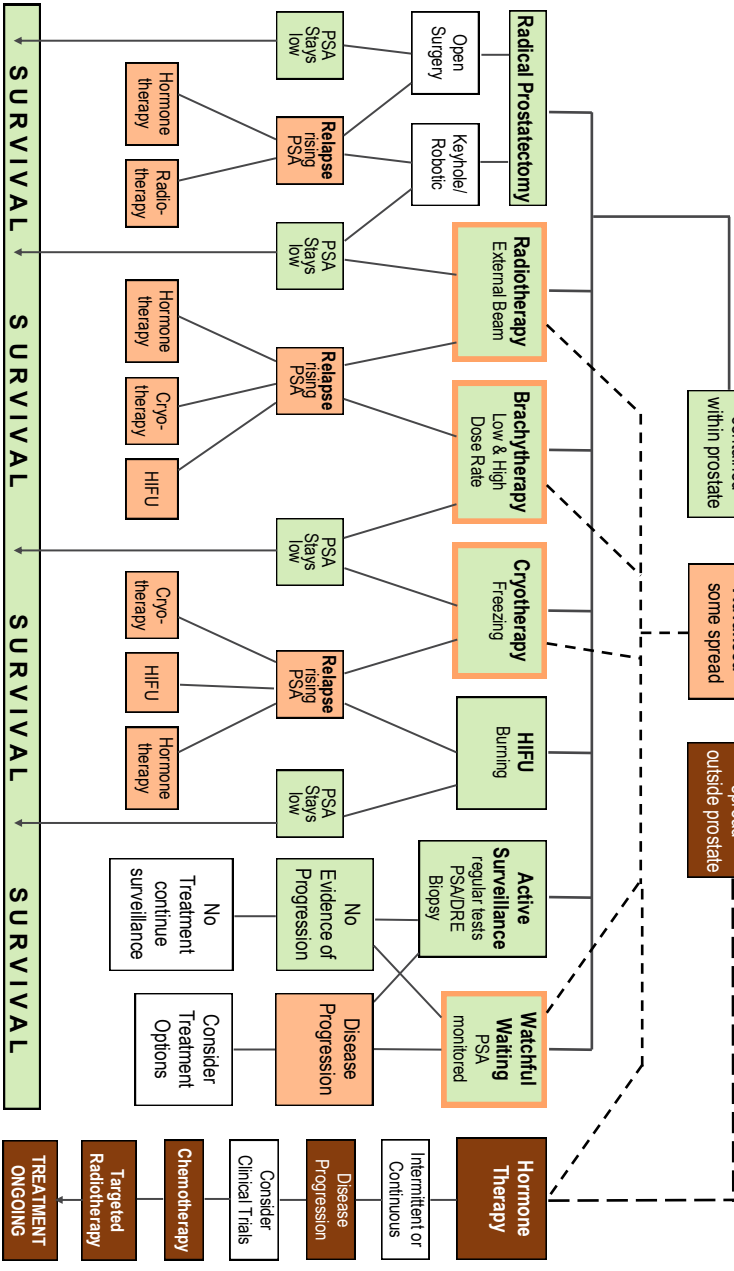
Flow chart of Treatment Options

Your patient profile will determine which treatment is best for you

DIAGNOSIS



* See page 47 for more detail on options for Advanced prostate cancer



2. Active Surveillance

Some men with localised (early stage) prostate cancer may not need any active treatment. The cancer will grow so slowly, if at all, that the man will live out his natural span and die of something else before the cancer causes any symptoms. Results suggest that many men on Active Surveillance will never need to be treated for their prostate cancer. Unfortunately, not all early prostate cancers behave like this. Some may progress at a significant rate, so that over a period of years the cancer will grow sufficiently to cause symptoms, and may then spread to other parts of the body and become life-threatening.

Active Surveillance (sometimes called **Active Monitoring**) is an alternative to immediate treatment. It is now the first-line approach for men found to have low grade prostate cancer. It is a pro-active method which monitors men with early prostate cancer who do not need immediate curative treatment, so as to spare them the side-effects that may be caused by a treatment that may later prove to have been unnecessary.

Men on active surveillance are closely monitored by their consultant. They would typically have an initial multi-parametric MRI scan, repeated every 1-2 years, and an annual PSA blood test. A repeat biopsy may only be needed if the MRI scan reveals any significant change. Some doctors now believe that the **Free-to-Total PSA Ratio** (see p. 6) is also an additional monitoring tool. Those cases that show signs of tumour progression will be advised to receive curative treatment, normally with surgery, radiotherapy or brachytherapy, dependent on age and other factors.

Advantages and disadvantages

- Active Surveillance may avoid unnecessary treatment, with its resultant side effects
- MRI scans now reduce any risks associated with repeat TRUS biopsies
- It may also give the opportunity for a change of diet and lifestyle which may help in keeping the cancer under control.

But:

- It can create on-going worry about 'having cancer' and 'doing nothing'
- It could happen that the 'window of opportunity' for curative treatment may be missed, should the cancer unexpectedly become more aggressive.

A change of lifestyle?

While on Active Surveillance, you may like to consider a change of diet, taking nutritional advice from an NHS Macmillan dietitian or a trained nutritionist, or an exercise programme, as it has been shown that regular exercise can help to control the rate at which cancers develop (see pp. 41-42).

Monitoring your PSA

PSA velocity (the rate at which the PSA increases) and **doubling time** (the period over which the PSA number doubles), together with other factors (e.g. MRIs), play an important part in any Active Surveillance programme, so it is important that you keep a careful record of your PSA results. You have the right, in co-operation with your consultant, to opt out of Active Surveillance and be treated at any stage.

3. Watchful Waiting

Watchful Waiting is usually offered either to older men, where the disease may grow so slowly that it may not affect the person's quality of life, or to those whose health may not allow them to undergo a treatment such as radiotherapy or surgery. Unlike Active Surveillance, the aim of any treatment will be to delay progression of the disease or to be palliative, i.e. not intended to cure the disease.

Watchful Waiting will involve attending an out-patients' clinic once or twice a year for regular PSA tests and possibly a digital rectal examination (DRE), where the doctor inserts a gloved finger into the rectum to feel the prostate. Should the cancer progress, the most likely treatment option would be hormone therapy (see p. 30), depending on any rise in PSA levels.

Watchful Waiting, however, does not necessarily mean doing nothing. You may like to consider:

- **changing your diet**
- **nutritional supplements**
- **an exercise programme**

These may help in slowing the growth of the cancer cells. Your NHS Macmillan dietician can advise you on diet and nutrition. You should, of course, consult your doctor before starting any new exercise regime.

Monitoring your PSA

PSA velocity (the rate at which the PSA increases) and **doubling time**, together with other factors, play an important part in Watchful Waiting. It is therefore important that you keep a careful record of your PSA results.

4. Surgery

A surgical operation to remove the whole prostate gland together with the seminal vesicles is called a **radical prostatectomy**. The prostate is normally taken out through the abdomen (called the 'retro-pubic approach'). For patients with intermediate grade prostate cancer the pelvic lymph nodes (part of the immune system) may be removed. For high grade cancers, they should be removed. Radical prostatectomy is normally offered to those with localised cancer, a life expectancy of 10 or more years, and where the man's age and general health allow. In some cases surgery may be considered for locally advanced cancer.

Nerve-sparing surgery, which aims to preserve erectile function, is normally undertaken where possible. This does not necessarily ensure that erections can be subsequently achieved, as the nerve bundles lie extremely close to the prostate.

Surgery is now only performed in larger specialist cancer centres, where a greater number of operations are done. **The greater the experience of the surgeon, the greater the likelihood of a satisfactory result.**

Advantages and disadvantages of surgery

- The cancer may well be completely eradicated
- You will know afterwards exactly how far the cancer had developed
- It will get rid of any age-related benign enlargement of the prostate (BPH)
- Follow-up is easier than other options
- Radiotherapy and/or hormone treatments can follow, if needed.

But:

- All major surgery has risks. The older you are, the greater the risk
- As with most radical prostate cancer treatments, you will lose fertility and ejaculatory function (but not necessarily the ability to reach orgasm)
- Nerve-sparing surgery does not necessarily guarantee potency
- Risk of long-term incontinence, however, is normally very low.

