

KNOWLEDGE EMPOWERS

tackle
prostate cancer
Action for patients and their families

Prostate Cancer
Information booklet
produced by PCaSO

Foreword



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I am pleased to recommend this booklet as a summary of the information that all prostate cancer patients, and their families, need to know, written from a patient's perspective, and based on real patients' experiences.

Prostate Cancer is a difficult and complex disease, and the choices facing a man who is diagnosed with it – what treatment to have, indeed whether to be treated at all – are complex, perhaps more complex than in any other major cancer.

For a man to make the right decisions, he and his family, need access to information at the right level of detail and presented in a way that is easily understood. That is what this booklet provides.

A handwritten signature in black ink, appearing to read 'C Parker'.

Written by patients, for patients,
this Information Booklet has been compiled by
PCaSO Prostate Cancer Support Organisation

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Prostate Cancer Information Booklet

Introduction

Prostate cancer is not generally well understood, yet each year in the UK over 47,000 men are diagnosed with the disease. In its early stages the cancer can develop quietly without obvious symptoms, and even changes such as difficulty or discomfort in passing water may be wrongly assumed to be simply the ageing process. Although there have been huge advances in the medical care and treatment of prostate cancer there is still no national screening programme, although cancer charities such as **PCaSO** (Prostate Cancer Support Organisation) and **Tackle** (National Federation of Prostate Cancer Support Groups) do lobby for national screening. Finding cancer early greatly increases the chance of a cure, whereas late diagnosis can limit the treatment options to containing the growth of the cancer.

The PSA (prostate specific antigen) blood test currently serves as the best indicator of prostate problems that may include cancer, and this booklet describes the PSA process. It also describes the 'patient pathways' in dealing with prostate cancer through diagnosis, treatment and dealing with any side effects of treatment. Although some treatments such as surgery and radiotherapy have been used for a long time, diagnosis and treatments for prostate cancer are still being refined and improved. Research continues with emerging new developments through trials that go through several stages and this booklet also mentions some of these.

Although all men are at risk of prostate cancer, a healthy lifestyle including mediterranean diet and physical activity and suitable exercise can help the body's general resistance to the disease and, where cancer is diagnosed, may also aid in fighting the cancer's growth.

Much has been written and published on the subject of prostate cancer treatment and prevention. This information booklet is intended as a comprehensive guide, from a **patient's perspective**, to most aspects of prostate cancer. It is hoped it will help you (and your partner, friends or family) understand about prostate cancer and its effects and it may help you when talking to health professionals, such as your GP, hospital consultants and specialist nurses.

It is for any man concerned about a rising PSA, but should be particularly useful for newly diagnosed men, whether they have been diagnosed at an early stage or only caught later when the cancer is more advanced. It can also be useful for more experienced patients, who may be facing some further treatment later in their prostate cancer 'journey'.

Each reader of this booklet will have a different level of experience and knowledge, thus needing to know different things. If you are new to prostate cancer we suggest you use the detailed Contents List to help you look for what you need to know for your particular circumstances, otherwise you may find you have too much information to absorb in one go. You can always read further sections later.

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

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Facts, Tests and Diagnosis



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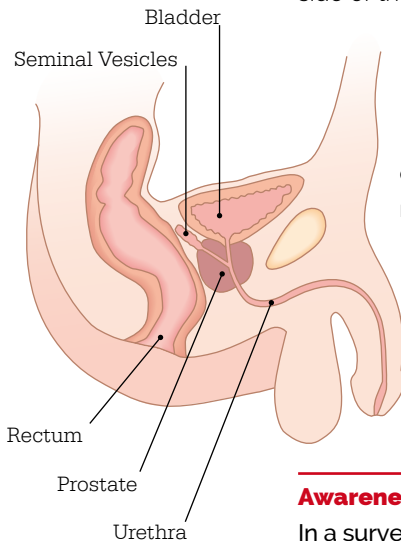
The Prostate and Prostate Cancer

What is the Prostate?

The prostate is a sex gland found only in men and it is important for reproduction. It supplies the fluid needed for sperm produced by the testes, to travel and survive. On each side of the prostate are bundles of nerves

and vessels which help to control erectile function. It lies at the base of the bladder, surrounding the tube called the urethra which carries urine or semen to the end of the penis. It is normally about the size of a walnut.

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.



Awareness is key

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

Risk Factors

There are four major risk factors that can influence your risk for developing prostate cancer. Prevention can hinge on awareness and appropriate screening—neither too early, nor too late. It's important to understand your personal risk profile.

Age – Once regarded as the curse of older men, younger men are being diagnosed in their 50s, and occasionally in their 40s. In the UK more men are diagnosed between the ages of 65 and 69 than any other age bracket.

Race – Men of African-Caribbean origin are especially at risk: 70% more likely to develop prostate cancer and twice as likely to die from it. Asian men who live in Asia have the lowest risk, but if they migrate to the west, their risk increases.

Diet and lifestyle – These can also be a factor, particularly a high-fat, highly processed carbohydrate diet. Research has shown that in obese men, recovery from surgery can be longer and more difficult, and the risk of dying from prostate cancer can be higher.

Family History and Genetic Factors – According to Cancer Research UK it is estimated that inherited factors explain around 5–9% of prostate cancers. The risk is 2.1-2.4 times higher in men whose father has/had the disease; 2.9-3.3 times higher in men whose brother has/had the disease; 1.9 times higher in men with a second-degree relative (grandfather or uncle, nephew, or half-sibling) who has/had the disease. Family genetic risk is higher in men aged under 65 compared with older men, and in men with more than one affected first-degree relative or with an affected relative diagnosed aged younger than 60.

Prostate cancer risk is 19-24% higher in men whose mother has/had breast cancer (but it is **not** associated with breast cancer in a sister).

Prostate cancer risk is up to 5 times higher in men with the BRCA2 gene mutation and among such men under 65 years old it is more than 7 times higher.

'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 be life threatening.

It often spreads first to tissues that are near the prostate, such as the seminal vesicles and the nearby lymph nodes, which are part of the lymphatic system. 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 and need more urgent treatment.

Most prostate cancers are found in the outer part of the prostate, called the peripheral zone, the back of the prostate and near the rectum. Most start when normal cells begin to grow out of control.

Slow-growing cancers, ('pussycats'), may stay within the gland, unnoticed and indolent, for many years. These may only require careful monitoring, without necessarily needing radical treatment, and can safely undergo Active Surveillance.

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 invade other areas of the body.

Prostate cancer is very treatable if it is detected early and contained within the gland. If prostate cancer spreads elsewhere it **remains** as prostate cancer. It can spread to the bones, but if it does it is **not** bone cancer.

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 11,800 die of it (source: Cancer Research UK)
- 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 slowed and controlled
- If prostate cancer spreads elsewhere it remains as prostate cancer. It can spread to the bones, but it is not bone cancer'

The PSA Test

PSA measures the level of Prostate Specific Antigen, a protein found mostly in the semen, but with small amounts secreted naturally into the bloodstream. When prostate cancer growth is present more PSA is released into the bloodstream. A PSA blood sample is normally taken at a GP surgery, it is not primarily a direct 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.

Not all prostate cancers are aggressive and need treatment, and PSA screening has, in the past, led to invasive investigation and 'over diagnosis' followed by 'over treatment' through radical surgery or radiotherapy and their associated side effects of impotence, incontinence and bowel disturbance. It is equally true, however, that many thousands of men have avoided a slow and painful death through early treatment of prostate cancer that was detected by PSA screening. Early detection is most important.

In the last few years there have been some developments:

The PROMIS trial showed that if an mpMRI scan of the prostate was normal in a man with a raised PSA, a biopsy was unnecessary and surveillance was all that

was required. This is now saving many unnecessary biopsies and preventing 'over-diagnosis' of non-aggressive prostate cancer; this has reduced the risk of 'over-treatment' to 4% and falling (National Prostate Cancer Audit 2018 report).

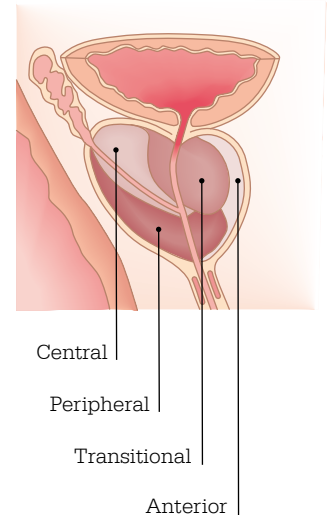
Secondly, **the ProtecT study** showed that for men actually found to have apparent non-aggressive prostate cancer, Active Surveillance alone was a safe treatment strategy.

The DRE

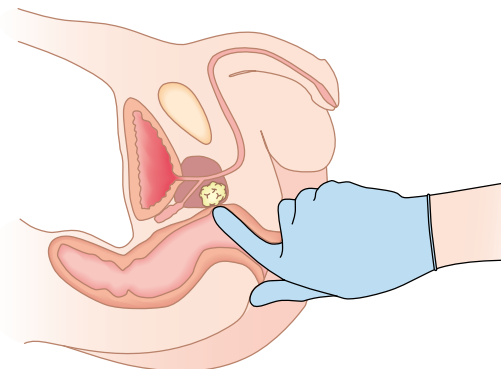
If your PSA reading is raised your doctor may give you a Digital Rectal Examination (or DRE). Although not a completely reliable test for prostate cancer, because not all of the prostate can be felt, it is however a useful check of your prostate.

The prostate is divided into several 'zones'. Most prostate cancers start in the peripheral zone, at the back of the prostate, which is why the DRE can be a useful screening test. It is done by feeling it with a gloved finger in the back passage. This only takes a few seconds and generally causes only a little discomfort. Your prostate should feel smooth and soft, not hard and lumpy. If any abnormalities are felt, it may be a sign of a problem.

Prostate 'Zones'



DRE (Digital Rectal Examination)



GP guidelines

The UK relies upon GPs to deliver PSA testing, both for symptomatic (with symptoms) and asymptomatic (without symptoms) men, in line with the recommendations of the Prostate Cancer Risk Management Programme (2016).

This Prostate Cancer Risk Management Programme (PCRMP) sheet helps GPs give clear and balanced information to asymptomatic men who ask about prostate specific antigen (PSA) testing. The PSA test is available free to any well man aged 50 and over who requests it. GPs should use their clinical judgement to manage asymptomatic men and those aged under 50

who are considered to have higher risk for prostate cancer.

PSA screening decisions should be made on an individual basis between the doctor and patient, based on a full examination of risk factors. Testing from age 40 onwards for those with higher risk is advised.

PSA after diagnosis

The PSA test is not 100% perfect, as elevated levels can be caused by other benign prostate problems. But the PSA test is widely accepted as an invaluable tool for monitoring prostate cancer disease activity and remission from prostate cancer after treatment.

Some Facts

Your GP consultation and the PSA Test

- The PSA test may reassure you if the reading is normal
- 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 long-term remission

But:

- A raised PSA level may lead to further 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
- Most men (typically two out of three) who have a raised PSA level may turn out not to have prostate cancer
- Around 15% of men with a 'normal' PSA result may actually have a rare form of prostate cancer that doesn't elevate the PSA reading

What can cause an elevated PSA reading?

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)
- an enlarged prostate that often comes as men age
- a medical condition called Benign Prostatic Hyperplasia, or BPH (sometimes now called BPE, standing for Benign Prostate Enlargement)
- an infection within the urinary tract
- ejaculation within the previous 48 hours before the test
- vigorous exercise within the previous 48 hours (particularly bike riding)

Some drugs may artificially lower PSA, such as finasteride (Proscar or Propecia) or dutasteride (Avodart).

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 1.0ng/ml to readings in the 1000s. Readings from 1 to 3 (depending on age) are generally normal. A single reading is of little value, unless it is high (say over 10.0ng/ml).

What if my PSA is higher than normal?

If the reading is marginal or borderline (say between 3.0 and 5.0ng/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) 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 0.75ng/ml in one year should be a warning signal.

Because expert opinions vary, there is no clear consensus regarding the optimal PSA threshold for recommending referral for further investigations. The Prostate Cancer Risk Management Programme (2016) issued

If a man has a diagnosis of prostate cancer, the PSA test is useful, because it can track prostate cancer growth well before any clinical signs or symptoms.

by Public Health England, recommends PSA levels greater than 3.0ng/ml for men in the 50-69 age group should be referred. There are no recommended referral levels for men aged 70 and over, or men aged under 50. Your GP and/or urologist should advise you on this. The chart below gives generally accepted guidelines that some NHS Hospitals use.

