

NCCN Guidelines for Patients®

Version 1.2015

Prostate Cancer



Available online at NCCN.org/patients





Prostate Cancer

Prostate cancer is the most common type of cancer in men living in the United States. Learning that you have prostate cancer can feel overwhelming. The goal of this book is to help you get the best cancer treatment. This book presents which cancer tests and treatments are recommended by experts in prostate cancer.

The National Comprehensive Cancer Network[®] (NCCN[®]) is a not-for-profit alliance of 26 of the world's leading cancer centers. Experts from NCCN have written treatment guidelines for prostate cancer doctors. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of prostate cancer. NCCN also offers patient books on colon and lung cancers as well as other cancer types. Visit **NCCN.org/patients** for the full library of patient books as well as other patient and caregiver resources.

Credits

NCCN aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Guidelines for Patients[®]. Each book presents the best practice for a type of cancer. The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]). Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients. Panels of experts create the NCCN Guidelines[®]. Most of the experts are from NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp. NCCN staff involved in making the guidelines for patients and doctors include:

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CALIFORNIA PROSTATE CANCER COALITION (CPCC)

"CPCC is pleased to endorse this important resource. We believe it to be the most understandable and comprehensive guide for men diagnosed with prostate cancer who want to really understand what the disease is about and what their specific treatment options are." prostatecalif.org

NATIONAL ALLIANCE OF STATE PROSTATE CANCER COALITIONS (NASPCC)

"NASPCC strongly endorses the NCCN Guidelines for Patients: Prostate Cancer, as an invaluable resource for patients and others. It is a reliable wealth of important information about prostate cancer, in a readable and understandable format." www.naspcc.org

PROSTATE HEALTH EDUCATION NETWORK (PHEN)

"Knowledge is the best defense against prostate cancer. This NCCN Guidelines for Patients will help patients gain the knowledge they need." prostatehealthed.org

ZERO - THE END OF PROSTATE CANCER

"Every 19 minutes a man loses his battle with prostate cancer. NCCN's Guidelines for Patients is a premier resource in helping men and their families to be proactive and make informed decisions. By advancing research, encouraging action, and providing education and support, we can create Generation ZERO - the first generation of men free from prostate cancer." zerocancer.org

Supported by NCCN Foundation®





The NCCN Foundation supports the mission of the National Comprehensive Cancer Network[®] (NCCN[®]) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of books for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

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Who should read this book?

This book is about treatment for an adenocarcinoma of the prostate. About 98 out of 100 men with prostate cancer have an adenocarcinoma. Women don't get prostate cancer because they don't have a prostate. Patients and those who support them caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with doctors what care is best.

Where should I start reading?

Starting with Part 1 may be helpful. It explains what prostate cancer is. Knowing more about prostate cancer may help you better understand its treatment. To learn how doctors plan treatment, read Parts 2 and 3. Parts 4 through 7 address prostate cancer treatment. Part 4 describes the treatments. Parts 5 through 7 are guides to treatment options. Part 8 gives tips for anyone making treatment decisions.

Does the whole book apply to me?

This book includes information for many situations. Your treatment team can help. They can point out what information applies to you. They can also give you more information. As you read through this book, you may find it helpful to make a list of questions to ask your doctors. The recommendations in this book are based on science and the experience of NCCN experts. However, these recommendations may not be right for you. Your doctors may suggest other tests and treatments based on your health and other factors. If other suggestions are given, feel free to ask your treatment team questions.

Making sense of medical terms

In this book, many medical words are included. These are words that you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don't be discouraged as you read. Keep reading and review the information. Don't be shy to ask your treatment team to explain a word or phrase that you do not understand.

Words that you may not know are defined in the text or in the *Dictionary*. Words in the *Dictionary* are underlined when first used on a page.

Acronyms are also defined when first used and in the *Glossary*. Acronyms are short words formed from the first letters of several words. One example is PSA for **p**rostate-**s**pecific **a**ntigen.



Prostate cancer basics

1

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1 Prostate cancer basics

6	What is the prostate?
7	How does prostate cancer start?
8	How does prostate cancer spread?
8	Review



You've learned that you have prostate cancer. It's common to feel shocked and confused. Part 1 reviews some basics about prostate cancer that may help you start to cope. These basics may also help you start planning for treatment.

What is the prostate?

The <u>prostate</u> is a gland that makes a white-colored fluid. Sperm mixes with this fluid and other fluids to form semen. Semen is ejected from the body through the penis during ejaculation. The fluid from the prostate protects sperm from the acid inside a woman's vagina.

As shown in **Figure 1.1**, the prostate is located below the bladder near the base of the penis. Urine from the bladder travels through the <u>urethra</u>, which passes through the prostate and into the penis. Above the prostate and behind the bladder are two <u>seminal</u> <u>vesicles</u>. Seminal vesicles are also glands that make a fluid that is part of semen.

Inside the prostate, 30 to 50 small sacs make and hold the white-colored fluid. The fluid travels in ducts to the urethra during ejaculation. Around the sacs and ducts is connective tissue.

The prostate begins to form while a baby is inside his mother's womb. After birth, the prostate keeps growing and reaches nearly full size during puberty. At this point, it is about the size of a walnut. <u>Testosterone</u> causes the <u>prostate</u> to grow slowly in most men. However, the prostate may grow to a large size in some men and cause problems passing urine.