How is the operation performed?

It is always performed under a general anaesthetic. The urethra is cut during the operation and, after removal of the prostate, is then reconnected to the bladder with stitches. The patient wakes with a catheter in the penis (which stays in place for a period after leaving hospital), tubes in the abdomen and arm drip(s), which are both removed during the hospital stay.

After the operation

Painkillers are prescribed as needed, and the wound dressings removed. Constipation can sometimes be a problem after surgery. Only prescribed laxatives

should be taken, and straining should be avoided. Blood in the catheter can be seen in some cases, often after opening the bowels, but this need not be a concern unless it becomes severe. Advice will be given on using the catheter.

After removal of the catheter (about 10 days later), some slight incontinence should be expected in many cases but, with the pelvic floor exercises that you will be given, this should return to normal over time. This could last from three to six months. You will be given incontinence pads to wear for this period. In very few cases incontinence is permanent. This can, however, be considerably improved by an operation to fit a device to help enable controlled urination (see p. 38).

Follow up care

After the operation the prostate will be sent to the pathology lab for analysis. This will reveal the extent and grade of the cancer, and whether it remained enclosed within the prostate, or whether it extended up to or beyond the cut edge of the prostate. The presence of cancerous cells in these surgical margins is called a **positive surgical margin**. If found, or if cancer is found to be outside the prostate, there is a greater likelihood of a recurrence of the cancer over time. Radiotherapy or hormone treatment may be recommended in this event.

Following a prostatectomy a **high sensitivity PSA** (down to 2 decimal places) is usually required. A sustained high sensitivity PSA result after the operation of less than 0.05ng/mL over several years will indicate the likelihood of a cure.* This test will be required quarterly for 12 months, then 6 monthly until five years after and thereafter annually for the rest of a man's life. Should PSA levels increase, further treatment, such as radiotherapy or hormone therapy, will be advised.

Side effects of surgery

1. Ejaculation. As the seminal vesicles that produce man's ejaculate as well as the prostate are removed, ejaculatory function is lost. Orgasm is always possible but it will be dry. Although this is a concern, some men report the experience as being enhanced. (Should a younger man who wishes to father children consider surgery, opportunities for sperm banking should be discussed.)

2. Erections. After nerve-sparing surgery partial erections normally occur, and better function can return over time. In some cases useful erections can take up to 3 years after the operation to return. To aid recovery, urologists now recommend the use of low-dose Viagra (or similar) on a regular basis. Other methods of obtaining erections are available on the NHS (see p. 36).

3. Continence. Some slight incontinence may occur for a few months, as the sphincter (the muscle that controls the urine flow) is tethered by dissolvable stitches. Pelvic floor exercises, done before and after the operation, may aid speedier return to normality (see p. 37). At the hands of a trained surgeon, incontinence is rarely permanent. Weight loss, if appropriate may help.

*The nationally agreed target standard, however, is <0.2ng/mL.

Methods of surgery

Three main methods of surgery are now used: **open, keyhole, and robotic**. Current research is showing no appreciable difference in long-term outcomes.

1. Open surgery

Until the last few years an **open radical prostatectomy** was the most common method to remove the prostate gland. It is a major operation which requires 3–6 days in hospital and several weeks of recovery time. The operation takes about 2–2½ hours. The surgeon will make a cut in the lower abdomen to remove the prostate. The catheter is removed after about two weeks. The wound will take 4–6 weeks to heal completely and the scar will fade and shrink over time. Driving can normally be resumed after 4–6 weeks.

2. Laparoscopic surgery

The removal of the prostate by keyhole surgery is known as a **laparoscopic radical prostatectomy** (LRP). It is considerably less invasive than open surgery, has less blood loss and less post-operative pain. It has been in use in the UK since 2000. The surgeon will first inflate the abdomen with gas in order to reduce blood loss and to gain a clear view of the area of the operation with a special camera, the image being transmitted to a video screen. Four or five small incisions will be made in the lower abdomen, and the prostate and seminal vesicles will be removed through an incision below the navel. At the hands of an experienced surgeon, the operation typically takes only a little longer than for open surgery.

3. Robotically assisted laparoscopic surgery

This method uses a 'Da Vinci'[®] robot. It uses similar techniques to the laparoscopic method, except that the operation is performed by the surgeon from a remote console, using both rotating handles and foot pedals to remotely control the five arms of the robot. The surgeon is assisted by a team of theatre nurses at the operating table.

Unlike laparoscopic equipment, the machine gives 3D vision and control of tremor. The learning curve for the surgeon is shorter than for a standard LRP procedure. More and more centres are investing in this highly expensive equipment. Results so far are proving as effective as, but no better than, the other two methods. In 2014 the majority of radical prostatectomies (56%) were done using this method.



Above: The robotic arms

The surgeon's console

5. External Beam Radiotherapy

Radiotherapy is the use of high energy rays, usually X-rays, to kill cancer cells. It is used:

- (1) with the aim of getting rid of the cancer (curative radiotherapy)
- (2) after or in conjunction with another treatment if there is a doubt whether the treatment has been successful, or
- (3) to reduce pain and other symptoms in advanced cancers (called ‘palliative radiotherapy’).

Cancer cells differ from normal body cells in that they reproduce faster and are thereby more susceptible to high energy rays. So repeated exposure to high energy rays will kill off cancer cells but allow normal cells to recover. Not all cancer cells act in the same way, so it is necessary to adjust the exposure and duration to achieve optimum effect. The treatment itself is painless. It normally involves daily attendance, 5 days a week, at a radiotherapy centre for short sessions for up to 7 weeks.

Radiotherapy has been proven to improve overall survival in treating locally advanced disease, and is an alternative to surgery for those men with localised prostate cancer. It may be recommended to men with adverse results shown after surgery as an additional treatment. Compared with hormone treatment alone, radiotherapy halves the risk of dying from prostate cancer.

Side effects of radiotherapy

For prostate radiotherapy, the short-term side effects can be bladder and/or rectal irritation, including blood in the urine or rectum. Long-term side effects can include alteration of bowel habit and impotence problems. As with other treatments, ejaculatory function is either lost or degraded. Because of damage to adjacent tissues, there is now some evidence of a small risk of developing bladder or rectal cancer 10 or more years after treatment. These side effects should be discussed in detail with your consultant oncologist prior to your agreement that the treatment should proceed.

Conformal radiotherapy

This has been in common use for many years and until recently has been the standard method of delivery for prostate cancer patients. The radiation beam is shaped to reduce the radiation to the surrounding areas, but it is unable to provide the detailed targeted coverage that newer technologies can offer.

Recent developments

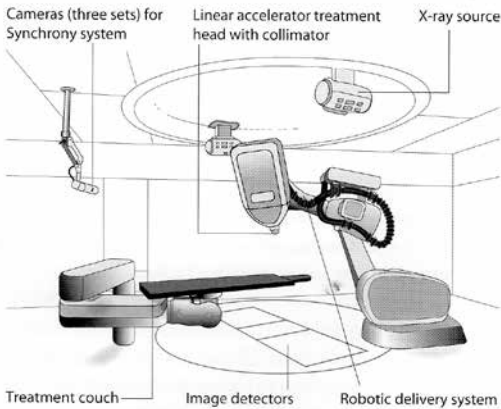
Intensity Modulated Radiation Therapy (IMRT) and Image Guided Radiation Therapy (IGRT)

IMRT and IGRT take conformal radiotherapy a step further in the precision in which the beam is shaped and directed at the body, typically from five different angles. A high degree of planning and computer control is involved in these processes, requiring more time in the treatment sessions. These methods help to reduce some of the side-effects listed above. Although not yet widely available in the UK, this equipment is impressive, with good short-term results. The National Radiotherapy Advisory Group has stated that IMRT should be available in at least one centre in each area. NHS prostate cancer patients are now becoming more able to access this new equipment.



Stereotactic Radiotherapy (CyberKnife)

CyberKnife® is one of several types of radiotherapy machine that delivers stereotactic radiotherapy. This form of radiotherapy uses pencil-like beams of radiation that are directed from different angles precisely on to the tumour. The X-rays are contained in a robotic arm, thus giving the advantage of being able to direct the beams to any part of the patient with greater accuracy, higher intensity and avoiding, to a large part, even greater collateral damage to nearby healthy tissue. The scanner moves with exceptional agility and is able to track any slight movement of the patient or his prostate.