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, or the rate of increase is higher than expected, 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.

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

Further tests for prostate cancer

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% 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 tests.

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.

MRI Scan

Following referral to a consultant urologist for suspected prostate cancer, you will be recommended for various tests, one of which could now be a non-invasive MRI scan. A Magnetic Resonance Imaging (MRI) scan creates a cross-section of the soft tissues around the selected part of the body by using magnetic fields.

In the past the test was normally done after a biopsy, as a further check to see whether there is any spread outside the prostate. Following advances in technology (both software and hardware), clinicians

are now using a multi-parametric MRI (mpMRI) scan of the prostate area before a biopsy is considered, for men with suspected clinically localised prostate cancer (NICE guideline 2019). This has improved considerably the diagnostic capabilities, enabling better detection of clinically significant cancers and reducing unnecessary biopsies and treatment.

Standardisation and consistency of interpreting these contrast enhanced scans has led to a PI-RADS/Likert grading system being adopted and used to evaluate mpMRI of the prostate. Based on a score of 1 to 5, grades 1 and 2 indicate that a significant cancer is unlikely to be present, grades of 3, 4 and 5 indicate an increasingly higher level of probability of cancer. However, the ability to interpret mpMRI depends on the radiologist's level of experience in this area. Before having an mpMRI scan, some hospitals inject a contrast agent in order to enhance the image, this can occasionally produce side effects that should be explained to you before having the procedure.

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 (PI-RADS/Likert grade 1 & 2) then there may be no need for an immediate biopsy.

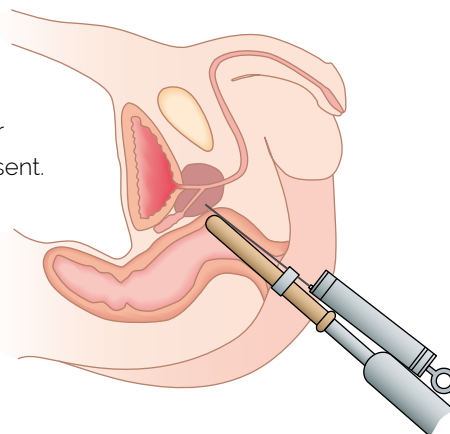
Recent advances in MRI scanning techniques and the introduction of advanced software have led to greater accuracy in identifying the position of any tumour and its potential aggressiveness. These are becoming the gold standard, though it will be some time before they come into use in all hospitals.

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 Ultra-Sound (TRUS) guided biopsy of the prostate is a short procedure that takes place at a hospital as an out-patient. 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 to reduce the 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.

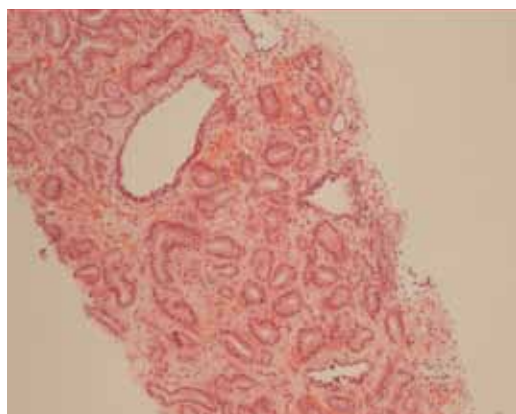


TRUS Biopsy

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. New techniques (see **Fusion Guided Biopsy**) mean that better accuracy is now possible.

Template (or Transperineal) 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 can be done when suspicions of cancer are high, or if a TRUS biopsy result is inconclusive. Many urologists now prefer to recommend this method to patients with high/intermediate risk. The procedure is



Section of Biopsy core Gleason 3 (x200 magnification)

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.

performed under either a general or local anaesthetic and may require an overnight stay in hospital. 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 (up to 60). As well as being more accurate, a template biopsy is considered safer, as there is less risk of infection from untreatable bacteria, compared to 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. It can lead to fewer samples being taken and, for those who may need further biopsies, fewer occasions where a repeat biopsy may be needed. Fusion Guided Biopsy may not be available at all hospitals.

Isotope 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 appear 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 offered when hormone treatment is part of a Watchful Waiting programme for people who are at high risk of developing bone complications. It is painless and quite harmless.

PET Scan

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 (choline), known as a radiotracer, is passed into your body 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.

The Gleason Score & ISUP Grading

(How aggressive the cancer is)

Gleason Score

This 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. Scores totalling 5 or less are insignificant and are not 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'

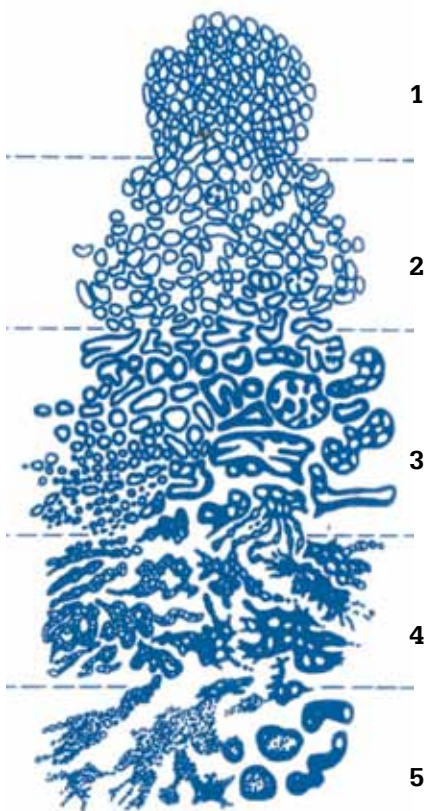
The consultant will give you a total score out of 10, which should be split down as two

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.

ISUP Grading

In 2014, the International Society of Urological Pathologists released supplementary guidance and a revised prostate cancer grading system called the ISUP Grade Groups. The ISUP Grade Group system is simpler, with just five grades, 1 to 5.

Your consultant may report your score either as a Gleason Score or an ISUP Grade Group, or you may receive both scores.



ISUP Grading

Risk Group	ISUP Grade Group	Gleason Score
Low	Grade Group 1	Gleason <6
Intermediate Favourable	Grade Group 2	Gleason 7 (3+4)
Intermediate Unfavourable	Grade Group 3	Gleason 7 (4+3)
High	Grade Group 4	Gleason 8
High	Grade Group 5	Gleason 9 - 10

Gleason patterns (Grade 5 is the most aggressive.)

Staging of Prostate Cancer

(How far the cancer has progressed)

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.

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.

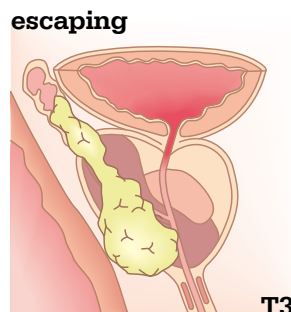
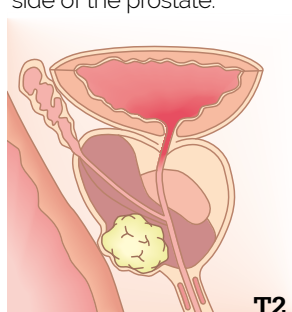
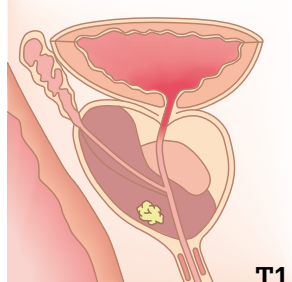
N and M Stages

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.

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.

Below 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.

confined



escaping

Risk Category

Your risk category is determined following all the diagnostic tests, before any treatment is undertaken. The NICE Guidelines for Prostate Cancer (2019) give three categories of risk:

Low risk, Intermediate risk and High risk

Depending on a combination of PSA, DRE, Gleason score, ISUP score and T stage, you will fit into a 'risk' category. Knowing this risk category will help decide the most appropriate treatment for you (see chart).

There can also be a subset of 'very high risk' in which the tumour has extended into the seminal vesicles (T3b) or the rectum or bladder (T4), or there are multiple biopsy samples with high grade cancer.

Currently, there are ongoing efforts to develop tests that can aid physicians more accurately to distinguish cancers that will become fatal from those that will sit in the prostate without spreading. Treatment options for each risk group are very different and you should ask your doctor which risk group you belong to, so you can better understand the options available to you.

The categories describing prostate cancer

Localised (or early stage) cancer - where the cancer has been found to be enclosed within the prostate.

TNM staging - either **T1** or **T2, NO, MO**

Risk stratification for people with localised prostate cancer

Level of Risk	PSA		Gleason score		Clinical Stage
Low	<10 ng/ml	and	≤6	and	T1 to T2a
Intermediate	10 to 20 ng/ml	or	7	or	T2b
High ¹	>20 ng/ml	or	8 to 10	or	≥T2c

1. High-risk localised prostate cancer is also included in the definition of locally advanced prostate cancer

NICE guideline, May 2019

Locally advanced cancer - where the cancer has been found to have broken through the outer capsule and begun to spread outside the prostate, e.g. into the seminal vesicles, the lymph nodes near the prostate, the rectum (back passage) or the bladder.

TNM staging - either **T3** or **T4, N1, MO**

Note: high-risk localised prostate cancer, PSA higher than 20ng/ml, or Gleason Score between 8 and 10, may also be included in the definition of locally advanced prostate cancer even though the cancer is still enclosed within the prostate.

Advanced cancer (sometimes known as metastatic cancer) will have spread from the prostate to other more distant parts of the body. See Section 4, which includes a diagram of the lymphatic system and a diagram showing possible areas of prostate cancer spread.

TNM staging - **T4**, any **N**, any **M**



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. No matter the exact words that describe the results of your prostate biopsy, a diagnosis of prostate cancer forever changes everything. It can be confusing and overwhelming.

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 in particular the 'stage' that you have been diagnosed with and what is likely to happen. As a newly diagnosed patient, you might be confused by arguments favouring one treatment over another or you may feel ill-equipped to make the decisions that are being required of you. 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 and should be able to advise. 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 often useful to talk to a 'professional stranger'. 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. If you or your partner find yourself badly affected by the stresses of your cancer, take action and seek further support from your GP, your local

mental health line, Macmillan Cancer Support or PennyBrohn UK.

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, bowel or urinary problems following treatment, see section 3. 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 of 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

treatment. 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 treatment, in some hospitals there is a specialist nurse who can do a 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 is one way of doing that.

Lifestyle changes

Adopting a healthy lifestyle can help your body recover from treatment, reduce the side effects of treatment, including fatigue, that affect many cancer sufferers and reduce risk of relapse. Some find that changing lifestyle increases confidence in living with, or even controlling, their disease. For prostate cancer sufferers, lifestyle change can reduce the rate of PSA progression, an important indicator of the state of the disease. It's also important to remember that cancer survivors often have more health problems than people of similar age and background. Lifestyle changes, such as healthy eating and regular exercise, can

Some Facts

- Psychological distress is currently not being assessed or managed well in men living with prostate cancer, despite just under a third of men reporting moderate or extreme anxiety or depression.
- Depression, anxiety, stress, fatigue, pain and psychosocial factors can affect patients with prostate cancer. These factors can occur as a result of impotence, erectile dysfunction, sexual issues and incontinence.
- Prostate cancer patients may also suffer a loss of self-confidence, which may be a particular issue in the period shortly after completion of primary treatment and this loss of self-confidence may be a significant barrier to accessing support

and do mitigate general health problems. For more see **Exercise, Diet and Lifestyle** on page 49.

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

Many men gain enormous benefit from talking to other men who have experienced the same problems and local prostate cancer support groups can help a great deal.



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 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 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 questions below and on the next page. 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 72). The team meet regularly to discuss all their patients. Each individual patient's treatment case is considered and approved by a range of senior clinicians, not just the doctor who happens to be seeing the patient when he comes for an appointment.

Some Questions for your Consultant

1. What is my Gleason score, and how is it split? (p. 13)
2. What T stage is my cancer? (p. 14)
3. Is my PSA increasing abnormally? (p. 9)
4. Can you tell me whether the cancer is fast or slow growing? (p. 6)
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. 10-12)

7. Is there a team and a Nurse Specialist managing my case? (p. 47)
8. What is the long-term situation for me? (You may prefer not to ask.)

Treatment Options and General Questions

1. What treatments are available for my type of cancer? (p. 23)
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. 41-46)
8. Can anything be done to ease the side effects?

Important Questions for Surgery

1. What type of surgery will I have – open, keyhole or robotic? (p. 28)
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. 28)
4. Will I need any other treatments?