How does prostate cancer start?

Cancer is a disease of cells—the building blocks of tissue in the body. Inside of cells are coded instructions for building new cells and controlling how cells behave. These instructions are called <u>genes</u>. Prostate cancer occurs when normal cells begin to grow faster or die slower. Either pattern causes a tumor to form. Some prostate cancers occur from changes, called <u>mutations</u>, in genes. Aging, being of African-American descent, and having family members with prostate cancer have been linked to a higher chance of getting prostate cancer. Other related factors include contact with Agent Orange, obesity, smoking, and poor diet. Not all men with these conditions get prostate cancer and some men without these conditions do. Prostate cancer is common among older men. However, prostate cancer in older men often doesn't become a problem.

Almost all prostate cancers are adenocarcinomas. Adenocarcinomas are cancers that start in cells that line glands and, in the case of prostate cancer, make semen. Adenocarcinomas of the prostate are the focus of this book.

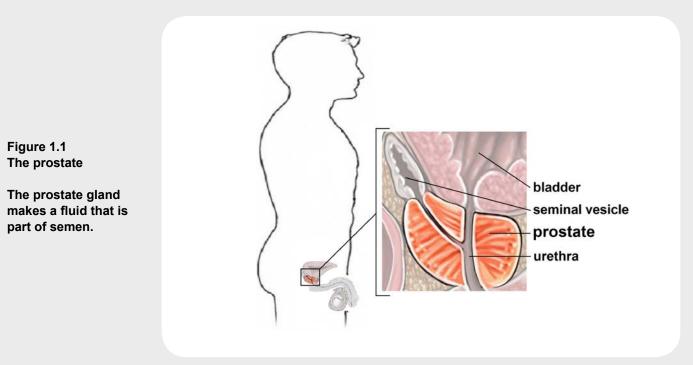


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How does prostate cancer spread?

Cancer cells don't behave like normal cells in three key ways. First, the changes in <u>genes</u> cause normal prostate cells to grow more quickly and live longer. Normal cells grow and then divide to form new cells when needed. They also die when old or damaged. In contrast, cancer cells make new cells that aren't needed and don't die quickly when old or damaged. Over time, cancer cells form a mass called the primary tumor.

The second way cancer cells differ from normal cells is that they can grow into (invade) other tissues. If not treated, the primary tumor can grow large and take over most of the <u>prostate</u>. It can also grow beyond the prostatic capsule and invade nearby tissues. This growth is called <u>extracapsular extension</u>. Third, unlike normal cells, cancer cells can leave the prostate. This process is called <u>metastasis</u>. Prostate cancer can then grow and form tumors in other parts of the body.

Prostate cancer can spread through blood or lymph vessels that are in the prostate. Lymph is a clear fluid that gives cells water and food. It also has white blood cells that fight germs. After draining from the prostate, lymph travels in vessels to lymph nodes. Lymph nodes are small disease-fighting organs that destroy the germs picked up by lymph. Lymph vessels and nodes are found all over the body.

Most men with prostate cancer will not die of this disease. However, prostate cancer is the second most common cause of death from cancer in men. Most prostate cancers grow slowly but some are aggressive and grow quickly. Why some prostate cancers grow fast is unknown and is being studied by researchers.

Review

- The prostate makes a fluid that is part of semen.
- Prostate cancer often starts in the cells that make fluid.
- Cancer cells may form a tumor since they don't die as normal cells do.
- Cancer cells can spread to other body parts through lymph or blood.
- Most men with prostate cancer will not die from it.
- Some men have prostate cancer that grows fast.

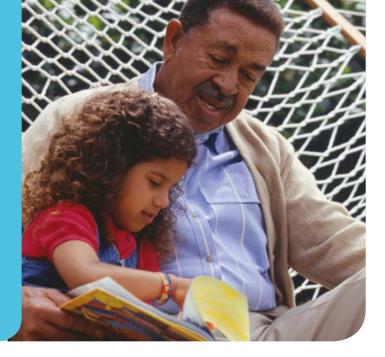


2 Cancer staging

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2 Cancer staging

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Cancer staging is a rating by your doctors of how far the cancer has grown and spread. The rating is based on test results. Doctors plan additional tests and treatment based on how much the cancer has grown. In Part 2, the tests and scoring system used for cancer staging are explained.

Prostate-specific antigen

<u>PSA</u> (prostate-specific antigen) is a protein made by the fluid-making cells that line the small glands inside the <u>prostate</u>. These cells are where most prostate cancers start. PSA turns semen that has clotted after ejaculation back into a liquid.

PSA levels can be measured from a blood sample since some of it enters the bloodstream. PSA levels are used for cancer staging, treatment planning, and checking treatment results. PSA levels discussed in this book include:

- **PSA level** is the number of nanograms of PSA per milliliter (ng/mL) of blood.
- **PSA density** is the PSA level in comparison to the size of the prostate. It is calculated by dividing the PSA level by the size of the prostate. The size of the prostate is measured with a <u>TRUS</u> (transrectal ultrasound).
- **PSA velocity** is how much PSA levels change within a period of time.

• **PSA doubling time** is the time it takes for the PSA level to double.