Stereotactic treatment is able to treat complex tumours wrapped around sensitive structures. It is used for a number of cancers where precise targeting is essential, and it is undergoing a trial for special prostate cancers that would benefit from this treatment. Fewer treatment sessions than for conventional radiotherapy are generally needed. However, it has not yet been proven whether this method is any safer or better than IMRT.

There are currently only a few NHS hospitals and private clinics in the UK that have CyberKnife. These include the Royal Marsden Hospital and London clinics.

Radiation dosage

This is measured in **Grays** (Gy). Depending on clinical indications, for conformal radiotherapy 74 Gy in daily 2 Gy doses or ‘fractions’ is used to the prostate. After prostatectomy, 66 Gy is used. Increased dosage over a shorter period in conformal radiotherapy has been shown to have detrimental results. However, increased dosage can be given with latest IMRT machines, where damage to surrounding tissues (e.g. bladder and rectum) is considerably reduced.

What happens should radiotherapy fail?

Curative radiotherapy can only be applied once; so, if there is a re-occurrence of the cancer at the same site, an alternative treatment method (such as hormone therapy or possibly HIFU or cryotherapy) has to be applied. Subsequent surgery at the radiated site is difficult and is only undertaken by specialised surgeons. Hormone treatment (see p. 30) can be, and is often used to shrink the cancer before radiotherapy starts. This also helps reduce the risk of recurrence.

Palliative radiotherapy and bone pain

Radiotherapy is sometimes used for the treatment of bone pain associated with secondary tumours (called palliative treatment). Treatment at a different dosage is given to the bone or area affected. Many men notice some pain relief within a few days whilst for others the relief may take several weeks to become effective. The radiotherapy may be given as a single treatment (usually of 8 Gy) or as several smaller treatments. If the cancer has spread to several areas, a treatment known as ‘hemibody irradiation’ is applied over a larger area. Although this is now seldom used, it normally gives good pain relief. The side effects, however, can be somewhat severe.

Note: When receiving radiotherapy, it is important to follow the dietary advice given by your radiologist.

Advantages and disadvantages

- There is no incision, wound, anaesthetic, or recovery time
- Normal work can often be resumed after each treatment.

But:

- You must be prepared to travel each day to the centre
- Surgery is more difficult should radiotherapy fail, though HIFU is possible
- There are possible long-term side effects (see p. 22 and pp. 36-37)
- Recognising recurrence is harder, as there is no target PSA level
- Radiotherapy may be difficult after a bilateral hip replacement.

6. Brachytherapy

What is brachytherapy?

Brachytherapy literally means 'short therapy'. There are two types of prostate brachytherapy: **low dose-rate** (LDR) and **high dose-rate** (HDR). (The term 'dose-rate' refers to the type of radiation source used and not to the actual radiation dose delivered.) Low dose-rate is most commonly used.

Who is suitable for brachytherapy?

This treatment is only suitable for organ-confined prostate cancer, for those whose prostates are not over-enlarged, and for those who have few, or mild urinary symptoms. Typically men with low or intermediate risk prostate cancer are treated with a LDR seed implant alone. Such patients would normally have a PSA below 15, a Gleason score of 6 or 7, and a cancer stage of T2b or less. Where there is a possibility of spread, or for higher risk disease, a short course of radiotherapy and/or hormone treatment is sometimes offered. HDR brachytherapy is normally given with a short external beam radiotherapy course and is more suited to men with a higher risk cancer which may have spread to the seminal vesicles (i.e. stage T3b).

1. Low dose-rate brachytherapy

Low dose-rate brachytherapy, unlike external beam radiotherapy, treats the cancer by permanently inserting tiny radio-active seeds of Iodine-125 into the prostate with the aim of destroying the cancer.

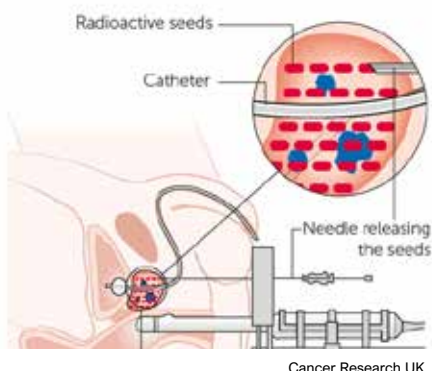
What is involved?

The process is done in three visits:

1) An outpatient appointment will assess your suitability for the treatment, and will consist of some simple tests, which would typically include a DRE examination and a trans-rectal ultrasound examination.

2) The first stage of the treatment will be done as a day case in order to identify the exact size and shape of the prostate by computer imaging, and to plan the radiation dosage required.

3) The second stage of the treatment consists of the actual implantation of the seeds under general anaesthetic by a series of 20–30 needles, each implanting



between 2 and 6 seeds. X-rays may be taken during the procedure. You will wake with a catheter in place, which is removed before you leave hospital. A CT scan may be done following the treatment in order to check that the right dose has been delivered. Patients are sent home the next day with antibiotics and other medicines.

Is the radiation dosage dangerous?

The major portion of the radiation is released from the seeds into the prostate over the first three months. Thereafter the radiation decreases so that it is negligible after nine months. While the seeds are radio-active, you are not. No special precautions are generally considered necessary, but it is suggested that you avoid near contact with pregnant women, and young children should not sit on your lap for the first two months after the treatment. When having intercourse, you may be advised to use condoms for the first two occasions.

Side effects

About 5–10% of patients may experience temporary urinary retention. Some may experience frequency and urgency, which are again generally temporary. Bowel problems (constipation or frequency) can occur 3–6 months after the treatment. Erectile problems can occur in up to 20-30% of men. These risks are claimed to be lower than with surgery or external beam radiotherapy and it has been shown that these have significantly improved with greater experience. There is evidence of a small risk of pelvic cancers after brachytherapy.

Advantages and disadvantages

- It allows a higher dose of radiation to be delivered directly to the prostate when compared with external beam radiotherapy
- There is only a short stay in hospital and in most cases no catheter after the treatment
- Incontinence is rare (less than 1%) and around 70-80% of patients retain their potency
- Only a few days off work are needed.

But:

- The result of the treatment will not be known for several months
- There may be temporary worsening of urinary symptoms for about three months after treatment
- There is a risk of a narrowing of the urethra after treatment
- Brachytherapy is not possible after external beam radiotherapy
- Surgery is more difficult, though rarely needed, after brachytherapy and may lead to poorer outcomes.

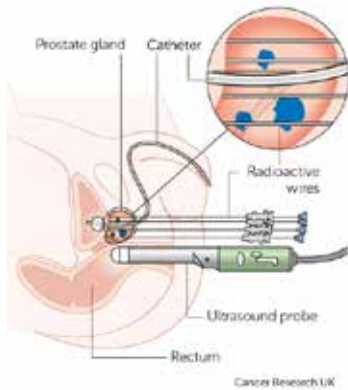
4D Brachytherapy

A newer method becoming more common in many hospitals is 4D brachytherapy. It only requires two visits – an initial outpatient assessment, followed by the seed implantation, during which the planning is performed, known as real-time planning. 4D brachytherapy uses two different types of seeds which come ready prepared in the correct implantation order. The whole procedure can be done more efficiently and accurately in under an hour, with a quicker recovery time and with fewer side effects for the patient.

2. High dose-rate brachytherapy

High dose-rate brachytherapy, sometimes called **temporary brachtherapy**, is suited for both early stage and some locally advanced prostate cancers, (up to stage T3b). It is used in conjunction with external beam radiotherapy and/or hormone therapy. In some instances high dose rate brachytherapy may be used as a sole treatment.

How does High dose-rate differ from Low dose-rate?



HDR brachytherapy involves the insertion a radioactive bead into tiny plastic rods which are temporarily placed into the prostate to deliver the appropriate dose (as opposed to Low dose-rate, in which the seeds are permanently implanted). 15-20 of these thin hollow rods are placed into the gland through the perineal area with the aid of a template, through which an iridium bead is inserted.