Important Questions for Radiotherapy

1. Will I be able to have the latest IMRT or IGRT radiotherapy? (p. 31)
2. What dosage will I receive, and over how many weeks? (p. 32)
3. Do I have Hormone treatment treatment as well? If not, why not? (p. 55)

Important Questions for Hormone Treatment

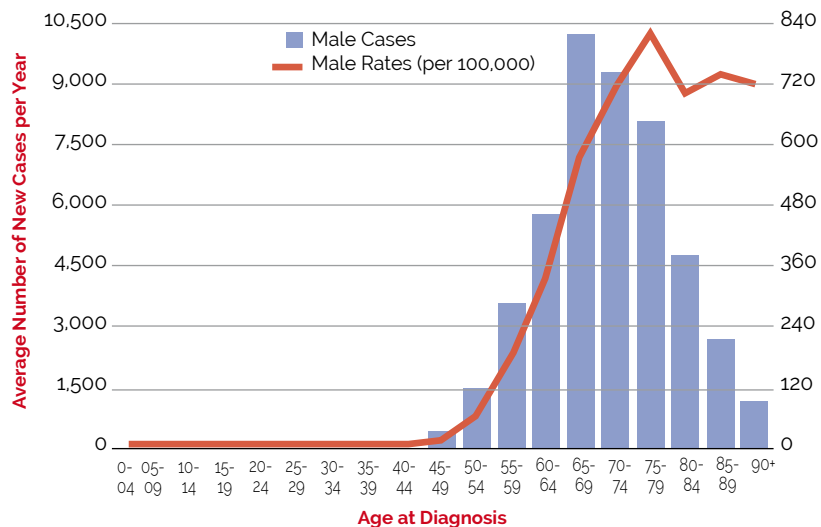
1. Do I need to have a bone density scan? (p. 12)
2. Will you recommend intermittent Hormone treatment if necessary? (p. 56)
3. What drugs can I have to ease any side effects?

Clinical Trials

1. Would I be a suitable candidate for a trial? (p. 69)

Support

1. Can I see my oncologist/urologist and Nurse Specialist? (p. 47)
2. Can I do anything to help myself with diet and supplements? (p. 49)
3. Can you give me details of any local support groups?



Average Number of New Cases per year per 100,000 males in UK

Age Range	Male Cases
30 to 34	2
35 to 39	6
40 to 44	79
45 to 49	436
50 to 54	1,510
55 to 59	3,575
60 to 64	5,807
65 to 69	10,242
70 to 74	9,302
75 to 79	8,095
80 to 84	4,772
85 to 89	2,721
90+	1,189
All Ages	47,740

Source: cruk.org/cancerstats, Prostate Cancer (C61): 2014-2016





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Brachytherapy	34
High Intensity Focused Ultrasound (HIFU)	37
Cryotherapy	38

Summary of Treatment Options for Localised and Locally Advanced Prostate Cancer

As detailed in Section 1, page 15, you will have been diagnosed with one of three categories of prostate cancer:

Localised (or early-stage) cancer - where the cancer has been found to be enclosed within the prostate. Localised disease has the most options available for a possible cure.

Locally advanced cancer - where the cancer has been found to have broken through the capsule and begun to spread outside the prostate. The treatment options are more limited, but the disease may still be potentially curable.

Advanced cancer (sometimes known as metastatic cancer) will have spread to other parts of the body. In this situation it is only possible to treat the cancer with drugs designed to delay the progression of the disease. (For Advanced Cancer treatment see Section 4)

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 on 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 or as part of a clinical trial. Some treatments may be used in combination (e.g. Hormone treatment 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, See Section 3. 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, with the intention to treat with curative intent if the disease progresses.

Watchful Waiting (L, LA, A):

regular check-ups, leading to hormone treatments or palliative care where necessary. The intention is disease control when symptoms arise.

Surgery (L):

an operation to remove the whole prostate.

External Beam Radiation Therapy (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 radio-active rods, removed after treatment.

HIFU (High Intensity Focused Ultrasound) (L):

the cancer cells are heated and destroyed by ultrasound.

Cryotherapy (or cryosurgery) (LA):

the freezing of cells in the prostate.

Hormone Treatments (Androgen Deprivation Therapy) (L, LA, A):

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

Chemotherapy (A):

drugs used with hormone therapy or after it has failed.

Comparison of the three main treatment options:			
People with low-risk or intermediate risk Localised Prostate Cancer (for whom radical treatment is suitable) - evidence from large UK trial	Active Surveillance	Radical Prostatectomy	Radical Radiotherapy
Survival and disease progression at 10 years:	%	%	%
People who had not died of prostate cancer	98	99	99
Disease progression (e.g. evidence of metastases, or T3 or T4 diagnosis)	21	8	8
Development of distant metastases	8	3	3
Urinary problems			
Urinary problems at 6 months	39	71	38
Urinary problems at 6 years	50	69	49
Moderate to severe urinary problems at 6 months	4	19	6
Moderate to severe urinary problems at 6 years	8	13	5
Erectile Dysfunction (ED)			
Moderate to severe Erectile Dysfunction at 6 months	29	66	48
Moderate to severe Erectile Dysfunction at 6 years	40	50	36
Bowel function problems			
Problems with faecal incontinence at 6 months	2	1	5
Problems with faecal incontinence at 6 years	3	2	4
Moderate to severe impact of bowel habits on quality of life at 6 months	3	3	10
Moderate to severe impact of bowel habits on quality of life at 6 years	4	3	2

This table has been assembled from information in Table 3 of NICE guideline 'Prostate cancer: diagnosis and management' published 9 May 2019. It is intended to be used for health professionals to discuss benefits and harms with patients.

Active Surveillance

Of the top 10 most common cancers, prostate cancer is the only cancer where many patients, over 30%, have a slow-growing tumour that does not warrant immediate aggressive treatment. The cancer will grow so slowly, if at all, that a man will die of something else before the cancer causes any symptoms. Active Surveillance (sometimes called Active Monitoring) is now the primary option for men that have a low-risk prostate cancer that is unlikely to cause harm or decrease life expectancy. It is a better choice than immediate radical treatment such as surgery or radiation as it is a pro-active method which monitors men with early prostate cancer.

If a man does choose Active Surveillance the NICE guideline recommends the protocol in the table below:

Active Surveillance Protocol	
Timing	Tests
Year 1 of active surveillance	Every 3 to 4 months: measure PSA
	Monitor PSA kinetics (PSA density and velocity)
	At 12 months: DRE (digital rectal examination)
	At 12 to 18 months: multiparametric MRI
Year 2 onwards	Every 6 months: measure PSA
	Monitor PSA kinetics (PSA density and velocity)
	Every 12 months: DRE (digital rectal examination)
Note: if clinical or PSA changes of concern arise during Active Surveillance, mpMRI and/or biopsy may be repeated.	

This table has been assembled from information in Table 4 of NICE guideline 'Prostate cancer: diagnosis and management' published 9 May 2019.

Advantages and Disadvantages

- Active Surveillance may avoid radical treatment, with its potential side effects
- mpMRI 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
- Active Surveillance offers men with localised cancer the same survival benefit as surgery or radiotherapy

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

Men with 'low risk' cancer are the ideal candidate for Active Surveillance

**Example:
Low volume cancer -
Stage 1c;
Gleason 6;
PSA less than 10ng/ml;**

who do not need immediate curative treatment. This spares them the side-effects that may be caused by a treatment which may later prove to have been unnecessary. It is now the first-line approach for men found to have low grade prostate cancer. Results suggest that many men on Active Surveillance will never need to be treated for their prostate cancer.

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 a 6 monthly or annual PSA blood test. A repeat biopsy may only be needed if the MRI scan reveals any significant change. 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.

A Change of Lifestyle?

Increasingly, research shows that lifestyle changes can reduce the side effects of

treatment and slow the growth of some tumours and reduce the risk of relapse. This means that you could benefit from lifestyle changes during Active Surveillance. Smokers should start by giving up and those of us that drink should ensure we consume no more than recommended levels. Regular exercise and, for many of us, changes to diet can be beneficial. See **Exercise, Diet and Lifestyle** on page 49 for more details.

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. mpMRIs), 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.

Watchful Waiting

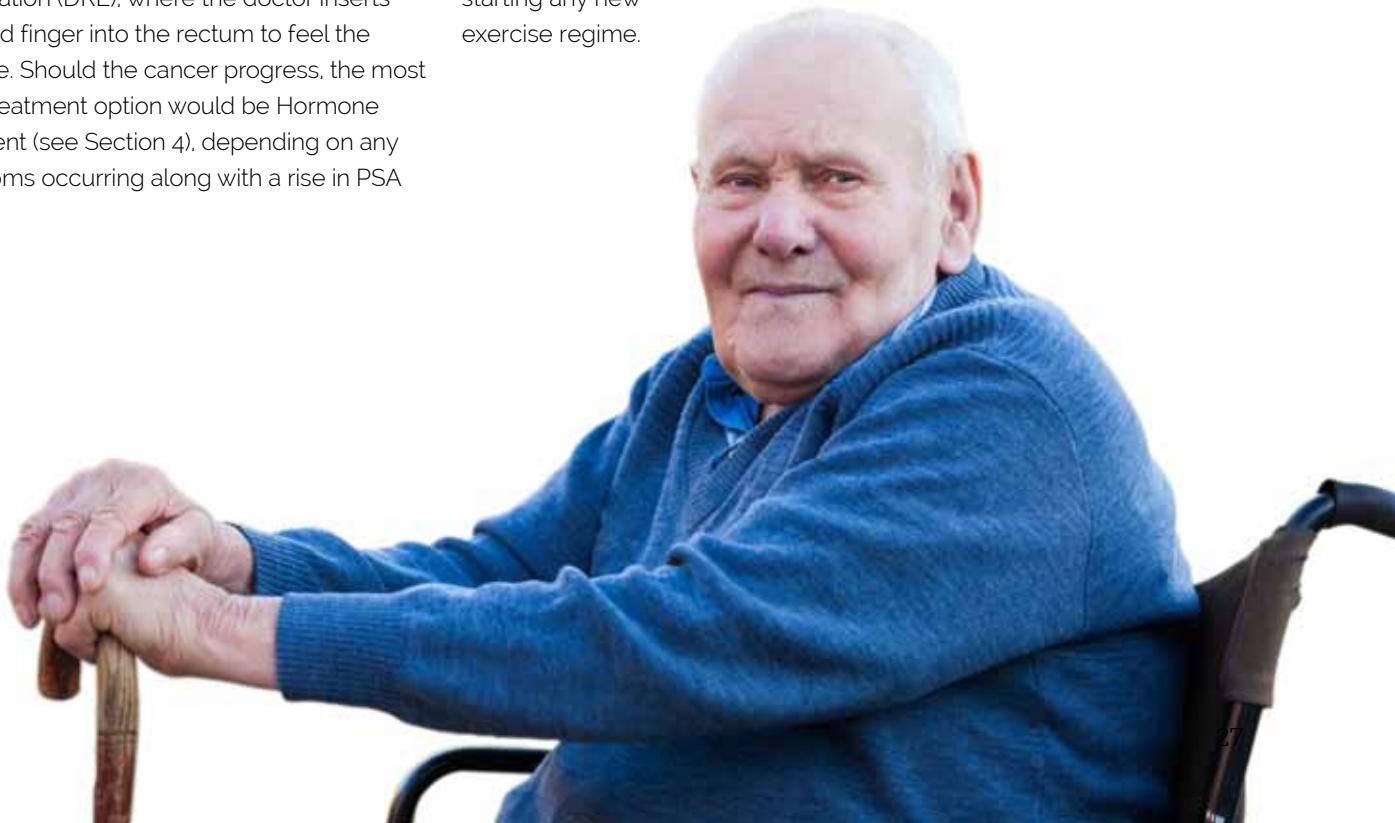
Watchful Waiting is usually offered either to older men, where the disease may grow so slowly that it may not affect the person's quality of life, or to those whose health may not allow them to undergo a treatment such as radiotherapy or surgery. Unlike Active Surveillance, the aim of any treatment will 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 treatment (see Section 4), depending on any symptoms occurring along with a 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 dietitian can advise you on diet and nutrition. You should, of course, consult your doctor before starting any new exercise regime.



Surgery – Radical Prostatectomy

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-risk prostate cancer the pelvic lymph nodes (part of the immune system) may be removed. For high-risk 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.

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, but evidence for robotic surgery is rapidly increasing and distinct differences may well be found in the future.