The larger the <u>prostate</u>, the more <u>PSA</u> it can make. Large prostates can be a result of cancer or other health problems of the prostate. Some medications can also affect the PSA level. PSA increases after ejaculations and vigorous exercise, especially running or bicycling. Thus, refrain from sex and exercise for 3 days before a PSA test. Then the PSA test will be more exact.

Digital rectal exam

Doctors use a <u>DRE</u> (digital rectal exam) to screen for cancer, rate the cancer stage, and assess treatment results. For this exam, your doctor will put a glove on his or her hand and then put lubricant on his or her index finger. Next, your doctor will insert a finger into your rectum to feel your prostate as shown in **Figure 2.1**. Your prostate can be felt since it is on the other side of the rectal wall. Bear in mind that not all parts of the prostate can be felt on this exam.

Figure 2.1 DRE

The prostate can be felt through the wall of the rectum.

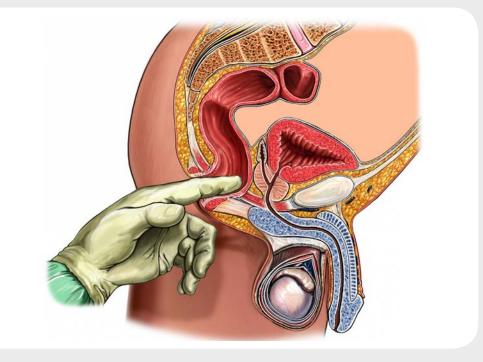


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Prostate MRI

Imaging tests make pictures (images) of the insides of your body. <u>MRI</u> (magnetic resonance imaging) uses a magnetic field and radio waves to make images. A 3-T, multi-parametric MRI of your <u>prostate</u> may help pinpoint where the cancer is in the pelvis and assess features of the cancer.

Prostate MRI can be used at many points of care. It is sometimes used for biopsies as discussed next. Prostate MRI may also be used to help decide whether to start and continue <u>active surveillance</u>. Active surveillance is discussed in Part 5. Another use for prostate MRI is to assess if you have cancer when other tests, given after treatment, suggest there's cancer. Read Part 6 for more information.

For MRI, you will need to lie on a table and be fitted with coil devices that emit radio waves. An endorectal coil may be used. However, the need for endorectal coil is debated among experts. An endorectal coil is a thin wire that is inserted into your rectum. To prepare for endorectal MRI, you may be asked to eat less and clean your bowel with an enema. A cover will be placed over the coil and gel will be applied before insertion. Once inserted, the device will be inflated to hold it in place.

During the MRI, you will be inside the MRI machine. Straps may be used to help you stay in place. You may be given a sedative beforehand if you feel nervous about the test. The machine makes loud noises but you can wear earplugs. After MRI, you will be able to resume your activities right away unless you took a sedative.

Prostate biopsy

Rising <u>PSA</u> levels and abnormal <u>DRE</u> findings may suggest cancer is present. However, the only way to know if you have prostate cancer is to remove tissue from your body and have a <u>pathologist</u> look at it with a microscope. A <u>biopsy</u> removes small samples of tissue for testing. Biopsies can also help your doctor assess how far the cancer has grown.

A prostate biopsy is a type of biopsy that removes tissue from the prostate. To prepare for the biopsy, your doctor may say to stop taking some medications and start taking others. Medications to stop taking include blood thinners like warfarin (Coumadin[®]) or antiplatelet drugs like aspirin or Plavix[®]. Your doctor may prescribe antibiotics to try to prevent an infection from the biopsy.

Right before the biopsy, local anesthesia may be given to numb the area. You'll feel a small needle stick and a little burning with some pressure for less than a minute. A numbing gel may also be applied to the area. You may feel pressure and discomfort during the biopsy but pain is often little or none.

The most common type of prostate biopsy is the transrectal method. To make sure the best samples are removed, a <u>TRUS</u> probe is inserted into your rectum. The TRUS uses sound waves to make a picture of your prostate that is seen by your doctor on a screen.

A newer method uses MRI along with TRUS. Before the biopsy, images with MRI will be made. These images will then be combined with TRUS during the biopsy. This allows for better tracking of the movement of your prostate. It also helps doctors pinpoint which tissue to remove. At present, this use of MRI is not common practice. More research is needed. A spring-loaded needle will be inserted through the <u>TRUS</u>. Your doctor will trigger the needle to go through the rectal wall and into your <u>prostate</u>. The needle removes tissue about the length of a dime and the width of a toothpick. At least 12 samples called cores—are often taken. This is done to check for cancer in different areas of the prostate. Prostate biopsies aren't perfect tests. They sometimes miss cancer when it's there. If no cause for the high <u>PSA</u> is found, your doctor may order more biopsies.

Prostate biopsies often occur with no problems. However, <u>side effects</u> are possible. Some people have allergic reactions to anesthesia. Tell your doctor if you've had any problems with anesthesia in the past. The prostate <u>biopsy</u> may cause:

Often

- Blood in your semen (hematospermia) or urine (hematuria),
- Rectal bleeding,

Sometimes

• Infection,

Rarely

- Swelling of your prostate (prostatitis) or epididymis (epididymitis),
- Inability to empty your bladder (<u>urinary</u> retention), and
- Hospitalization.