A computer-controlled machine pushes the bead into the rods one by one. It also controls the length of time the radiation is given through the rods. The procedure is performed once. If given with external beam radiotherapy it is usually performed first and the radiation follows approximately two weeks later. At the end of the treatment the rods are withdrawn, with no radio-active material remaining in the prostate.

There is currently no evidence that results for High dose-rate brachytherapy are any better than for Low dose-rate treatment.

How will I know whether the treatment has been successful?

As with any radiotherapy treatment, the potential success of brachytherapy will not be known until about 36 months after the treatment has finished, when the PSA will have reached its lowest level. If there is a steady rise of more than 2.0ng/mL above this low point in a six-month period, your consultant should be advised.

7. HIFU

What is HIFU?

High Intensity Focused Ultrasound is a technique that is non-invasive and aims to retain good quality of life for the patient. It is suitable for locally confined prostate cancer T1 or T2. It is not suited for men with an enlarged prostate, although hormone treatment may be first recommended to reduce its size. HIFU can be undertaken as a primary treatment with curative intent, though it is normally used to treat recurrence after radiotherapy.

What does the treatment involve?



The probe used for HIFU treatment

The treatment is done under a spinal (epidural) or general anaesthetic and lasts about two hours. A probe, which emits an ultrasound beam, is placed in the back passage. The tightly focused beams raise the temperature of the prostate tissue to destroy the cancer cells in the targeted area without damaging the surrounding tissue. The process is repeated until the cancerous cells have been destroyed. As the prostate swells immediately after the treatment, a catheter needs to be inserted and remains in place for up to two weeks.

Focal HIFU

Results obtained in treating the whole prostate have not been ideal. However, HIFU offers the option of treating just the part of the gland where the cancer is localised to a particular area, called **Focal HIFU**. Precisely locating the cancer can nevertheless be difficult despite modern diagnostic techniques. The many trials looking at this approach which, although not proven, may offer advantages to some patients. NICE supports the procedure as being safe, although the effect on quality of life and long-term survival is unproven.

Advantages and disadvantages

- Repeat treatments are possible if the cancer recurs
- Normal activity can be resumed within a few days
- No incisions are required, and there is no radiation toxicity
- Impotence rates, against other treatments, are often better.

But:

- Repeat treatments carry a greater risk of impotence and incontinence
- There may be temporary urinary retention, urgency or leakage
- The catheter may be in for longer than for surgery
- It is not always certain that that cancer is all localised to the treatment area
- Occasionally self catheterisation may temporarily be needed.

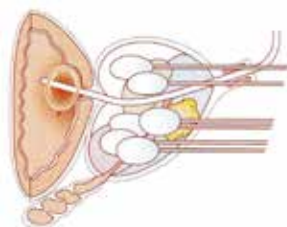
8. Cryotherapy

What is Cryotherapy?

Cryotherapy, Cryosurgery, or Targeted Cryo-ablation of the Prostate (TCAP) involves inserting, under ultrasound guidance, a number of probes into the prostate gland. Argon gas is passed down these probes under pressure and, at the tips, it is allowed to expand and flow back down other channels of the probes. Ice balls are formed which destroy the tissues and the tumour in close proximity to the tips. By suitable positioning of these probes, either the tumour itself or the whole prostate gland can be treated. The process also involves the use of a second gas (helium) to thaw the area; two (or sometimes more) freeze/thaw cycles may be used. Additional probes are used to measure the temperature so as to ensure adequate control.

Who is it for and what is involved?

Cryotherapy is normally considered by most urologists only as an option when radiotherapy has failed but cancer is still found in the prostate. As well as targeting the whole prostate, it can now treat small areas identified on a special mpMRI scan. Cryotherapy is not suitable for those with an over-enlarged prostate.



Ice balls forming in the prostate after insertion of the needles

The treatment requires close teamwork between radiologists and urologists, who use trans-rectal ultrasound for the insertion and guidance of the five to eight needles. This is done under general or spinal anaesthetic, lasting about 1–2 hours. The patient will normally be discharged from hospital within 24 hours after treatment but with a catheter in place, which will remain in for two weeks. PSA levels should gradually drop to an acceptable level after treatment.

Focal Cryotherapy

The development of refined MRI and biopsy techniques has made it possible to target small areas of cancer within the prostate. This minimises side effects and can be more easily repeated. Focal treatment is only used in clinical trial centres.

Advantages and disadvantages

- It is a relatively non-invasive technique with minimal blood loss
- There is a short recovery time and the operation can be repeated if it is not totally successful
- Side effects can include soreness of the perineum, some incontinence and a high rate of erectile and ejaculatory dysfunction.

Note: There is no long-term data on the effectiveness of this treatment. It is only available at a few centres in the UK and is only obtainable on the NHS in the context of a clinical trial.

9. Hormonal Therapies

Hormonal therapy is the first-line treatment for prostate cancers that cannot be treated at a curable stage. It is mainly used in two situations:

- (1) when the cancer is at the advanced stage and has spread outside the prostate to other areas of the body
- (2) when the cancer has recurred after other treatments, or

It can also be used for men with curable cancers prior to radiotherapy or other treatments, which may make the treatment more effective.

In order to grow, most prostate cancers need the male hormones (androgens), the most common of which is **testosterone**. Most testosterone is produced in the testicles, though a small amount is also produced in the adrenal glands, which lie above the kidneys. By inhibiting the generation of testosterone, the cancer will be starved and shrink.

The standard methods to control the production of testosterone are:

- (1) an operation to remove the testicles, called an **orchidectomy**. This treatment is effective, but understandably is not favoured by most patients and is rarely performed nowadays.
- (2) treatments with hormones, which are designed to control the production of testosterone. These are described below.

Hormone treatment is also called **androgen deprivation therapy**. Hormone treatment alone does not cure the cancer but may control it for anything from 2 to 10+ years. A marked lowering of the PSA is usually a good indication of the effectiveness of hormone treatment.

However, the cancer will eventually no longer respond to the hormone drugs. This is called **Hormone Relapsed prostate cancer** (still sometimes referred to by the medical profession as ‘castration resistant’ or ‘hormone resistant’ prostate cancer). A rise in PSA level is the first sign of the treatment becoming ineffective. When this happens, there are several second-line treatments, described later in this section.

There are two main types of hormone treatment:

LHRH analogues and **anti-androgens**.

LHRH analogues

This is short for **Luteinising Hormone-Releasing Hormone**. These drugs can decrease the amount of testosterone produced by the testicles as effectively as surgical removal. Two common examples of these drugs are **Zoladex** (Goserelin) and **Prostap** (Leuprorelin). They are administered by the injection of a slowly

dissolving pellet either monthly or three monthly.

Less common is **Decapeptyl** or Gonapeptyl (Triptorelin). This is another drug that can be used, especially in cases of aggressive advanced prostate cancer. This is administered in 1, 3 or 6-monthly injections. When first administered, these drugs cause an initial surge of testosterone, which is counteracted by a short course of anti-androgen tablets shortly before and after the first injection.

Degarelix (Firmagon) works in a slightly different way to LHRH analogues but has been shown to be just as safe and effective. The advantage of this drug (as opposed to others listed above) is that there is no tumour flare and thus no need for an anti-androgen before an LHRH analogue treatment. It is approved by NICE for cases of advanced prostate cancer where it has spread to the spinal column. It is administered by injection under the skin.

Anti-androgens

These drugs do not stop the production of testosterone but block the effects of androgens produced by the testes and adrenal glands. Two common examples of these drugs are **Cyprostat** (Cyproterone acetate) and **Casodex** (Bicalutamide).

They are usually taken in pill form, which makes them attractive to those who do not like the thought of regular injections. Anti-androgens can be used as a stand-alone therapy (referred to as ‘anti-androgen monotherapy’), or can be used in combination with LHRH analogues, referred to as ‘combined androgen blockade’. Some men may prefer anti-androgens because of the reduced side effects, but evidence shows that they are not quite as effective as LHRH analogues.

Intermittent hormone therapy

Intermittent hormone therapy is a process in which the hormone treatment is started and stopped for periods while monitoring the PSA. When the PSA rises, treatment is restarted. The aim is to reduce the side effects of the treatment. Some trials have shown that intermittent treatment can be as effective as continuous treatment, and with fewer side effects.