Open surgery

Until around 2014 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

Advantages and disadvantages of surgery

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

But:

- All major surgery has risks. The older you are, the greater the risk
- Risk of urinary incontinence and/or erectile dysfunction
- As with most radical prostate cancer treatments, you will lose fertility and ejaculatory function (but not necessarily the ability to reach orgasm)

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.

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. In the hands of an experienced surgeon, the operation typically takes only a little longer than for open surgery.

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 more accurate fine movements. Results so far are proving



as effective as, but no better than, the other two methods. The majority of radical prostatectomies are now done using this method and any man choosing surgery as his option is highly likely to have robotic surgery.

After the Operation

The patient wakes with a urinary catheter in place, an intravenous infusion of fluid in the arm, and may have an abdominal drain. 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



DaVinci Robot

expected in most 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 (p44-45).

Assessing the Spread of the Cancer

Following 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 was enclosed within the prostate, or whether it extended up to or beyond the cut edge of the prostate. The presence of cancerous cells all the way to the edge of the tissue that was removed, is called a positive surgical margin.

If cancer is found just outside the prostate, there is a greater likelihood of a recurrence of the cancer over time. This may not be a cause for concern, dependent on the grade of the cancer found at the edges of the gland. The cancer at the centre of your tumour may have been aggressive, but at the margins may have been of low grade. You should discuss options with your consultant following surgical pathology.

Follow up Care

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. (The nationally agreed target standard, however, is <0.2ng/ml)

PSA levels should be checked no earlier than 6 weeks after treatment, at least every 6 months for the first 2 years and then at least once a year after that (NICE Guideline 2019).

Side effects of Surgery

Ejaculation. In addition to the removal of the prostate gland, the seminal vesicles are removed at the same time. These glands help to produce a man's semen in addition to the prostate itself. Orgasm is always possible, but it will be dry. Although this is a concern, some men report the experience or quality of orgasm as being enhanced. (Should a younger man who wishes to father children consider surgery, opportunities for sperm banking should be discussed.)

Erections. After nerve-sparing surgery partial erections normally occur, and better function can return over time. It is important that efforts are made as soon as practicable after surgery to resume erectile function. 'Use it or lose it' is the motto (See Sexual Function on page 41).

Continence. A degree of incontinence may occur for a few months, as the urinary sphincter (the muscle that controls the urine flow) is removed during surgery. Pelvic floor exercises, done before and after the operation, may aid speedier return to normality (See Urinary Function on page 43). Weight loss, if appropriate, may help.

External Beam Radiation Therapy (EBRT)

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

- with the aim of getting rid of the cancer (curative radiotherapy)
- after or in conjunction with another treatment
- 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 4 weeks and in some cases up to 7 weeks.

Radiotherapy has been proven to improve overall survival in treating locally advanced disease. Compared with hormone treatment alone, radiotherapy halves the risk of dying from prostate cancer. The ProtecT trial has shown that radiotherapy is as effective as surgery for men with localised prostate cancer. It can be

used in combination with Brachytherapy and Hormone treatment for men with intermediate or high-risk localised prostate cancer.

Conformal Radiotherapy

This has been in common use for many years and until recently was 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 in the field of radiotherapy include: Intensity Modulated Radiation Therapy (IMRT) and Image Guided Radiation Therapy (IGRT). These are described in detail below.

IMRT

This takes conformal radiotherapy a step further in the precision by 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. This technique uses multiple beams of varying intensity to achieve complex shaping of the radiation dose around the prostate. Many small 'beamlets' from various angles contribute to the total dose administered. These methods help to reduce some of the possible side effects. Now widely available in the UK, this equipment is impressive, with good short-term results.



IMRT Linear
accelerator

The latest data from the National Prostate Cancer Audit shows 90% of patients in England and 100% in Wales are treated with IMRT. Tomography is also a form of intensity modulated radiation therapy (IMRT)

IGRT

is a form of IMRT but even more accurate, the technique uses regular imaging of the tumour or a marker inserted into the prostate before treatment, it is used to confirm that the target and surrounding organs are truly in a position appropriate for the therapy. In prostate cancer, IGRT can be achieved by implanting small inert seeds (fiducial markers) or a cone beam CT scan can be taken once the patient is in the treatment position.

Fractionation or 'Radiation Dosage'

The dose of radiation is measured in Grays (Gy). Recently announced outcomes from the CHiPP clinical trial, NICE Prostate Cancer guidelines (2019) confirm that for low and intermediate-risk localised prostate cancer patients, hypofractionated radiotherapy (60 Gy delivered in 3 Gy fractions), requiring 20 treatment sessions should be offered. The previous standard of 74 Gy delivered in 37 sessions of 2 Gy fractions may be used in certain cases.

For cancer recurrence after radical prostatectomy, a total of 66 Gy in 2 Gy fractions is normally used, requiring 33 treatment sessions.

Radiation with Hormone treatment

Clinical trials have shown a benefit in patients who receive Hormone treatment with radiation treatment: studies have shown that this combination increases long-term survival. It is now becoming the standard treatment for men with certain types of intermediate-risk prostate cancer and nearly all high-risk.

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 may be either lost or degraded. Because of damage to adjacent tissues, there is 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

Advantages and disadvantages of Radiotherapy

- 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 rarely undertaken, should radiotherapy fail, though salvage HIFU is possible in selected cases
- There are possible long-term side effects (pp 41-46)
- Radiotherapy may be difficult after a bilateral hip replacement
- It is now usually combined with Hormone treatment for 6 months or longer depending on the level of risk

consultant oncologist prior to your agreement that the treatment should proceed.

Note: When receiving radiotherapy, it is important to follow the dietary advice given by your doctor and radiographers who are treating you daily.

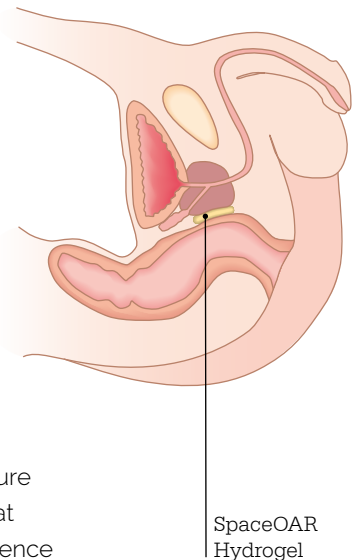
SpaceOAR Hydrogel®

This procedure can benefit prostate cancer patients receiving radiotherapy and has been designed to reduce radiation exposure to organs surrounding the prostate. This therefore might reduce the potential of long-term side effects and damage that can cause rectal bleeding, bowel dysfunction, urinary incontinence and in potency.

The Hydrogel is a soft gel, injected into the area between the rectum wall and the prostate, a

minimally invasive new procedure performed under local or general anaesthetic. The gel pushes the rectum about 1cm further away from the prostate and hence away from any potential damage from radiation. It stabilises the rectum and prostate against movement during treatment, with the hope of minimising harmful side effects.

It remains in place for three to six months, after which it is absorbed by the patient's body and cleared in the patient's urine. Permitted by NICE, but individual NHS Hospital Trusts are deciding whether to include the procedure within their treatment pathway, given that currently there is little good-quality evidence for this technique.



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 speed of radiation source used and not to the actual radiation dose or level delivered.) Low dose-rate is most commonly used.

Who is suitable for Brachytherapy?

This treatment is only suitable 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 LDR seed implant alone. Such patients would normally have a PSA below 15, a Gleason score no more than 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, Gleason 8-10.

Low Dose-Rate Brachytherapy (LDR)

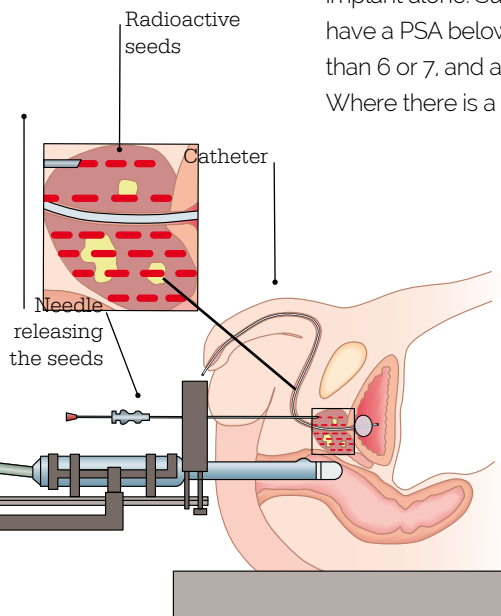
Low Dose Rate Brachytherapy, unlike External Beam Radiation Therapy, treats the cancer by permanently inserting tiny radio-active seeds of Iodine-125 into the prostate with the aim of destroying the cancer.

What is involved?

The process is done in two or 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.

Low Dose Rate
Brachytherapy (LDR)



Most centres now would combine stages 2 and 3 in one visit. Some centres offer a 'brachy boost' whereby low dose-rate brachytherapy is combined with a course of external beam radiation.

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, to avoid the risk of passing a radio active seed.

**Men with low or intermediate
-risk prostate cancer are
treated with LDR.**

**HDR Brachytherapy is
normally given with a short
external beam radiotherapy
course and is more suited to
men with a higher
risk cancer.**

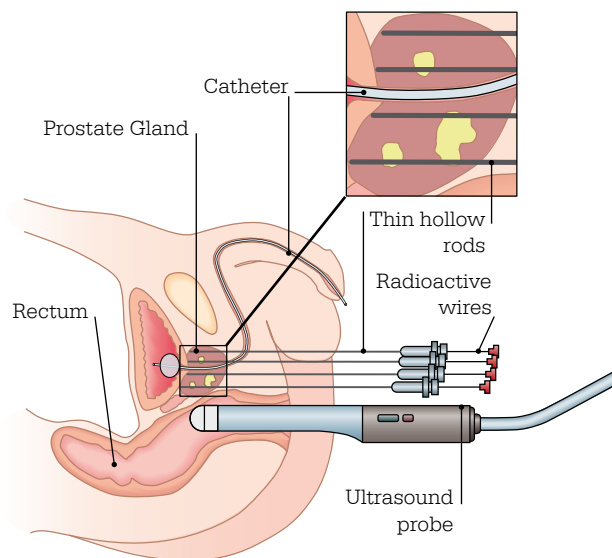
High Dose-Rate Brachytherapy (HDR)

Sometimes called temporary Brachytherapy, 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 treatment. In some instances, HDR Brachytherapy may be used as a sole treatment.

How does High Dose-Rate differ from Low Dose Rate?

HDR brachytherapy involves the insertion of 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 beads into the rods one by one. It also controls the length of time the radiation is given through the rods.

At the end of the treatment the rods are withdrawn, with no radio active material remaining in the prostate. If combined with



High Dose-Rate
Brachytherapy (HDR)

External Beam Radiation Therapy, it is usually performed first, and the radiation follows approximately two weeks later. Results for High dose-rate Brachytherapy are similar to those 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.

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 they have significantly improved with greater experience. There is evidence of a small risk of pelvic cancers after brachytherapy.

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.

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. The treatment works by delivering high-frequency sound waves. These waves deliver a strong beam that is focused directly onto the cancer within the prostate and, by heating the cells, it kills them.

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 given 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 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 mpMRI diagnostic techniques. There are 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.

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.

Advantages and disadvantages

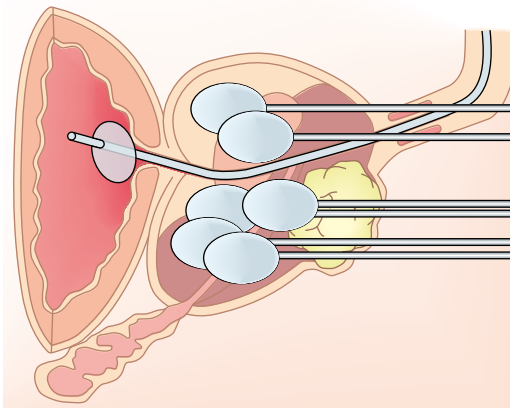
- Repeat treatments are possible if the cancer recurs
 - Normal activity can be resumed within a few days
 - No incisions are required, and there is no radiation toxicity
 - Impotence rates, against other treatments, are often better
- But:**
- Repeat treatments carry a greater risk of impotence and 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

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.

Ice balls forming in the prostate after insertion of the needles



Who is it for and what is involved?

Cryotherapy is normally considered by many urologists only as an option when radiotherapy has failed but cancer is still found in the

prostate. However, it can be offered as a primary treatment. 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. The patient

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

But:

- Side effects can include soreness of the perineum, some incontinence and a high rate of erectile and ejaculatory dysfunction

will normally be discharged from hospital within 24 hours after treatment but with a catheter in place. 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.