Gleason score

The grading system for prostate cancer is called the <u>Gleason score</u>. The Gleason score is used by doctors to plan treatment. **Chart 2.1** briefly describes what the scores mean.

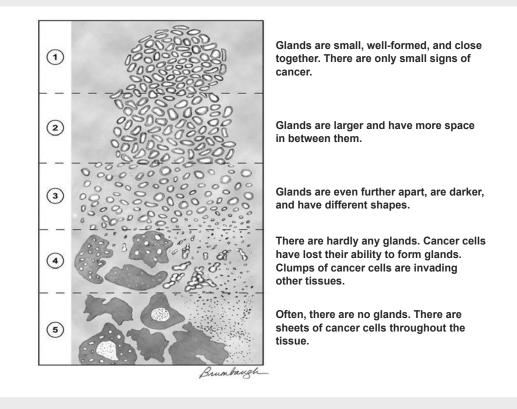
Results from the prostate <u>MRI</u>, <u>biopsy</u>, or both are used for scoring. First, the cancer is assigned two <u>Gleason grades</u>. The <u>primary grade</u> is the most common Gleason pattern. The <u>secondary grade</u> is the second most common Gleason pattern. Gleason grades are depicted in **Figure 2.2.** Glands comprised of cells with a grade of 1 or 2 can't be scored on a prostate biopsy. Therefore, Gleason grades range from 3 for glands made of cancer cells that look almost normal to 5 for cancer cells that aren't able to form glands.

The primary and secondary grades are added together to get the Gleason score. Gleason scores range from 2 to 10, but most prostate cancers are scored 6 to 10. Higher Gleason scores mean the cancer is more likely to grow and spread.

Chart 2.1 Gleason score summary

Gleason score	What does this score mean?
2–6	The cancer is likely to grow and spread very slowly. If the cancer is small, many years may pass before it becomes a problem. Thus, you may never need cancer treatment.
7	The cancer is likely to grow and spread at a modest pace. If the cancer is small, several years may pass before it becomes a problem. To prevent problems, treatment is needed.
8–10	The cancer is likely to grow and spread fast. If the cancer is small, a few years may pass before the cancer becomes a problem. To prevent problems, treatment is needed now.

Figure 2.2 Gleason grades Cancers with higher Gleason grades are more likely to spread and need treatment.



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TNM scores

The AJCC (American Joint Committee on Cancer) staging system is used to stage prostate cancer. In this system, the letters T, N, and M describe a different location of cancer growth. Your doctors will assign a score to each letter. These scores will be combined to assign the cancer a TNM stage.

T = Tumor

The T score is a rating of the size and extent of the primary tumor. T1 tumors can't be felt or seen with imaging tests. They are found in tissue removed by biopsies or surgical treatment. For example, prostate cancer may be found in men who had an abnormal <u>PSA</u> level or who had an operation for urinary problems caused by an enlarged <u>prostate</u>. Prostate cancer discovered as a result of an operation for voiding problems is called an incidental finding.

- **T1a** means that incidental cancer was found in 5% or less of the removed tissue.
- **T1b** means that incidental cancer was found in more than 5% of the removed tissue.
- **T1c** tumors are found by needle <u>biopsy</u> that was done for a high PSA level.

T2 tumors can be felt by your doctor during a <u>DRE</u>. They also may be seen with an imaging test. T2 scores are based on cancer growth within the lobes—the left and right halves of the prostate. **Figure 2.3** displays the lobes. T2 tumors haven't grown outside the prostate gland.

- **T2a** tumors haven't grown beyond half of one lobe.
- **T2b** tumors have grown beyond half of one lobe but not to the other lobe.
- T2c tumors have grown into both lobes.

T3 tumors have grown outside the prostate. They have reached the connective tissue around the prostate, the <u>seminal vesicles</u>, or the neck of the bladder. This group is subdivided into T3a and T3b.

- **T3a** tumors have grown outside the prostate but not into the seminal vesicle(s).
- **T3b** tumors have grown outside the prostate and into the seminal vesicle(s).

N = Nodes

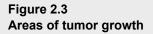
The N category reflects if the cancer has spread within nearby <u>lymph nodes</u>. Nearby lymph nodes include the hypogastric, obturator, internal and external iliac, and sacral lymph nodes. These nodes are shown in **Figure 2.4**. N scores for prostate cancer include:

- **NX** means it is unknown if there is cancer in lymph nodes.
- **N0** means that there is no cancer within the nearby lymph nodes.
- N1 means that the cancer has spread into the nearby lymph nodes. Most often, prostate cancer spreads to the external iliac, internal iliac, or obturator nodes.

M = Metastasis

The M category tells you if the cancer has spread to distant sites. Para-aortic, common iliac, inguinal, supraclavicular, scalene, and cervical lymph nodes are distant from the prostate. These nodes are shown in **Figure 2.4**. Prostate cancer tends to metastasize to bone then the lungs and liver. M scores for prostate cancer include:

- **MX** means it is unknown if cancer has spread to distant sites.
- **M0** means that there is no growth to distant sites.
- **M1** means that the cancer has spread to distant sites.
 - **M1a** is cancer that has spread to distant lymph nodes.
 - **M1b** is cancer that has spread to bone(s).
 - **M1c** is cancer that has spread to distant organs.



The primary tumor may grow throughout the prostate and into nearby organs.