Side effects of hormone treatments

A common side effect, particularly of LHRH analogues, is hot flushes for short periods, which can occur at night, affecting sleep, for which a short course of low-dose anti-androgens may be prescribed. Eliminating alcohol, tea and coffee (or using decaffeinated drinks) and going on a soya diet (to replace milk) may also help. Weight gain, bone or muscle pain, joint pain, numbness and tingling in hands and feet, and possible hair loss on face, arms, legs or underarm are other listed side effects. Some may find these hard to live with, but with time many will reduce in severity as the body adjusts. Medication can, of course, be changed should these become a problem.

LHRH analogue side effects. The main side effect is that the patient will be impotent and lose his sex drive; but unlike orchidectomy the process is gradually reversed if the patient stops taking the drug. Some men may suffer from decreased size of testicles and some slight penile shrinkage. Initially these drugs can produce a flare in testosterone, which settles after a few weeks.

Anti-androgen side effects. A common side effect of these drugs is tender or enlarged breast tissue (gynaecomastia), which may subside if treatment is ceased. Low doses of Tamoxifen (an anti-oestrogen) can reduce this side effect. Other possible concerns may be nausea, diarrhoea, itching, feeling weak, and problems with the liver. As the drugs affect your hormone levels, this may cause some anxiety or depression. Although there is still a risk of impotence and other adverse sexual side effects with anti-androgens, these are less severe than with LHRH analogues (or with orchidectomy, where it is permanent).

When Standard Hormones Fail

When the 'first line' hormone drugs referred to above lose their effectiveness, there are other, newer drugs which have been shown to work on many patients. These 'second line' drugs are often used in combination with the first line hormone drugs. You may find chart on page 35 helpful.

Abiraterone Acetate (Zytiga)

This has done well for many patients with advanced cancers that have become resistant to hormone treatments. Abiraterone is currently authorised for use in the NHS as a treatment before or after chemotherapy. It is highly effective in improving survival of some types of prostate cancer, but not all, so it doesn't work for every patient. Some men have to be taken off the drug when an adverse reaction in the liver is found.

Enzalutamide (Xtandi)

This is an advanced anti-androgen that is showing outstanding results, similar to Abiraterone. It is approved by NICE before or after chemotherapy (see below). However, it cannot currently be given after Abiraterone, unless Abiraterone has caused toxicity problems within the first three months of it being given.

Both these drugs are generally well tolerated. Tiredness is the most common side effect associated with them.

Steroids

Steroids have been in use for many years and have proved to be effective, though only for a limited period of time. These include **Dexamethasone** and **Prednisolone**. These drugs stop the adrenal glands from producing other male hormones. A recent trial has shown Dexamethasone to be twice as effective as

Prednisolone; so Dexamthasone should now be considered the preferred option. The main side effect of steroids is an increased appetite.

Bone pain

For bone pain a radioisotope called **Strontium 89** may be used. Given as an intravenous infusion, it is taken up by the affected bones. Most men feel the benefit within a few weeks, although for some the pain may get slightly worse before it gets better. It is now rarely used, as it can damage surrounding healthy tissue.

Radium-223 (Xofigo)

Formerly known as Alpharadin, Radium-223 is proving an excellent treatment for bone metastases associated with advanced prostate cancer. This is a much safer treatment, as it only targets the cancerous areas. It is very similar to calcium and, when injected into the bloodstream, is rapidly taken up in the bone. It emits very high-energy alpha particles that cause lethal damage to adjacent tumour cells and has undergone a trial with nearly 1,000 patients with hormone relapsed prostate cancer. The results show that Radium-223 improves survival by a similar amount to Abiraterone or Enzalutamide and is now a standard treatment for men with hormone resistant prostate cancer and bone metastases. It has been approved by NICE for all patients who need it.

11. Chemotherapy

When is chemotherapy used?

Chemotherapy has traditionally been used as a treatment when all second- and third-line therapies have failed. However, results of the STAMPEDE trial released in 2015 have shown that chemotherapy is most effective when used at an early stage in conjunction with standard first-line hormone therapy. This has the advantage that the patient may be fitter and more able to withstand the side effects of chemotherapy treatment.

However, you may be recommended chemotherapy when standard hormone treatments have become ineffective and the more advanced drugs such as abiraterone and/or enzalutamide have shown not to have worked. There is no 'right time' to start chemotherapy. The treatment will affect your quality of life for 6 months. On the other hand, delaying having chemotherapy until you are seriously ill and unfit may mean worse side effects. It is best to be as strong and as fit as you can beforehand.

Prostate Cancer chemotherapy is usually administered with the drug **Docetaxel** (Taxotere), which is always used in combination with a cortico-steroid such as **Prednisolone**.

What can the patient expect?

Docetaxel is administered as a one-hour infusion every three weeks, usually for up to ten infusions, depending on the patient's tolerance and response. It acts like a poison to prostate cancer cells, causing cell death. Prednisone given at the same time aims to reduce any inflammation and pain. A patient's hormone treatment may be continued in parallel. In trials, 50% of patients after chemotherapy achieved a 50% reduction in PSA on average, though many men achieve much lower PSAs. As prostate cancer seems to present itself in a variety of forms, every patient's experience will be different. When Docetaxel is successful, patients could expect their lower PSA to remain for several months or even some years.

Side effects of chemotherapy

Because Docetaxel is toxic, and not specifically targeted at *prostate* cancer cells, it can and does damage normal cells as well. The number of side effects listed is quite large, common ones being temporary hair loss, damage to finger and toenails, and bone marrow.

Patients' experiences vary. A lucky few are fairly free of side effects; in others, they can be quite severe. Aches and pains, extreme fatigue, particularly in the first week after the infusion, are quite common. Because of the damage to bone marrow, red blood cells can be depleted, leading to anaemia; white blood cells are also reduced, which means that the immune system is compromised.

Other side effects can include loss of appetite, feeling sick and mouth ulcers. Any infections during the chemotherapy cycle have to be dealt with immediately and may even interrupt the treatment cycle. In this event you must contact your GP straight away.

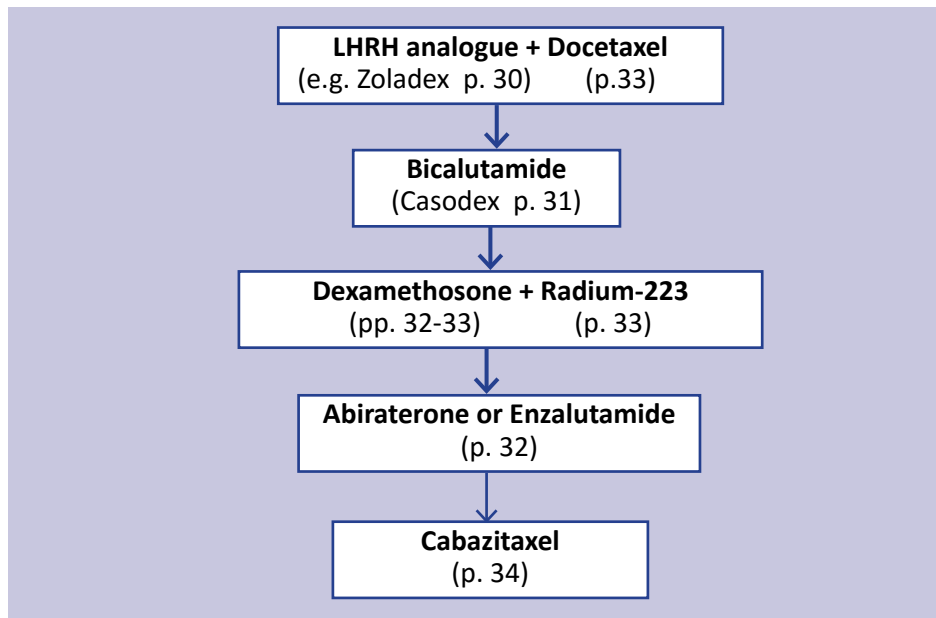
A newer drug building on the success of Docetaxel is **Cabazitaxel**. This is a 'second generation' Docetaxel. It has recently been passed for use for patients who have previously been given Docetaxel. The side effects are similar to those of Docetaxel.