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.



three

Living with and Surviving Prostate Cancer



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Sexual Function

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 will affect sexual function and the ability to achieve a firm erection, which is controlled by the nerves and vessels that are intimately associated with the prostate and structures near the penis. Any treatment that damages the prostate will also result in loss or severe impairment of ejaculatory function and hence fertility.

Fertility

If fertility is important to you, you should discuss creating a sperm bank with your consultant. After any of the most common prostate cancer treatments – surgery, radiation therapy, or Hormone treatment – you will become infertile. During surgery to remove the prostate, the seminal vesicles and part of the vas deferens are also removed, which disrupts the connection to the testes. Orgasm may still occur, but ejaculation will be dry and natural conception will not be possible. Radiation therapy similarly destroys the prostate and seminal vesicles; chemotherapy and Hormone treatment are both harmful to sperm production.

Erectile Dysfunction

It is thought that around half of men over 40 may have a degree of erectile dysfunction (ED). ED

can limit your intimacy, affect your self-esteem and impact your relationship with your partner. As the nerves that control erections cover the surface of the prostate, any trauma to the area can result in a change in nerve function. 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. Penile size however, (both flaccid and erect) is often reduced post treatment particularly after surgery. Radiotherapy treatments may initially have less of an impact on erections, compared to surgery, but this can decrease over time rather than improve. Brachytherapy is similar to or slightly better than external beam radiotherapy in this respect. Results from HIFU have been fairly encouraging, especially where the treatment has been focussed specifically on the tumour area, called Focal HIFU. Few patients achieve erections after cryotherapy.

Men that have other diseases or disorders that impair their ability to maintain an erection, such as diabetes or vascular problems, will have a more difficult time returning to pre-treatment function. 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. Penile rehabilitation /physiotherapy using a vacuum pump is often recommended.

Treatments for Erectile Dysfunction

There are a variety of treatments for erectile dysfunction, these include:

Viagra, Cialis, Levitra pills - all of which are available on normal prescription through your GP and are also available across the counter in chemists. They work by enhancing the effects of chemicals that increase blood flow into the penis. They rely on there still being some degree of activity in the nerves concerned with sexual function. There are different strengths and side effects can be experienced.

Alprostadil (MUSE) - available as a small pellet that is inserted into the urethra at the tip of the penis. It works because alprostadil acts directly on the penile blood vessels to increase blood flow and then potentially produce an erection. It may be successful where nerve function is completely lost. Around 40% to 60% success rate has been reported. There are different strengths and side effects can be experienced.

Alprostadil (Caverject) - uses the same drug as MUSE but is delivered by injection into the penis. Around 60% to 85% success rate is reported. There are different strengths and side effects can be experienced.

Alprostadil (Cream) - this is fairly new to the market. Applied to the tip of the penis, it works again to stimulate blood flow.

Vacuum Pump - by creating a vacuum, it forces blood into the penis, the subsequent erection is maintained by rolling a rubber ring onto the base of

the penis so that the blood does not escape. Around 80% to 90% success rate reported.

Penile Implant - a surgically inserted penile implant that can be almost 100% successful. It uses a small pump in the scrotum, which when pressed, releases fluid from a small balloon into a plastic tube inserted in the penis, which pulls it up into an erection. The procedure is now available on the NHS.

It's important to know there are treatment options beyond medication that are safe and effective. Each treatment option has varying degrees of success and reliability, with some maybe more effective or satisfying than others. Most treatments can be at some cost to spontaneity. A penile implant is a unique permanent solution, because it allows you to have intimacy wherever, whenever and for as long as you want, with no medication side effects. Consult your doctor to see which option could be right for you. Discussion with your partner is essential.

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.

Hormonal treatments particularly can 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.

Urinary Function

Problems with passing urine can often result from prostate cancer treatments, other conditions such as diabetes, multiple sclerosis, Parkinson's disease, stroke or simply the ageing process. Urinary incontinence tends to fall into three categories:

Stress Urinary Incontinence – involuntary leakage when coughing, sneezing or physical exertion.

Urge Incontinence – leakage with an overwhelming need to urinate.

Mixed Incontinence – leakage with both exertion and urgency.

Urinary incontinence after surgery can affect most men, but over time the majority of men will gain control of leakage problems once muscles have recovered.

There are two sphincter muscles that keep men continent, the internal urethral sphincter and the external urethral sphincter. The internal sphincter is found at the bottom of the bladder, called the 'bladder neck,' and in the prostate. During surgery this is removed, because the prostate cannot be taken out without removing this sphincter.

The external sphincter is the muscle used to stop the urine stream and can

be strengthened with pelvic floor muscle exercises. Normally, an intact, healthy external sphincter is sufficient to provide continence. However, after radical prostatectomy, there can be some damage or dysfunction of this sphincter, which can prevent a man recovering bladder control. This may be due to damage to the nerves, blood supply, supporting structures, or the muscle itself, as the external sphincter is located at the apex of the prostate gland. Nearly all men will have some form of leakage immediately after the surgery, but this will improve over time with strengthening exercises.

Radiation therapy targets the prostate and the urethra runs through the middle of the gland, so both will receive radiation. Long-term leakage is rare, but frequency and urgency can be experienced. Radiation cystitis occurs when the lining of the bladder and urethra has been irritated by the radiation. Symptoms include frequency or difficulty in urinating, also a burning sensation while urinating, and passing blood. Cystitis can appear within the first few days of treatment, but some men don't get symptoms until months or even years after treatment.

Brachytherapy can cause the prostate to swell and block the urethra, leading to urine retention. It can also cause the urethra to become narrow – this is called a stricture.

Some lifestyle modifications can help:

- Try to avoid drinks containing caffeine
- Fizzy drinks may exacerbate symptoms
- Alcohol can increase urgency
- Try to increase time between visits to the toilet, as this will help the sphincter muscle to strengthen
- Do not try to hold out at night – it will only keep you awake
- If you are overweight, try to lose a few pounds
- Carry out regular pelvic floor exercises.

Pelvic floor muscle training

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.

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 performed 100+ times each day, 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 pelvic floor exercises prior to

treatment are beneficial, they can do no harm, and they may well help you get into the habit of routinely exercising the right muscles.

Long-term Severe Incontinence

It must be emphasised that severe long-term incontinence is rare, and nearly all men recover continence after treatment within a few 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 external 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, and men usually gain full continence after 3–6 months or less. In up to 5% of cases, however, this can remain a problem after a year, requiring the daily use of incontinence pads. 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 synthetic mesh and is implanted entirely inside the body during an operation under general anaesthetic. Through a small cut in the skin, the two ends of the sling are passed underneath the urethra and out through the pelvic area into the

upper thigh on each side. It is then tightened enough to lift and partially compress the waterpipe. It is a minimally invasive procedure, the device operates automatically and most patients are continent immediately following the operation.

There can be some inflammation, pain and bruising at the wound site, but this will diminish with time. Very occasionally, urinary retention occurs, usually caused by incorrect sling tension, and then a catheter may be needed for a short period and further surgical intervention may be required if normal urination is not restored after the catheter is removed.

Success rates of 54.6% to 94.6% have been reported from six clinical studies involving more than 500 patients. In a study of 42 patients, 94.4% would recommend the procedure to a friend.

Note: Following the MASTER trial (AUS v. SLING) that took place in 2017/18 the 'sling' operation has been suspended in some NHS centres until a report has been finalised on the outcomes of the procedure. It may very well be reintroduced as an alternative to the AUS at a later date.

The Artificial Urinary Sphincter (AUS)

The simplest way to describe this device is that it is like a miniature blood pressure cuff that is inserted around the urethra at the base of the bladder. The fitting of an AUS requires an operation done under full anaesthetic.

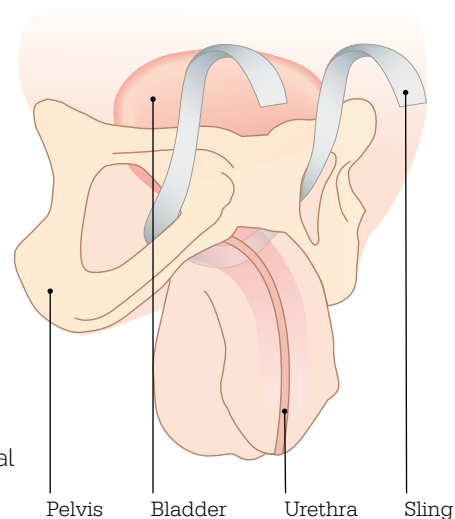
There are three parts to fitting this urinary control system:

- an inflatable cuff fits around the urethra
- a pump with a switch, is implanted in the scrotum
- a small balloon reservoir is implanted in the abdomen

The device works by pressing the switch in the scrotum several times, this deflates the cuff around the urethra by pushing fluid from it into the balloon. The pressure on the urethra is thereby released allowing urine to flow, after a few minutes the cuff self-closes once the balloon reservoir refills the cuff with fluid, closing off the urethra again.

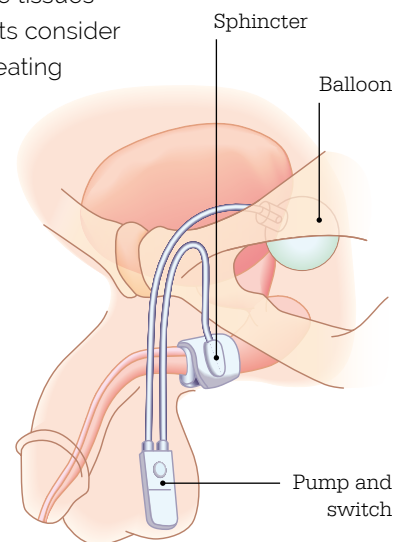
After the insertion of the device it is not used for several weeks to allow the tissues involved to recover. Many urologists consider this to be the 'gold standard' for treating male urinary incontinence. Following the operation there can be some pain, discomfort and bruising at the wound site, but the procedure can help restore quality of life and should alleviate the problem considerably.

In a study of 50 patients, 90% reported satisfaction, 96% would recommend the implant to a friend.



The Sling

Artificial Urinary Sphincter





Bowel Function

Damage to the rectum during prostate cancer treatment can result in bowel problems, including rectal bleeding, diarrhoea, or urgency. With a radical prostatectomy it is very rare (less than 1%) for men to have altered bowel function after this surgery. However, with radiation therapy, damage to the rectum is more likely to occur. The older forms of radiation therapy (called 3D conformal) can increase rectal side effects significantly. Using more modern radiation therapy (IMRT or IGRT), it is now very rare to

have moderate or severe bowel problems, but the possibility still exists.

During radiation therapy you may experience softer stools and diarrhoea (less than 10%). A new NICE approved technique called SpaceOAR Hydrogel® uses a gel that is injected between the prostate and the rectum to increase the distance between them. It has been shown to reduce the possibility of rectal damage from radiation in men where increased risks of rectal damage have been identified (see page 33).

The Clinical Nurse Specialist

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 a Nurse Specialist:

"From the time of diagnosis, each patient should have access to a specialist cancer nurse who can offer psychosocial support and continuity of care. Patients should, whenever possible, be offered contact details for others who have experienced similar cancers or treatments".

The 2019 NICE Prostate Cancer guideline also states:

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

"A Urologist or specialist nurse should advise people with prostate cancer about potential longer-term adverse effects of treatment and when and how to report them".

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

'Offer people 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!



Health of Survivors of Prostate Cancer

Survivors of prostate cancer treatment tend to suffer more health problems than other men of a similar age. After cancer treatment, particularly if on Hormone treatment, patients can lose previous fitness levels and put on weight. More than 30% will die of cardiovascular disease.

Health related problems caused by your prostate cancer treatment are likely to be even greater if you are overweight, have high blood pressure or are a smoker. Some cancer treatments can also cause an increase in weight, blood pressure, blood sugar and cholesterol levels, all of which can lead to an increased risk of heart disease, stroke and type 2 diabetes.