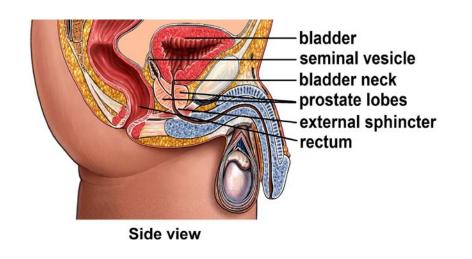


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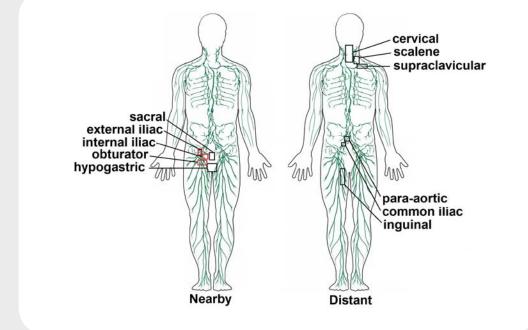


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Figure 2.4 Nearby and distant lymph nodes

Prostate cancer may spread in the body by traveling in a fluid, called lymph, to small disease-fighting organs, called lymph nodes.

2 Cancer staging

Review

- Prostate cancer is grouped into stages.
- Cancer stages are defined by the growth and spread of the tumor.
- PSA, DRE, and a prostate biopsy can help doctors assess the size of a tumor.
- The Gleason score is a grading system for how much prostate cancer cells retain their ability to form glands.
- Doctors rate the extent of cancer with T, N, and M scores.

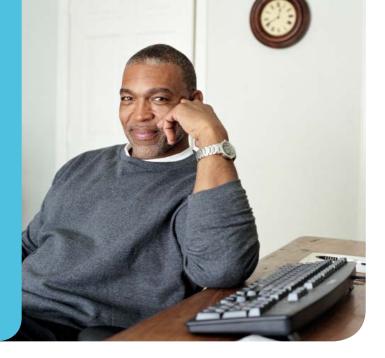


3 Treatment planning



3 Treatment planning

20	Life expectancy
21	Risk assessment
22	Imaging for metastases
24	Review



There are many sources of information that doctors use to plan treatment. The tests and the grading and staging systems used to assess the extent of the cancer were described in Part 2. The side effects of treatment that are listed in Part 4 and your personal preferences are other sources. Here, in Part 3, three more sources of information that doctors use are explained.

Life Expectancy

To help assess what tests and treatments you need, your doctor may determine the number of years you will likely live. These years are called your <u>life expectancy</u>. It may be hard to talk with your doctor about how long you might live. However, this information is very important for your health care.

Prostate cancer often grows slowly. If you're likely to die of other causes, having more tests and cancer treatment may have little or no benefit. Likewise, if the cancer isn't causing symptoms, there may be no benefit to having more tests.

How many years you may live is estimated with two sources of information. First, research on the general population tells how long the average man may live based on his age. See Part 8 for website information. The second source is your general health.

If you're in excellent health, the number of life years from the general population research is increased by half. If you're in poor health, the number of years is decreased by half. If you have average health, no change is made. See **Figure 3.1** for examples. This method may correctly predict length of life for a large group of men, but it can't predict without a doubt what will happen to you. Even so, it gives a starting point for suggesting treatment options.

Most prostate cancers diagnosed in America are found using <u>PSA</u> and are slow growing. Growth of prostate cancer can be estimated with tests. You and your doctor should begin talking about prostate cancer by comparing your <u>life expectancy</u> versus the threat to you by the prostate cancer.

Risk assessment

To plan the best treatment for you, your doctors will like to know:

- If and how far the cancer has spread,
- · How fast the cancer will grow,
- · How the cancer will respond to treatment, and
- Whether cancer will re-appear on tests after treatment (called a <u>recurrence</u>).

However, this information often can only be known over time or after cancer treatment has started. As such, your doctors will assess your chances (also called risk) for such events. <u>Risk groups</u> and <u>nomograms</u> are two tools that doctors use. Molecular testing is a newer tool that needs more research.

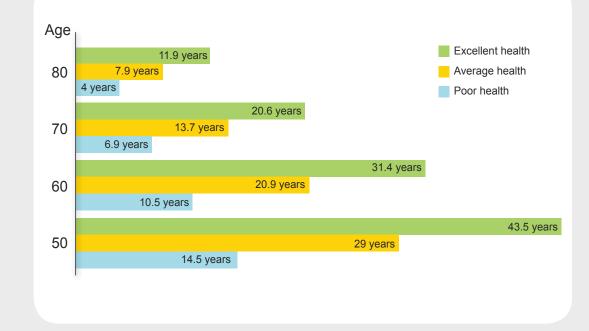


Figure 3.1 Examples of life expectancy

How many years a man is likely to live depends on his age and health.

Risk groups

<u>Risk groups</u> divide people with cancer into smaller subsets based on their chances of an event. Some risk groups are based on one piece of information while others use multiple pieces of information. In Part 5, treatment options are presented by risk groups for <u>prognosis</u>. Risk is based on TNM scores, <u>Gleason</u> <u>score</u>, and <u>PSA</u> values. NCCN experts recommend that these risk groups be used as a foundation to start talking about treatment options.