The next step

When the PSA starts to rise beyond acceptable levels and both the drugs above and chemotherapy have been shown to be ineffective, your consultant may have access to the **Cancer Drugs Fund**. This is a scheme managed by NHS England whereby NHS patients can get drugs not routinely available and not yet approved by NICE. It is a fast track route for cancer patients shown to have special needs, but has limited financial resources.

12. A Treatment Path for Advanced Prostate Cancer

Below is a suggested treatment route for those with advanced prostate cancer. It may not be applicable to every man, so it is always important to follow the advice of your medical professional.



Now that the first results of the STAMPEDE trial have shown the efficacy of using chemotherapy at the same time as first-line hormone therapy, men can now receive this with their LHRH analogue (e.g. Zoladex or Prostag). The PSA should fall dramatically to an acceptable level. Treatment with these hormone drugs will continue, either continuously or intermittently, until such time as PSA begins to rise.

At this stage an anti-androgen such as Casodex may be used. The steroid Dexamethosone could follow, which can be used in conjunction with Radium-223. As steroids are only effective for a limited amount of time, newer drugs such as Abiraterone or Enzalutamide can follow; for some, but not all men, these may be very effective. Cabazitaxel, a more recent chemotherapy treatment, may be used if the advanced drugs prove ineffective.

The programme above is flexible and can continue over many years. New treatments are being developed in many different countries. Keep optimistic.

1. Sexual Problems

The prostate is a sex gland. Diseases affecting it and its treatment inevitably impact on a man's sex life. Prior to any treatment, your consultant should advise you of the impact of the disease and of each treatment type, so that you can make an informed choice. All radical treatments affect sexual function. Any treatment that damages the prostate will result in loss or severe impairment of ejaculatory function and hence fertility. If fertility is important to you, you should discuss creating a sperm bank with your consultant.

Erectile dysfunction

As the nerves that control erections cover the surface of the prostate, most treatments will affect erectile function to a greater or lesser degree. Surgery often has a significant initial impact but, where the surgery is nerve-sparing, this normally improves over time. Radiotherapy treatments may affect erections less but, unlike surgery, there is generally no gradual post-treatment improvement. Brachytherapy is similar to or slightly better than external beam radiotherapy in this respect. Results from HIFU are fairly encouraging. Few patients achieve erections after cryotherapy. It should be noted that, with some treatments, orgasm is normally achievable in spite of these problems. After treatment, it is important to get the system back into working order as quickly as possible. 'Use it or lose it' is the motto.

There are a variety of treatments for erectile dysfunction. These include pills (e.g. **Viagra**, **Cialis**, **Levitra**, **Spedra**), all of which are available on normal prescription through your GP. Asking for a repeat prescription can avoid any possible embarrassment. In addition there is **Alprostadil**, available as a pellet inserted into the end of the penis (called **MUSE**), as a cream or by injection. Other methods include vacuum pumps, a penile implant and a treatment using a small pump in the scrotum, now also available on the NHS. You should be aware that all treatments can be at some cost to spontaneity.

You and your partner

Discussion with your partner is essential. Hormonal treatments in particular cause lack of interest in sex, and this can become a barrier to discussion. In such circumstances your partner may be in for a particularly distressing time, as the cause of the problem, if not discussed, may not be apparent.

Psychological and sexual counselling

Problems can be mental as well as physical. Many hospitals now have staff with expertise in this area, and you should not be frightened to ask. If you wish it, you and your partner are entitled to sexual counselling. Remember that treatments for sexual problems caused by prostate cancer are available free under the NHS.

2. Problems with Continence

Problems with our waterworks often result from diseases of the prostate, treatments, or simply the ageing process. These tend to fall into two categories: urgency and lack of control.

Some guidelines

- Do not reduce your fluid intake – this can make the problem worse
- Try to avoid drinks containing caffeine
- Fizzy drinks may exacerbate symptoms
- Alcohol can increase urgency
- Avoid passing urine ‘just in case’ and try to increase time between visits to the toilet
- Do not try to hold out at night – it will only keep you awake
- Practise holding on in the daytime, which will help your night-time problems
- If you have been given water tablets, you must continue to take them, unless advised otherwise by your doctor
- If you are overweight, try to lose a few pounds
- Carry out regular pelvic floor exercises.

Pelvic floor exercises for men

The muscles of the pelvic floor are kept firm and slightly tense to stop leakage of urine from the bladder or faeces from the bowel. Pelvic floor muscles can become weak and sag because of surgery, radiotherapy, being overweight, lack of exercise, poor posture, or just getting older. Weak muscles give you less control, and you may leak urine, especially with exercise or when you cough, sneeze or laugh. (This is called ‘stress incontinence’.)

Pelvic floor exercises help strengthen these muscles and involve tucking your bottom in and pulling your pubic bone up in front and holding it there for a few seconds. This should be repeated 100+ times daily, so self-discipline is needed to keep at these exercises. Fast walking can also help. Both the exercises and fast walking have also been shown to improve erectile function.

Although there is no firm evidence that doing pelvic floor exercises prior to treatment is beneficial, this can do no harm, and it may well help to you get into the habit of routinely exercising the right muscles.

3. Long-term Severe Incontinence

It must be emphasised that severe long-term incontinence is rare, and nearly all men recover continence after treatment within months. So do not despair.

Note: The section that follows only applies to men who experience serious long-term incontinence problems that severely affect quality of life.

The **sphincter** is a natural on/off valve associated with the urethra, which can become weakened or even damaged, usually during prostate surgery. In nearly all cases nowadays this strengthens over time (often with the help of pelvic floor exercises described on the previous page), and men usually gain full continence after 3–6 months or less.

In up to 3% of cases, however, this can remain a problem after a year. If this is the case, there are two methods which are now used – a male sling (an implant for mild to moderate incontinence) and an operation to fit an artificial sphincter for more severe cases.

The Sling

The sling is made from polypropylene mesh and is implanted during a small operation, under general anaesthetic, through a small incision in the perineal area. It acts as a support for the urethra. A catheter may be needed for a short period, but normal urination should gradually be restored after this is removed.

The artificial sphincter

There are two parts to fitting an artificial urinary sphincter (AUS), an operation done under full anaesthetic: the fitting of the sphincter, a cuff around the urethra, and an incision (like a hernia operation) in the groin to fit a pump in the scrotum attached to a small balloon. When the need to urinate is felt, a switch is pressed in the scrotum, which releases the urine, and after a few minutes the device self-closes.

After the operation, the device cannot be used for six weeks, when it is activated by the nurse. Thereafter it should alleviate the problem considerably.

4. Bone Health

Our bones are living matter. They are constantly dying and regenerating. As we grow older we need to maintain strength in our bones through use. Weight-bearing exercise and brisk walking or swimming are particularly important to avoid osteoporosis, a deterioration of bone tissue which can lead to fractures. Unfortunately this deterioration is made worse by

- (1) certain hormone treatments for locally advanced and advanced prostate cancer (e.g. Zoladex) designed to lower testosterone levels
- (2) metastasis of the cancer to the bones in the advanced stages, particularly to the ribs, hips and spine.

Bone Density

If it is not offered, you should ask for a **Bone Mineral Density test (BMD)** or **DEXA** (short for dual energy X-ray absorptiometry) **scan** at the start of long-term hormone treatment to establish a baseline. This should be repeated every 24 months. The doctor will get the results, which will come in the form of T-scores:

- **between 0 and -1.0 is normal**
- **between -1.0 and -2.5 indicates low bone mass (osteopenia)**
- **below -2.5 indicates osteoporosis.**

If osteoporosis is found, you should be treated for this under NICE guidelines for osteoporosis. Unlike breast cancer, there are no guidelines for treatment of osteoporosis for prostate cancer.

Calcium and Vitamin D

Calcium intake is one of the keys to maintaining good bone health. If you are avoiding dairy products, calcium may be found in many other foods: green fruit, vegetables, soya milk and baked beans.

Note: Too much salt, caffeine or alcohol will deplete your calcium

Vitamin D3 is vital to help fix calcium in your body. It can be obtained naturally via careful and limited exposure to sunlight, and in oily fish and supplements. Most men in the UK are deficient in Vitamin D3, due to inadequate sunlight in the winter months and precautions against sunburn in the summer. So some men could find Vitamin D3 in tablet form helpful in the fight against prostate cancer, alongside other treatments.