Low Testosterone

Around 50 per cent of prostate cancer patients receive hormone treatment which lowers the levels of testosterone in the body (prostate cancer thrives on testosterone). Unfortunately low levels of testosterone encourage the body to store fat around the abdomen (tummy), a bit like a 'spare tyre'. We need fat under the skin to keep us warm, but fat stored around the abdomen is different. Having a lot of abdominal fat is linked with an increased risk of advanced or aggressive prostate cancer. Abdominal fat produces substances which cause inflammation and also prevents sugar

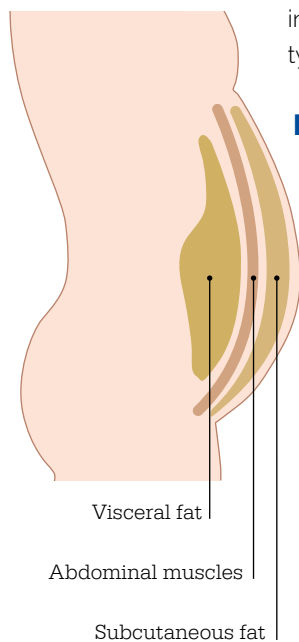
getting into the parts of the body it needs to reach. To compensate, insulin production increases and this promotes insulin-like growth factor (IGF) which can stimulate the growth of prostate cancer.

Low testosterone levels caused by some prostate cancer treatments can also cause muscle wastage which, combined with an increase in weight, makes exercise more difficult. So a cycle often develops where a man becomes heavier and more unfit as time goes on, leaving him vulnerable to health problems even if his prostate cancer has been successfully treated.

Hormone treatment can change the way your body handles fat in as little as three weeks, so these health changes can happen quickly.

For a man, if your waist size is 94cm (37 inches) or more, you're likely to be overweight. This means you have a higher risk of health problems, possibly including aggressive or advanced prostate cancer.

Abdominal Fat



Exercise, Diet and Lifestyle

Your waist-to-hip ratio is also a good indicator of health; research has shown that people with 'apple-shaped' bodies (with more weight around the waist) tend to face more health risks than those with 'pear-shaped' bodies (more weight around the hips). For a man, a waist-to-hip ratio of 0.9 or less is good. Men with a ratio greater than 0.9 will face a higher risk of heart disease and stroke.

Can Lifestyle influence Prostate Cancer Progression?

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. Many biochemical pathways are triggered during and after exercise, most of them having direct or indirect anti-cancer effects.

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. See his latest book 'Keep Healthy after Cancer' 2020 edition available via www.cancernet.co.uk.

Physical Activity and Exercise

Many trials evaluating exercise programmes have concluded that moderate activity can reduce fatigue, and 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 men on active surveillance, and a reduced risk of relapse after radical treatments.

Physical activity and exercise improve the flow of blood supply, even gardening (the green gym) or cleaning the house can be beneficial. A minimum of 30 minutes of exercise a day, 5 times a week is recommended, a combination of moderate and vigorous exercise. If you can do it, 3 to 5 hours a week of mostly vigorous exercise can be more beneficial.

There is growing evidence of the beneficial effects of exercise. In a USA study of 2705 men over a 10-year period, the number of deaths were 36% lower in men who walked on average one hour per day; recurrence of

Nordic walking and walking football are some of the exercises that you can take part in to help with keeping fit.



cancer was 49% lower in men taking 3 or more hours of vigorous activity per week; and 61% fewer died from cardiac events.

You might find it more fun to exercise with other people. Ask a friend to come with you or join a sports team or running group. If you often drive or take the bus for short journeys,



try taking a brisk walk instead. Try to spend less time sitting down. You could move about while you watch TV or choose more active video games. And don't forget to stand up regularly if you sit down to work.

You may think you are fit, but could you run for a bus or climb several flights of stairs? As we get older our muscles become weaker, but partly because we do less.

To keep fit you need to do more. Just walking may not be enough. As well as aerobic exercise one needs strengthening and toning exercises and activities to maintain joint mobility, flexibility, balance and coordination. At least 2 days a week should include resistance training to help strengthen your muscles.

Find a sport or activity you enjoy or do lots of different ones so you don't get bored. Do not try too much at first, build up gradually.

Physical activity and impact on Prostate Cancer

- For adults, at least 150 minutes (2.5 hours) of moderate intensity activity (in bouts of 10 minutes or more) a week...or 75 minutes of vigorous intensity activity spread across the week
- or combinations of moderate and vigorous intensity activity
- Adults should also undertake physical activity to improve muscle strength on at least 2 days a week.

Aerobic
Exercise

Strengthening and
toning exercises

Exercise
Program

Joint mobility
and flexibility

Balance and
coordination

Going to the gym is commendable, with a personal trainer if affordable, but here are some other ideas: brisk walking, running e.g. find a 'park run' near you at www.parkrun.org.uk/, walking football, golf, Nordic walking, dancing, swimming, using fitness bands at home, or attending organised exercise classes such as Pilates or Tai Chi.

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.

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 and 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.

A Mediterranean diet has enormous health benefits and improves the immune system. It can reduce the risk of cardio-vascular disease.

It is plant-based, rich in fruits and vegetables, nuts and oily fish. It provides for moderate intake of poultry and only low intakes of red or processed meat, low intake of dairy foods and the avoidance of fizzy drinks.

Gut health is also very important. Live yoghurt can help to maintain the correct levels of healthy bacteria within the gut.

Pomi-T Trial

A substantial percentage of prostate cancer survivors and those on Active Surveillance are attracted to the potential benefits of a food supplement, 'Pomi-T', which is made from polyphenol-rich whole foods, namely pomegranate seed, green tea, broccoli and turmeric. This combination of food extracts has been shown, in a controlled trial, to help fight prostate cancer and slow PSA rise.



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 (National Cancer Research Institute) has stated that long-term vitamin and mineral consumption should be discouraged. Saw palmetto and genistein have not shown any benefit for either prostate cancer or BPH. Likewise, the two most recent trials of lycopene extracts among men on active surveillance or watchful waiting found no difference in PSA

We each have natural internal resources that, when supported in the right way, can have a powerful effect on our health and well-being.

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.

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.

Penny Brohn Cancer Care

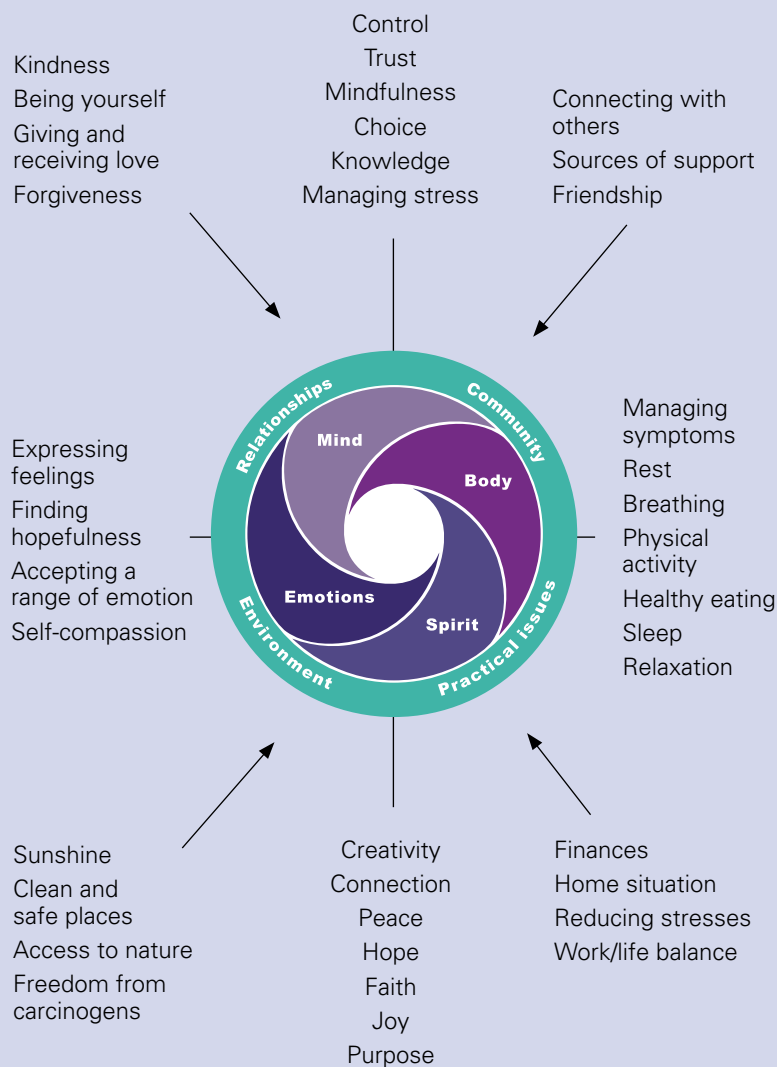
Based in Bristol, their Whole Life Approach recognises that to be healthy we need to pay attention to all parts of ourselves. Specifically, our mind, body, spirit and emotions, which are all closely connected and work together to support our immune system and its ability to keep us well. We strengthen our immune system by eating well, physical activity, doing the things we love and managing stress.

By learning how to self-care and increase our resilience, we are better able to face whatever life throws at us. This powerful knowledge offers hope and a sense of control for those with a cancer diagnosis. It doesn't mean we are offering the promise or expectation of cure, but it does mean we can confidently say we each have natural internal resources that, when supported in the right way, can have a powerful effect on our health and well-being.



What is the Bristol Whole Life Approach?

- The Bristol Whole Life Approach recognises that to be healthy we need to pay attention to all parts of ourselves. Specifically, our mind, body, spirit and emotions, which are all closely connected and work together to support our immune system and its ability to keep us well.
- We strengthen our immune system by eating well, physical activity, doing the things we love and managing stress.
- By learning how to self-care and increase our resilience, we are better able to face whatever life throws at us.
- This powerful knowledge offers hope and a sense of control for those with a cancer diagnosis.
- It doesn't mean we are offering the promise or expectation of cure.
- It does mean we can confidently say we each have natural internal resources that, when supported in the right way, can have a powerful effect on our health and well-being.



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



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Hormone Treatment

Androgen Deprivation Therapy (ADT)

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. By reducing the amount of testosterone in the man's body the cancer will be starved and shrink.

Hormonal treatment reduces the production of testosterone by the body. It is commonly called androgen deprivation therapy (ADT). It is mainly used in the following 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
- 3) It can also be used for men with curable cancers prior to radiotherapy or other treatments, which may make the treatment more effective.

Men whose tumours have already spread by the time they are first diagnosed with prostate cancer will often not undergo such treatment as surgery or radiation. Instead, their treatment journey will start with primary Hormone treatment, which initially should lower the PSA level considerably and stop the cancer progressing. Regular PSA readings are again adopted in order to monitor the cancer and make sure the treatment is effective.

If the 'first-line' hormone drugs 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 the chart on page 59 helpful. These drugs have different mechanisms of action and side effects.

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.

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®) administered by the injection of a slowly dissolving pellet either monthly or three monthly. The other is **Prostap** (leuporelin®) administered in liquid form.

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, all of 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 testicles 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 treatment

Intermittent Hormone treatment 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 become impotent and lose his sex drive; but unlike orchidectomy (surgical removal of the testicles) the process gradually reverses 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).

The STAMPEDE trial has shown that some men with high-risk cancer can benefit from a combination of chemotherapy and Hormone treatment. After completion of chemotherapy, hormone treatment with drugs such as **Zoladex** or **Prostap** will continue, either continuously or intermittently. 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. At this stage an anti-androgen such as Casodex may be used. The steroid

dexamethasone could follow, which can be used in conjunction with Radium-223. As steroids are only effective for a limited amount of time, newer drugs are now being used.

Abiraterone Acetate (Zytiga®)

This has helped 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 if an adverse reaction in the liver occurs.

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. However, it cannot currently be given after abiraterone, unless abiraterone has caused toxicity problems within the first three months of it being started. 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.

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 on the bones. It is very similar to calcium and, when injected into the bloodstream, is rapidly taken up in the bone. It is not taken up by lymph nodes and visceral metastases (such as liver or lung). 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 length of time as 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.

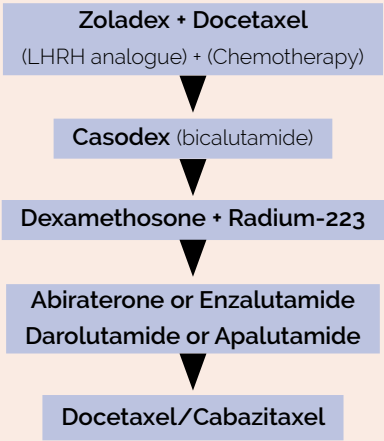
PSMA

Prostate-Specific Membrane Antigen (PSMA) radiotherapy - dubbed a 'search and destroy' method of treatment is based on imaging techniques which light up tumours, in order to plan future treatment. This new technique simultaneously delivers a radioactive payload, which experts described as delivering 'a bullet instead of a light'. It uses radioactive isotope, which binds to a protein on the surface of malignant cells, attacking them without damaging surrounding tissues.