Nomograms

A <u>nomogram</u> uses data from a large number of men and complex math to predict risk. It can predict one person's risk better than a risk group. A nomogram predicts an event by taking into account similarities and differences among pieces of information. In this book, test and treatment recommendations are sometimes based on nomograms that predict how likely the cancer has spread to <u>lymph nodes</u>. Also, NCCN experts recommend that nomograms be used in addition to risk groups to better plan treatment. Websites with information on nomograms are listed in Part 8.

Molecular testing

Any of your body's molecules that can be measured to assess your health is known as a biomarker. There are ongoing biomarker studies for detecting prostate cancer and predicting its growth and spread. Molecular (or biomarker) testing can be used with risk groups and nomograms to predict how aggressive prostate cancer will be.

The Prolaris test and Oncotype DX GPS are molecular tests of prostate cancer. They have been studied and used more than other tests. Still, more research is needed. Both predict cancer progression among men with prostate cancer in or near the prostate (localized cancer). The tissue that was removed by the <u>biopsy</u> for diagnosis will be used for molecular testing.

Imaging for metastases

Imaging tests can help show if the cancer has spread to the lymph nodes or bones. If your <u>life expectancy</u> is more than 5 years or you have cancer symptoms, testing for <u>metastases</u> may help with treatment planning. Signs of metastases are listed in **Chart 3.1**. If you have these signs, you may get a 1) bone scan or 2) <u>CT</u> (**c**omputed **t**omography) or <u>MRI</u> scan of your pelvis. Your doctor may change his or her rating of the cancer stage based on these test results.

Most men have minor, if any, problems with imaging tests. There are usually no <u>side effects</u>. Depending on the test, you may need to stop taking some medicines, stop eating and drinking for a few hours, and take off any metal objects from your body. After an imaging test, you will be able to resume your activities right away unless you took a sedative.

You may not learn of the results for a few days since a <u>radiologist</u> or <u>nuclear medicine specialist</u> needs to see the pictures. A radiologist is a doctor who's an expert in reading images. A nuclear medicine specialist is a doctor who's an expert in tests that use radioactive substances.

Bone scan

A bone scan is suggested if you have signs or symptoms of bone metastases. For this test, a radiotracer will be injected into your vein. The most common radiotracer used for bone scans is technetium. A special camera will then take pictures of the dye in the bones. The radiotracer can be seen in your bones 2 to 3 hours after it is injected. You may be asked to drink water and empty your bladder to wash out any of the radiotracer that is not in your bones. **Figure 3.2** shows a machine that is used to take the pictures. You will need to lie still on the padded table for 45 to 60 minutes to complete the pictures. Prostate cancer in bone can damage the bone causing the bone to try in vain to repair itself.

Areas of bone repair take up more of the radiotracer than healthy bone and thus show up as bright or "hot" spots in the pictures. However, other health conditions besides cancer can cause bone repair. A <u>radiologist</u> can often tell what is and is not cancer in an abnormal bone scan.

Chart 3.1 Deciding factors for imaging tests

Test	Signs of metastases
Get a bone scan if you have a:	 T1 tumor and your PSA levels >20 ng/mL, T2 tumor and your PSA levels >10 ng/mL, Gleason score of 8 or higher, T3 or T4 tumor, or You have symptoms that suggest cancer is in bone
Get a pelvic CT or MRI if you have a:	 T3 or T4 tumor, or T1 or T2 tumor and nomogram results show >10% risk of cancer spread to the lymph nodes



Gamma Camera by Brendaicm available at commons.wikimedia.org/wiki/File:Gamma_ camera.jpg under a Creative Commons Attribution-Share Alike 3.0 Unported.



Figure 3.2 Bone scan machine

Doctors use bone scans to assess if cancer has spread to the bones.

CT or MRI

<u>CT</u> or <u>MRI</u> of your pelvis may show if your <u>lymph</u> <u>nodes</u> are enlarged. MRI was described in Part 2. MRI images are made with a magnetic field and radio waves. A CT scan takes many pictures of a body part from different angles using x-rays. A computer combines all the x-rays to make detailed pictures.

Getting a CT scan is like getting a MRI scan. Before CT, you may need to drink enough liquid to have a full bladder. A full bladder helps to keep the bowel away so the prostate can be better seen. During the scan, you will need to lie face up on a table. The table will move through the imaging machine. As the machine takes pictures, you may hear buzzing, clicking, or whirring sounds.

Fine-needle aspiration

If the CT or MRI scan suggests that the cancer has spread into your lymph nodes, a <u>fine-needle</u> <u>aspiration</u> can confirm if cancer is present. A fineneedle aspiration is a type of <u>biopsy</u>. It uses a very thin needle to remove very small pieces of tissue. A CT scan, MRI, or ultrasound machine is used to guide the needle into the lymph node. With a local anesthetic, this test causes little discomfort and doesn't leave a scar.

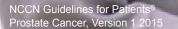
Review

- Doctors plan treatment using many sources of information.
- Life expectancy is the number of years you will likely live. It is sometimes used to plan treatment.
- Risk groups can be used to start talking about initial treatment options.
- Nomograms predict one person's risk better than risk groups and should be used to plan treatment.
- Imaging tests may be used to see if the cancer has spread beyond the prostate.
- A fine-needle aspiration may be done to test for cancer in lymph nodes.