Osteoporosis

Many osteoporosis treatments combine calcium and vitamin D3 in tablet form. **Bisphosphonates** such as **Zoledronic acid** (Zometa) are usually prescribed for osteoporosis. **Denosumab**, given by injection, is not yet approved by NICE for prostate cancer. It is recommended that all patients receiving these drugs consult their dentist, as they can affect the jaw and teeth.

1. The Clinical Nurse Specialist

One of the recommendations published in the newly updated NICE guidance on Prostate Cancer (2014) is:

'Offer men with prostate cancer individualised information tailored to their own needs. This information should be given by a healthcare professional (for example a consultant or specialist nurse) and may be supported by written and visual media (for example, slide sets or DVDs).'

Urological Clinical Nurse Specialists play an important role as keyworkers in caring for a prostate cancer patient. They have specialist knowledge which can be invaluable to a patient and his family, enabling them to ask detailed questions which they may feel uncomfortable posing to a consultant, with whom they will generally spend less time. Similarly, nurse specialists should be on hand to help manage more complex symptoms or side effects associated with prostate cancer.

Most Urology departments have specialist nurses dealing with incontinence and erectile dysfunction problems. Prostate cancer is by far the most common form of tumour for which a urological nurse specialist will be responsible. Unfortunately there is a shortage of these nurses across the country.

The Improving Outcomes Guidance for Urological Cancers is explicit on the importance of Nurse Specialists:

'All patients with urological cancers should be managed by multidisciplinary urological cancer teams. These teams should function in the context of dedicated specialist services... Nurse specialist members of urological cancer teams will have key roles in these services.'

The 2014 NICE guidelines also state:

'Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England ... Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professional.'

You are only able to make an informed decision if you have been given and understand the full facts about your cancer by a nurse specialist or a consultant. The guidelines go on to state:

'Offer men with prostate cancer advice on how to access information and support from websites, local and national services, and from cancer support groups.'

A Clinical Nurse Specialist can play a vital role in your cancer journey – make sure one is looking after you!

2. Diet and Lifestyle

Can patient's lifestyle influence the course of prostate cancer?

There is now emerging evidence to suggest 'yes' but probably not for everyone. Each patient and their stage, grade and biological pattern of their disease is unique. What works for one person may not work for another. The good thing is though, even if a healthy living programme does not help your cancer it will certainly help with many of the side effects of cancer treatments, help your body in other ways and empower you with a sense of self determination.

Evidence

The latest NICE guidelines (2014) on prostate cancer now show the evidence for exercise after prostate cancer is strong enough to include it as a peer reviewed recommendation for oncology units throughout the UK. Every week major journals are publishing trials which highlight the benefits of lifestyle after cancer. The most important of these trials have been collected in a formal evidence review, commissioned by Macmillan Cancer Support led by Professor Robert Thomas, consultant Oncologist at Bedford and Addenbrooke's Cambridge University Hospitals. He has also summarised the lessons learnt from these trials into evidence-based recommendations within his book *Lifestyle and Cancer – The Facts*, available via www.cancernet.co.uk.

Examples include:

- Keep physically active every day with moderate exercise at least 3 hours per week
- Avoid being overweight or obese
- Cut out smoking
- Avoid excessive alcohol: 1 glass of red wine 5 days a week is fine
- Eat more polyphenol-rich healthy foods (e.g. herbs, spices, teas, berries, fruit and vegetables)
- Eat less of the unhealthy foods (those high in processed carbohydrates, salt and bad fats)
- Reduce processed meat and burnt meats
- Try to eliminate processed sugar.

Physical activity

Many trials evaluating exercise programmes have concluded that moderate activity can reduce fatigue, improve mood, psychological well being and body composition. Other trials have linked exercise, especially if combined with other lifestyle manoeuvres, with a reduced rate of PSA progression in active

surveillance, and a reduced risk of relapse after radical treatments. There is insubstantial evidence, however, that fewer men gain benefit after radiotherapy.

Most of these trials indicate that 30 minutes a day or around 3-4 hours a week is the most beneficial, but any level of exercise is better than no exercise. Clearly, most of us do not get enough exercise. This should be a major lifestyle priority.



Exercise should be enjoyable if it is going to be sustained. Fortunately there are so many choices including gardening (the green gym), dancing, brisk walking, golf, running, cycling, swimming or formal exercise classes. You can search for exercise facilities in your area by postcode using a tool on cancernet.co.uk/exercise.htm. You may also be able to ask your doctor for a referral to the local municipal gym on the National Exercise Referral Scheme for

a 12-week supervised programme. If you are unfit, build up gradually; a fitter body will help you live longer and better.

Obesity

Being overweight increases the risk of developing prostate cancer in the first place. There is also evidence that obese men present with more aggressive types (higher Gleason grades), increasing the complexity of treatments. This means they have to take hormone therapies for longer, increasing the risk of hot flushes and further weight gain. Obese men also have a higher risk of PSA relapse after radical treatments. A recent study from USA has demonstrated an important link between lifestyle and genetics, which may explain why for some men obesity is bad and for others it has no effect. Overweight men with prostate cancer whose tumours were positive for the TMRSS2:ERG genetic mutation had more than a 50% increased risk of dying from cancer after their diagnosis compared with normal-weight men.

Diet

There is an increasing emphasis on reducing calorie (energy) excess. Not only does this lead to obesity, but it produces changes in the blood stream, such as a rise in insulin-like growth factor (IGF), which cancers love. As well as total calorie intake, the type of food is important. Foods which are rapidly absorbed, such as processed sugar, refined wheat in bread and pasta are the worst culprits. Colourful fruits, berries and tomatoes have a lower risk of prostate cancer; flavanoid-rich



foods such as beans, pulses, legumes show a lower risk of aggressive types of prostate cancer. Foods grilled at high temperature are known to be carcinogenic, and should be avoided.

Four foods in particular have been shown to work against the onset of prostate cancer in different ways: **Pomegranate**, rich in ellagic acid, has been shown to directly inhibit cell growth and can actually induce cell death in androgen sensitive and aggressive human prostate cancer cells. **Green tea**, rich in epigallocatechin gallate, blocks an enzyme which signals cells to proliferate faster, and metastasise. **Broccoli**, rich in isothiocyanate, has been found to inhibit prostate cancer cell growth; and **curcumin**, which gives turmeric its yellow colour, slows cancer cell growth by blocking the cell cycle, preventing the invasion and migration of cells.

Whole food supplements and the Pomi-T trial

These four foods have been concentrated into a pill (**Pomi-T**). After an extensive and approved trial it is now commercially available. The trial was sponsored by Prostate Cancer UK, approved by the National Ethics Committee and the National Cancer Research Institute Committee (NCRI). Cancer survivors are attracted to the potential health benefits of a food supplement, with over 70% reporting regular intake. Pomi-T provides a wide spectrum of polyphenol nutrients whilst at the same time avoiding over-consumption of any one particular type.



The trial showed a 63% reduction in PSA progression rate for those taking the pill against the control group who took a placebo. In addition, men on active surveillance taking the supplement have been shown to be less likely to opt for early invasive treatments.

Despite these findings Pomi-T is still classed as a food supplement, so can never become a recognised medicinal product or find its way into routine management. Further trials are hoping to look at the advantages of Pomi-T for men on hormone treatment, as well as for other cancers and conditions.

Another trial found that grapeseed extract was linked to a lower risk of prostate cancer after regular intake.

Minerals, vitamins and other chemical extracted foods

Vitamin E and **selenium**, once thought to be helpful have now been shown to have an increased prostate cancer incidence. High doses of **zinc** were also associated with an increased risk of prostate cancer in the study. The NCRI has stated that long-term vitamin and mineral consumption should be discouraged

unless correcting a known deficiency. **Saw palmetto** and **genistein** have not shown any benefit for either prostate cancer or BHP. Likewise, the two most recent trials of **lycopene** extracts among men on active surveillance or watchful waiting found no difference in PSA progression, nor were there any links with the reduction in the risks of breast cancer with regular intake.

There is still a lot of research needed in this area, especially as there may be benefits for selected vitamin and mineral supplements in cases of known deficiencies; so it is important not to throw the baby out with the bathwater.