Suggested treatment path

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.

The programme is only a guide and is flexible and can continue over many years. New treatments are being developed in many different countries. Keep optimistic. New second generation drugs to Abiraterone and Enzalutamide are currently being trialled, these are Darolutamide and Apalutamide.

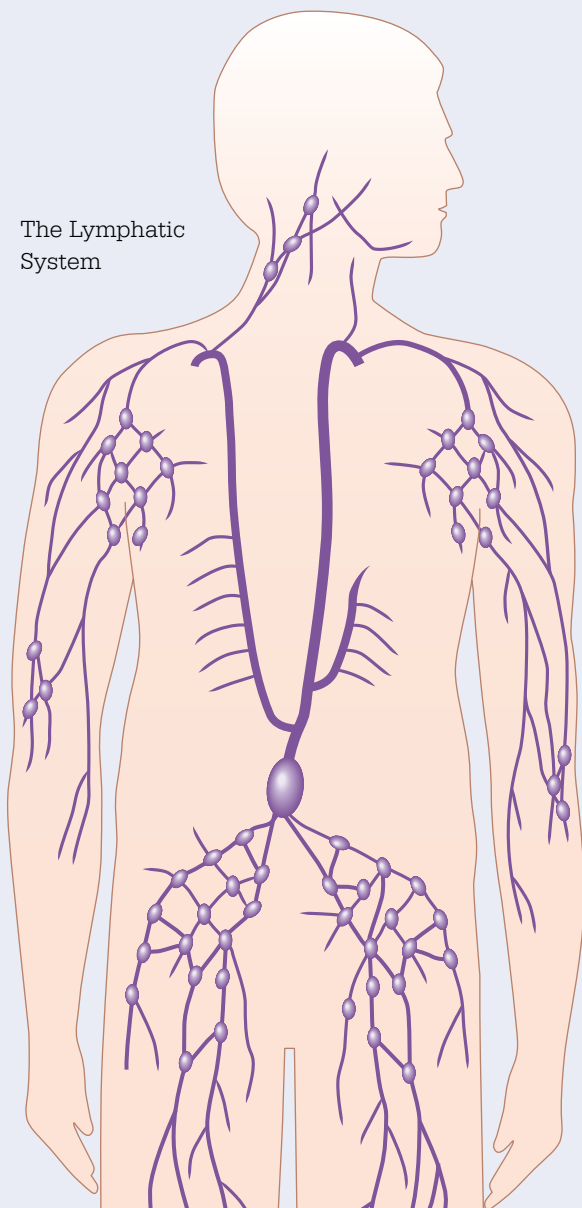


Spread of Prostate Cancer

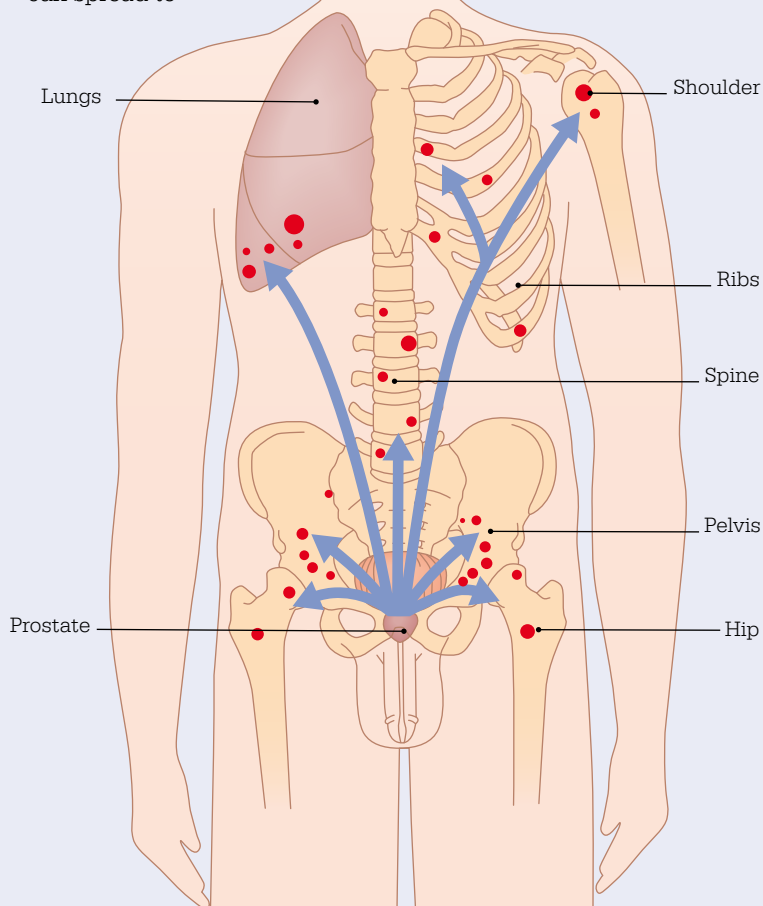
In time, prostate cancer cells may invade local tissues, or break away and spread to other areas of the body via the bloodstream or lymphatic system.

When these cells reach a new site they may form a new cancer, called a secondary tumour or metastasis. The areas most commonly affected are the lymph nodes, bones and lungs

The Lymphatic System



The areas where Prostate Cancer can spread to



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. Weightbearing 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, Prostop), designed to lower testosterone levels
- 2) metastasis of the cancer to the bones in the advanced stages, particularly to the ribs, hips and spine.

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.

Palliative Radiotherapy and Bone Pain

Radiotherapy is sometimes used for the treatment of bone pain associated with secondary tumours (called palliative treatment). 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 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.

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 early for men with metastatic and men with high risk non-metastatic cancer in conjunction with standard first-line Hormone treatment. This also has the advantage that the patient may be fitter and more able to withstand the side effects of chemotherapy treatment.

Commonly you may be recommended chemotherapy when standard hormone treatments have become ineffective and the more advanced drugs such as abiraterone and/or enzalutamide have not 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. The 'early chemotherapy' option should be discussed with your oncologist in detail following your diagnosis and full staging of the disease.

Prostate Cancer chemotherapy is usually administered with the 'first line' drug **docetaxel** (Taxotere®), which is always used in combination with a cortico-steroid such as

prednisolone, an anti-inflammatory that helps reduce nausea.

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. Prednisolone 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 can 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 fingernails 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, and 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 or 'second line' treatment. It has been approved by NICE for patients who have previously been given docetaxel. The side effects are slightly different, in particular, cabazitaxel does not tend to cause problems with numbness and tingling, that is common with docetaxel.



Recurrent Cancer

After your initial treatment for localised or locally-advanced prostate cancer is complete, the next stage of your recovery is monitoring and checking that all the cancer has been eradicated from the body. Some prostate cancer cells might have been able to spread outside the treatment areas before they could be removed or killed. At some point these cells may begin to multiply and produce enough PSA to become detectable by a blood test. Monitoring for recurrence or 'relapse' typically involves regular PSA tests, which are usually repeated every 6 months for the first 5 years, then yearly. A DRE prostate exam is sometimes performed every year but may be omitted if the PSA level is undetectable. If your PSA starts to rise, it could be a sign of your cancer returning, or it could be a sign of something else, dependent on which treatment you have had.

Surgery

If you had the prostate removed by surgery, your PSA should be undetectable with a reading of less than 0.01ng/mL, which is effectively zero, but by definition can never get all the way to zero. Following a prostatectomy, the most recognised confirmed PSA reading relating to recurrence is >0.20ng/mL. It is important to use the same lab for measuring your PSA result, as PSA levels can fluctuate from lab to lab dependent on machine calibration.

Radiation Therapy

Following radiation therapy, your consultant will need to look for confirmation from several PSA tests, because PSA can jump or 'bounce' for a short period, before returning to its low level, which is called your 'baseline' reading (as measured on two consecutive tests). PSA bounces can typically occur between 12 months and 2 years following the end of your initial therapy. If your PSA rises more than 2.0ng/mL above your baseline reading, that can be an indication of cancer recurrence.

The rate (or velocity) at which your PSA rises after prostatectomy or radiation therapy can be a significant factor in determining how aggressive your cancer is and can therefore be useful in deciding how aggressively it might need to be treated.

Recurrent Prostate Cancer after Surgery

Should your PSA start to rise after surgery, then 'salvage' radiation therapy could be right for you. EBRT is delivered to the area that the prostate used to occupy (called the prostate bed), the object being to eradicate any cancer cells that were left behind after surgery. Approximately 80% of men with a rising PSA after surgery have a regrowth contained within the prostate bed.

If the cancer has spread to other areas of the body and become metastatic then salvage radiation therapy is unlikely to be the best choice, as it will only target the prostate bed and potentially the nearby lymph nodes. Salvage radiation therapy (like all salvage therapies) is likely to cause an increase in side effects on top of those previously experienced with surgery.

Recurrent Prostate Cancer after Radiotherapy

Many patients now have a course of Hormone treatment in addition to radiation (EBRT), but should your PSA start to rise after this treatment has finished, there are options. Low dose-rate brachytherapy (seed implant), can treat the prostate provided there is no

spread outside the gland. Likewise, it would be possible to have cryotherapy (freezing), although men with higher-grade disease do not respond well to treatment. Surgery to remove the prostate is difficult after EBRT and very few surgeons would take this on, it would depend on several factors such as age and aggressiveness of the tumour.

Salvage HIFU can be used after several first-line treatments such as EBRT, brachytherapy, cryotherapy; and also if HIFU itself has been used as a first treatment. Men with a rapidly rising PSA are likely in the first instance to be given Hormone treatment in order to arrest the cancer growth, and imaging scans will then detect any spread outside of the prostate bed.



Emerging Therapies and Treatment Options

Because every cancer profile is different, each cancer needs a custom treatment.

Worldwide, there are many emerging therapies being tested on patients in clinical trials. There are some already showing highly promising results in those trials for the treatment of prostate cancer.

Precision Medicine

Scientists are working on ways of matching specific treatments to the particular genetic make-up of the patient and the tumour.

Cancer cells are mutations and each mutation is unique with its own weaknesses. Analysing the cancer and then having a custom-tailored treatment to attack those specific weaknesses has been shown to have the potential to be effective. But the scientists themselves say there is a long way to go.

PARP Inhibitors

PARP is an enzyme that helps repair DNA when it becomes damaged. A PARP inhibitor blocks the enzyme and keeps cancer cells from repairing their damaged DNA, causing them to die. PARP inhibitors, which include **olaparib** (Lynparza®), **rucaparib** (Rubraca®), **niraparib** (Zejula™), and others, are a class of precision medicine treatments that are effective against cancers with mutations in genes that repair damaged DNA. These 'DNA damage

repair' (DDR) genes include the breast and ovarian cancer risk genes BRCA1 and BRCA2. Approximately one-third of metastatic prostate cancer patients have these mutations in their tumours and may be candidates for treatment with PARP inhibitors. These drugs need further studies and trials, before being approved by NICE for use in this country, but it is hoped that in the future, screening of metastatic prostate cancer patients to identify those who have gene mutations and may benefit from PARP inhibitors will become common practice.

The Immune System

Our immune system works by protecting the body and is trained to fight infection, illness and disease; it can also protect us from cancer developing. It is doing this continually and is daily killing cancer cells without us realising it, by means of its killer T-cells. T-cells have proteins on them that turn on an immune response and other proteins that turn it off. These are called checkpoints. The immune system includes the lymph glands, spleen and white blood cells. Normally it can detect and destroy faulty cells in the body, stopping cancer developing. However, tumours have a few tricks they can play on our immune system such as:

- The cancer cells produce signals that stop the immune system from attacking it

- The cancer cells hide or escape from the immune system
- The immune system recognises cancer cells but is too weak to kill them

What is Immunotherapy?

Immunotherapy has become a standard treatment for some types of advanced cancer, both lung and skin cancers have been treated with immunotherapy drugs. It is now being developed for advanced prostate cancer patients. It works by helping the immune system to recognise and attack cancer cells and can be delivered on its own or with other prostate treatments such as chemotherapy or radiotherapy. Some treatment types of immunotherapy are also called targeted treatments or biological therapies.

Some men with otherwise untreatable prostate cancer can benefit from an immune system-stimulating treatment which could help prolong their life, or even stop their cancer growth entirely. Previous trials using immunotherapy in prostate cancer have been unsuccessful, but the latest research examined the genetics of the tumours.