Overview of cancer treatments

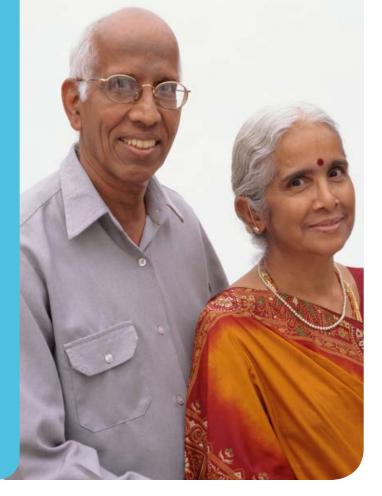
4



4 Overview of cancer treatments

26	Active surveillance
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Part 4 describes the main treatment types for prostate cancer. This information may help you understand the treatment options listed in Parts 5 through 7. It may also help you know what to expect during treatment. Not every man with prostate cancer will receive every treatment listed. Before any treatment, talk with your doctor about sperm-banking if you plan to have children.



Active surveillance

Small prostate tumors often have been found with <u>PSA</u> screening tests. They are also found in <u>prostates</u> removed because of benign prostatic hyperplasia. If small tumors grow slowly, they may not ever cause health problems, especially if you're older. Thus, some men would suffer needlessly from treatment <u>side effects</u> if all men with prostate cancer were treated. Another option is <u>active surveillance</u>. Active surveillance involves ongoing testing until treatment is needed. More information about this option can be found in Part 5.

Surgical treatment

Surgical treatment may be an option if you are healthy enough to have an operation. The goal of an operation is to remove all the cancer from your body. To do so, the tumor will be removed along with some normal-looking tissue around its rim. The normallooking tissue is called the <u>surgical margin</u>. Other tissue may be removed along with your prostate as described next.

Radical prostatectomy

A <u>radical prostatectomy</u> is an operation that removes the entire <u>prostate</u>, <u>seminal vesicles</u>, and sometimes other tissue. It is often used when the cancer appears not to have grown outside the prostate—T1 and T2 tumors. Less often, it is used when the cancer has grown outside the prostate but not into other organs.

There are four main types of radical prostatectomy. These types are described below. Results of a prostatectomy may be related to the experience of the surgeon. Surgeons who are experienced have better results. When choosing your surgeon, ask how many of these operations he or she has done. Going to a surgeon who has and continues to do many radical prostatectomies may result in a better outcome. Talk to other men with prostate cancer about their experiences.

There are a few steps to prepare for an operation. You may need to stop taking some medications to reduce the risk of severe bleeding. Eating less, changing to a liquid diet, or using enemas or laxatives will empty your bowel. Right before the operation, you will be given anesthesia. Anesthesia may be general, spinal, or epidural.

After a radical prostatectomy, a catheter will be inserted into your <u>urethra</u> to allow your urethra to heal. It will stay in place for 1 to 2 weeks. You will be shown how to use it while you're at home. If removed



too early, you may lose control of your bladder (urinary incontinence) or be unable to urinate due to scar tissue.

Open retropubic prostatectomy. This operation removes tissue through a cut that runs from your belly button down to the base of your penis. During the operation, you will lie on your back on a table with your legs slightly higher than your head. Before removing your prostate, some veins and your urethra will be cut to clear the area. Your seminal vesicles will be removed along with your prostate. After removing your prostate, your urethra will be reattached to your bladder.

Your cavernous nerve bundles are on both sides of your prostate. They are needed for natural erections. A <u>nerve-sparing prostatectomy</u> will be done if your cavernous nerves are likely to be cancer-free. However, if the cancer involves them, one or both bundles of nerves will be removed. If removed, good erections are still possible with aids, and orgasms can occur with or without these nerves.

It takes between 90 minutes and 3 hours to complete this operation. You may stay 1 to 2 days in the hospital. It takes about 2 weeks to feel very well, and 4 to 6 weeks to resume all normal activities. Open perineal prostatectomy. This operation L removes tissue through a cut in your perineum. The m

perineum is the area between your scrotum and anus as shown in **Figure 4.1**. During the operation, you will lie on your back with your legs spread open and supported with stirrups.

Your <u>prostate</u> and <u>seminal vesicles</u> will be removed after being separated from nearby tissues. Nerve sparing is possible but more difficult. <u>Lymph nodes</u> can't be removed. After your prostate has been removed, your <u>urethra</u> will be re-attached to your bladder.

This operation is completed in 1 to 3 hours. You may need to stay 1 to 2 days in the hospital. It takes about 2 weeks to feel very well, and 4 to 6 weeks to resume all normal activities. Laparoscopic prostatectomy. A newer retropubic method is the <u>laparoscopic prostatectomy</u>. This operation makes five small cuts, called ports, in your pelvis. Tools are inserted into these cuts to see and remove tissue. It takes between 90 minutes and 4 hours to complete this operation. You will likely leave the hospital the next day. It may take another 2 weeks at home to recover.

Robot-assisted laparoscopic prostatectomy.