Most of us, for example, are deficient in **Vitamin D3**. Sunshine is the best source (up to half an hour per day is sufficient), so a moderate supplement in the winter months may be logical. Vitamin D can also be obtained from oily fish, whole grains, nuts, seeds and eggs.

Dairy versus non-dairy



Although there is no clear evidence that dairy products are harmful, it is now looking increasingly likely that there is a case for at least considering either complete avoidance, or reduced intake, of these.

The Chinese do not consume any dairy products, but if they start to adopt a western diet, the incidence of western diseases increases. It is believed that IGFs (Insulin-like Growth Factors) in dairy products are a possible cause. Significant evidence, however, is still lacking. Nevertheless many prostate patients keep off dairy (including cheese, yoghurts etc.), switching to alternatives based on soya, oats, rice and almond. If not, consider changing to organic dairy products.

PSA doubling time

PSA doubling time remains the most sensitive measure of response to a lifestyle initiative. To aid its calculation an app, **PSACalc**, has been developed and is currently available for the iPhone and iPad.

We hope that the guidance given in this section will encourage you to take positive action to improve your cancer journey.

PCaSO is grateful to Professor Robert Thomas for contributing much of this article. For a full account of the trials and supporting evidence for this information please see his article, printed as a supplement to PCaSO Newsletter 46 (February 2014). A copy can be requested from PCaSO.

3. Clinical Trials

Clinical trials

Clinical trials are organised into four phases, of which Phases 2 and 3 are perhaps the most relevant. Phase 2 trials normally recruit a relatively small number of patients (typically 50-100) in order to establish whether the new drug/method is showing some useful activity. Phase 3 trials recruit a much larger number of patients. Patients are divided into those receiving the new drug or treatment method and those having standard treatment (the 'control arm'). In 'blind' or 'double-blind' randomised trials even the doctor may not know which arm the patient is on.

There are a high number of trials currently undergoing evaluation, too many to list in this booklet. A list can be found on the following website address:

<http://tinyurl.com/97w4abw> or from the Cancer Research UK site: <http://tinyurl.com/974gyaq>.

Trials are run across many of the teaching hospitals of the UK. An individual trial may also be accessed across different UK trials units. So it is important to find the unit that is most conveniently located to you, and to check whether or not any travel expenses are paid.

Advantages and disadvantages

- Even if you are on the control arm, you will be receiving the very best conventional treatment, which will be monitored closely – perhaps more closely than if you were not on the trial programme, and by some of the best specialists in the field.
- You may, however, have to set time aside for regular travel to a more distant centre than your local hospital, but in some cases all expenses are covered.
- You will need to be happy with the fact that the treatment may be 'blinded', i.e. you may not know on which arm of the trial you have been placed.

How to Get on a Trial

From the website addresses highlighted above, select a suitable trial and request your GP to forward your name to the appropriate unit for evaluation. The trials website is not always up to date, so a call to the unit to ensure the trial is still recruiting is worth the time.

Some Trials for specific therapies

High Intensity Focused Ultrasound, as a primary curative treatment, has to date mainly been offered in the private medical sector. The National Health and Clinical Excellence Agency (NICE) have yet to approve its use in the NHS. The trial, based in London at the University College of London Hospital under the leadership of Professor Mark Emberton, has a simple aim: to see how efficient this therapy is for treating localised prostate cancer.

PACE

The PACE trial is comparing a new type of radiotherapy, stereotactic body radiotherapy (SBRT – see p. 23) against standard treatment for men with localised prostate cancer. SBRT has the advantage that it is given in just 5 or 6 treatments rather than the conventional 20 treatments (see p. 22). The trial is open in many UK centres.

STAMPEDE, or Systematic Therapy in Advancing or Metastatic Prostate cancer: Evaluation of Drug Efficacy. This trial is multi-centre and is open in over 100 hospitals throughout the UK. It has already recruited over 8,000 patients. Its aim is to improve survival by adding other drug components to the standard hormone therapy. As one component is completed, another treatment is added. The outcome will be the most efficient combination.

Some new drugs on trial for advanced prostate cancer

There are a number of trials testing new drugs for men who have advanced prostate cancer and have already received standard drug treatments. Most of these are phase 2 trials. The most promising agents are taken on into phase 3 trials. **Olaparib**, a drug that is already used to treat ovarian cancer, is about to enter a phase 3 trial in multiple UK hospitals.

4. Some New Developments

PET Scanning

A PET scan (Positron Emission Tomography) is taken to produce a detailed, three-dimensional picture of the inside of the body. Choline PET-CT scans have been shown to be effective for prostate cancer, especially for determining whether there is any spread outside the prostate. Before the scan takes place, a radioactive substance, known as a radiotracer, is passed into your body either by injection, by an inhaler, or a small tablet that you swallow. In future, choline PET scans may be replaced by PSMA (Prostate specific Membrane Antigen) PET scans.

Proton Beam Radiotherapy

By 2018 the UK should have 3 or 4 Proton Beam centres. The potential advantage of *protons* over *photons* is that there may be significantly less collateral damage. Currently the therapy is employed for eye and some brain cancers. To

date, prostate therapy has not been tested against standard radiotherapy for prostate cancer.

Photo-dynamic therapy (PDT)

Photo-dynamic therapy has been under trial at University College London for some years. It uses a drug, which is injected into the patient. Needles (like cryotherapy) insert laser light into the prostate to activate the light-sensitive drug, with the object of killing the cancer. It has currently been discontinued as a trial, but may be available privately.

New developments to improve initial diagnosis

A urine-based test called **EN2** has been under development for some while. This will not replace PSA but, if available, it could be an additional tool in the armoury of the doctor. More recent is the **Stockholm 3 (STHLM3)** test. Instead of PSA alone, this consists of a combination of 6 blood markers (including PSA), genetic profiling, and patient characteristics (age, family history, previous prostate biopsy, prostate examination). In a large trial it found that it could reduce the number of men having biopsies by 32%, without compromising the ability to diagnose significant prostate cancer.

Caution:

While these drugs and treatments may be currently showing promising results in trials in or outside the UK, there is no guarantee that they will become approved for use in the NHS.

Acknowledgements

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5. Glossary of Terms and Abbreviations

antioxidant	a substance that protects us from the dangerous free radicals
biopsy	the removal of small samples of tissue for analysis
catheter	a small tube inserted (usually via the penis into the bladder)
Gleason score	the rating of the aggressiveness of the cancer
impotence	the inability to achieve a useful erection
incontinence	the inability to control urination
laparoscopy	looking into the abdomen by means of a tiny camera
lymph nodes	small organs that filter and destroy harmful bacteria and viruses
metastasis	the spread of cancer outside the primary site
nocturia	the need to urinate frequently at night
oncologist	a specialist in the medical treatment of cancer
orchidectomy	an operation to remove the testicles
perineum	the area between the scrotum and the anus
prostatectomy	an operation to remove the prostate
seminal vesicles	organs that contribute fluid to the ejaculate
testosterone	a male hormone secreted by the testes
urethra	the tube through which urine and semen flow
urologist	a specialist in disorders of the kidneys/bladder/prostate systems
BMD	bone mineral density test
BPH	benign prostatic hyperplasia (enlargement of the prostate)
CT	computerised tomography scan
DRE	digital rectal examination
EBRT	external beam radiotherapy
ED	erectile dysfunction (problems with erections)
HIFU	high-intensity focused ultrasound
HR	hormone relapsed (prostate cancer)
IMRT/IGRT	intensity modulated/image guided radiation therapy
LHRH	lutening hormone-releasing hormone
LRP	laparoscopic radical prostatectomy
MDT	multi-disciplinary team
MRI	magnetic resonance imaging scan
NICE	National Institute for Health and Clinical Excellence
PET	positron emission tomography – a form of body scanning
PDT	Photodynamic therapy
PSA	prostate specific antigen
RP	radical prostatectomy
RALP	robotically assisted laparoscopic prostatectomy
TCAP	targeted cryo-ablation of the prostate (i.e. cryotherapy)
TNM	tumour/nodes/metastases: a scale for measuring tumour spread
TRUS	trans-rectal ultrasound scan
TURP	trans-urethral resection of the prostate (an operation for enlargement)