A UK trial of 258 men using a drug called pembrolizumab, found that immunotherapy can benefit some patients with advanced prostate cancer, most likely those patients who have specific DNA repair mutations within their tumours. When treated they lived much longer. As the therapy will not work for

all patients, the next stage is to predict who would best respond to the treatment.

Still at a very early stage, an emerging treatment is CAR-T cell therapy which involves taking out a person's own immune T-cells, altering their DNA to spot cancer cells, and then putting them back into the patient to seek out and destroy tumours.

Immune Checkpoint Inhibitors

Immune checkpoint inhibitors are a class of immunotherapy that activate tumour-killing immune cells. **Pembrolizumab** (Keytruda®) is one of a range of drugs called 'checkpoint inhibitors' being developed by pharmaceutical companies; they are also described as a Monoclonal Antibody (MABs) or targeted treatment. Antibodies are found naturally in our blood and help us fight infection. MAB therapies mimic natural antibodies, but are made in the laboratory. MABs trigger the immune system by attaching themselves to proteins on cancer cells, making it easier for our own cells to find and attack the cancer cells. By stopping the cancer turning off the immune system, the body can keep on attacking the tumour.

Many studies are underway in prostate cancer to test other checkpoint inhibitors, including pembrolizumab, **ipilimumab** (Yervoy®), **nivolumab** (Opdivo®), **durvalumab** (Imfinzi™), **atezolizumab** (Tecentriq®), and **avelumab** (Bavencio®) alone and in combination with various therapies including PARP-inhibitors, cancer vaccines, and radiation therapy.

Vaccines

Researchers are also testing vaccines to treat cancer. Normally vaccines help protect us from disease and are made from weakened or harmless versions of the disease they are intended to fight. A vaccine can stimulate the immune system into action, by recognising and attacking the harmless versions of the disease. Once the body has made these attacking antibodies, it can recognise the harmful versions of the disease and mount an attack against those cells. Researchers are developing vaccines to recognise proteins that are on particular cancer cells, which helps the immune system to recognise and mount an attack against those particular cancer cells.

Genetic Testing and Counselling

It has been known for a while that around 5% of men with prostate cancer inherit from their parents mutations in the genes responsible for repairing damaged DNA (which include BRCA 1 and BRCA2 but there are many more). Newer research suggests the percentage increases to over 11% in men with advanced prostate cancer. Men with these mutations are more likely to do better on certain types of treatment.

These results suggest that, in the future, men with advanced prostate cancer should be tested for DNA damage repair mutations as it could improve their chances of getting the right treatment. In those cases where such a mutation is found the man's family may then be offered genetic counselling and testing for the DNA damage repair mutations.

Proton Beam Therapy

For men with early-stage, localised prostate cancer, conventional radiotherapy uses photons that produce high-energy radiation beams that destroy the cancer cells, but to get to them the beams must pass through healthy tissue and the beams also carry on beyond the tumour site, this can cause damage to other organs, particularly the rectum, and create side effects.

The potential advantage of **protons** over **photons** is that there may be significantly less collateral damage. The proton beam can be very accurately focused such that the major part of the energy is targeted at the cancer to be treated. Damage to tissues surrounding the cancer is significantly reduced. It should be noted that this type of therapy is only suitable for around 15% of all cancers.

Currently the therapy is employed for eye and some brain cancers, but a small number of patients have been treated for prostate cancer with promising results. By 2020 the UK should have 4 Proton Beam Centres: two NHS units in Christie Hospital Manchester and University College Hospital, London; two privately funded units at the Rutherford Cancer Centres in South Wales and Reading.

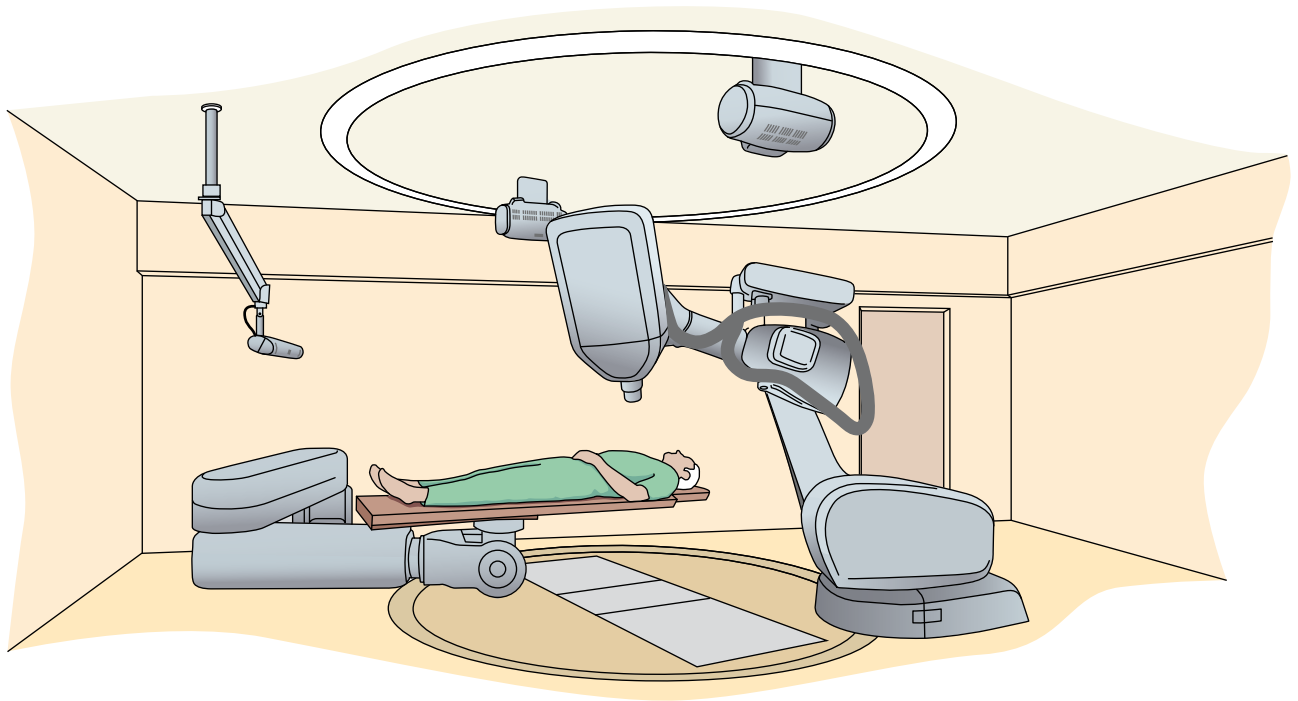
Proton beam therapy is yet to be widely used in the UK, but considerable experience has been gained in other countries. Long-term outcomes are promising and increasing data will become available.

Stereotactic Ablative Radiotherapy (SABR)

CyberKnife® is one of several types of radiotherapy machine that can deliver SABR. This form of radiotherapy uses pencil-like beams of radiation that are directed from different angles precisely onto the tumour. The X-rays are contained in a robotic arm, 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, 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 can 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 certain prostate cancers that would benefit from this treatment. Fewer treatment sessions, using a higher dose than conventional radiotherapy, are generally needed. However, it has not yet been proven whether this method is any safer or better than IMRT or IGRT.

There are currently only a few NHS hospitals and private clinics in the UK that have CyberKnife®. These include the Royal Marsden Hospital, St Bartholomew's Hospital and some London clinics.



Clinical Trials

About Clinical Trials

Every year in the UK, many people take part in clinical trials and every trial is reviewed by an Ethics Committee before being allowed to take place. All trials are designed so risk to those taking part is kept to a minimum. Each trial has strict criteria, relating to those people allowed and suitable to take part and everyone on a trial is monitored carefully, with safety and well-being a priority. Anyone taking part can withdraw from a trial at anytime and it will not affect your NHS treatment programme. Results of a trial are made available to those taking part.

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 that could run into thousands.

Patients are divided into different 'arms' of a study: 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.



Trials are run across many of the teaching hospitals of the UK. An individual trial may be recruiting across different UK trials units, as well as worldwide. So, it is important to find the trial 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, select 'prostate cancer' in the search box and find a suitable trial. In the first instance it is best to request your GP to forward your name to the appropriate unit for evaluation. The trials website is not always up to date, so it

is worth a call to the unit to ensure the trial is still recruiting.

There are a high number of prostate cancer trials currently recruiting and under evaluation, too many to list in this booklet. Comprehensive information about trials and a list of prostate cancer-specific trials can be found on the following website address:

<https://www.cancer.gov/about-cancer/treatment/clinical-trials> or visit the Cancer Research UK website: **<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial>**

Should you want to enter a trial, remember you have to fit the trial criteria and need to be referred by either your hospital consultant or GP.

Other Sources of Support and Information

National Federation of Prostate
Cancer Support Groups (Tackle)
Helpline **0800 035 5302**
www.tackleprostate.org

Prostate Cancer UK
National Help line: **0800 074 8383**
www.prostatecanceruk.org

Macmillan Cancer Support
Help line: **0808 808 0000**
www.macmillan.org.uk

Cancer Research UK
Help line: **0808 800 4040**
www.cancerresearchuk.org

Penny Brohn UK
Help line: **0303 3000 118**
www.pennybrohn.org.uk

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Glossary of terms

antioxidant a substance that protects us from the dangerous free radicals

biopsy the removal of small samples of tissue for analysis

catheter a thin tube inserted into the bladder, usually via the penis

Gleason score the rating of the aggressiveness of the cancer

impotence the inability to achieve a useful erection

incontinence the inability to control urination or bowels

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

pathologist a scientist who studies the causes and effects of diseases, especially one who examines laboratory samples of body tissue for diagnostic or forensic purposes

perineum the area between the scrotum and the anus

prostatectomy an operation to remove the prostate

radiologist a person who uses X-rays or other high-energy radiation, especially a doctor specializing in radiology.

seminal vesicles organs that contribute fluid to the ejaculate

testosterone a male hormone secreted by the testicles

urethra the tube through which urine and semen flow

urologist a specialist in disorders of the kidneys/bladder/prostate systems

Abbreviations

ADT androgen deprivation therapy

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 Luteinising 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

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 to treat an enlarged prostate)

About PCaSO

Who we are

PCaSO Prostate Cancer Support Organisation was formed in 2002 from PSA Solent. During the last 18 years it has become one of the largest such groups in the country. We cover Sussex, Hampshire and Dorset, though we have a number of members throughout the UK. It is run entirely by volunteers who, with their families, have been affected by this cancer.

We hold regular support meetings in the south from Bexhill to Bournemouth, and have a membership of around 1,000. Our meetings are supported by many urologists, oncologists, dietitians and researchers in the area, who come along to give us talks on a variety of prostate cancer related topics. Meetings are open to all, and there is always the opportunity to meet and talk to fellow sufferers over refreshments at one of our patient forums. Our help line and website are available for anyone with concerns.

Our newsletter **Updates** keeps members informed of our activities with a range of articles. We raise money for support to our members, for free PSA Testing awareness events, for equipment needed in local hospitals, and for research. Besides this information booklet, we produce a number of individual leaflets to help raise awareness. .

Membership.

Our membership fee is currently just £12 life membership, which includes both you and your partner, though we invite donations and standing orders. If you would like to join us, please contact our membership secretary, whose address is on our website, or download a membership form direct from our site www.pcaso.org or phone our help line 0800 035 5302.

Tackle Prostate Cancer

PCaSO is one of some 90 group members of Tackle Prostate Cancer, the campaign name of The National Federation of Prostate Cancer Support Groups which is the only national independent voice for prostate cancer patients. They campaign nationally on our behalf and run regular workshops for member groups.



National help line number: 0800 035 5302.

Website: www.tackleprostate.org



www.pcaso.org

info@pcaso.org

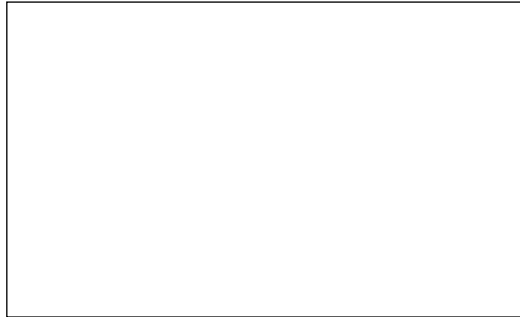
Medical Advisors to PCaSO

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Prof. Chris Parker, BA MRCP, MD, FRCR

Dr Angus Robinson, MBBS, MRCP, FRCR

Your local Support Group contact:



tackle

prostate cancer

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HELPLINE 0800 035 5302

Manned by prostate cancer patients 365 days of the year

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