A laparoscopic prostatectomy can be done with the help of a "robot." During this surgery, the surgeon will be in the room with you but not by your side. Instead, he or she will be at a desk that is equipped with a computer system. This system allows the surgeon to move robotic arms which hold the surgical tools used to perform the operation. **See Figure 4.2**. Robotic arms make more precise cuts compared to a surgeon's hand. However, surgeons can detect changes in the tissue by touching your organs during an open prostatectomy. These changes aren't detected when a robot is used.

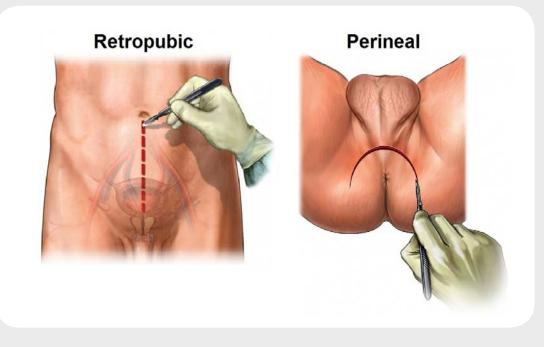


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Figure 4.1 Open prostatectomy

A prostate may be removed through one large cut in the pelvis or between the legs. Figure 4.2 "Robotic" prostatectomy machine

A prostate may be removed by a surgeon through "robotic" arms that hold surgical tools. The surgeon moves the robotic arms through a computer system instead of with his or her hands.



Laproscopic Surgery Robot by Nimur available at commons.wikimedia. org/wiki/File:Laproscopic_Surgery_Robot.jpg under a Creative Commons Attribution-Share Alike 3.0 Unported



Pelvic lymph node dissection

A <u>PLND</u> (**p**elvic lymph **n**ode **d**issection) is an operation that removes <u>lymph nodes</u> from your pelvis. In Part 5, PLND is recommended if you have a T1 or T2 tumor, you choose to have a prostatectomy, and a <u>nomogram</u> predicts you have a 2% or greater risk for cancer in your lymph nodes. Using a 2% cutoff, nearly half of men (48 out of 100) will be spared having a PLND. **See Figure 4.3**. Also, almost all men in this group who have cancer in their lymph nodes will be correctly staged and treated.

An extended PLND removes more lymph nodes than a limited PLND. It finds <u>metastases</u> about two times as often as a limited PLND. It also stages cancer more completely and may cure some men with very tiny metastases that haven't spread far. Therefore, an extended PLND is recommended if you're to have a PLND. It can be done with an open retropubic, laparoscopic, or robotic method.

Side effects of surgical treatment

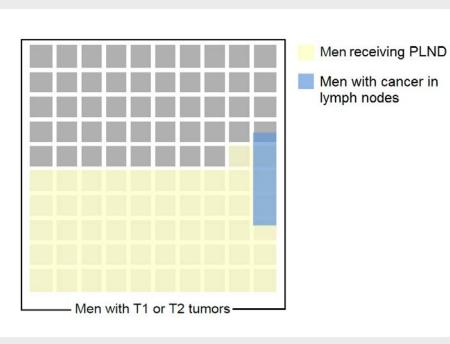
<u>Side effects</u> are unhealthy or unpleasant physical or emotional responses to treatment. You may experience side effects from the general anesthesia, prostatectomy, or the PLND. During the operation, you may have a serious loss of blood and require a blood transfusion. Serious risks of anesthesia and prostatectomy include heart attack and blood clots.

After the operation, general anesthesia may cause a sore throat from a breathing tube, nausea with vomiting, confusion, muscle aches, and itching. From the operation, you will have pain and swelling that often fade away within weeks. The PLND may rarely cause swelling in the legs due to the buildup of <u>lymph</u> (lymphedema) that will resolve over several weeks.

Almost every man has <u>urinary incontinence</u> and <u>erectile dysfunction</u> after a <u>radical prostatectomy</u>. These two side effects may be short lived, but for some men they are lifelong issues. You're at higher risk for erectile dysfunction if 1) you're older; 2) you

Figure 4.3 Nomogram results

When using a $\geq 2\%$ risk cutoff, most men with cancer in their lymph nodes will be correctly staged because they received a PLND.



Radiation therapy

have erectile problems before the operation; or 3) your cavernous nerves are damaged or removed during the operation. If your cavernous nerves are removed, there is no good proof that nerve grafts will help restore your ability to have erections. Aids are still needed.

Removing your prostate and seminal vesicles will cause you to have dry orgasms. You will no longer be able to father children through sex. Your prostatectomy essentially includes a vasectomy. Although not as common as erectile dysfunction, other sexual changes may include pain during orgasm (dysorgasmia), inability to have an orgasm (inorgasmia), curving of your penis (penile curvature), and a smaller penis (penile shrinkage).

Bladder control often returns within months after the operation, but you may not have full control. Stress incontinence is leakage of a little urine when coughing, laughing, sneezing, or exercising. It is caused by damage to the muscle at the base of the bladder. Overflow incontinence occurs when there is too much urine in the bladder because scarring blocks the full release of urine. Some men also have problems with bowel movements (defecating) for awhile after the operation.

Not all side effects of surgical treatment are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

Radiation therapy

Radiation therapy uses high-energy rays to treat cancer. The rays damage DNA (deoxyribonucleic acid). DNA is a chain of chemicals in cells that contains genes. This either kills the cancer cells or stops new cancer cells from being made. Radiation therapy is an option for many men with prostate cancer. Radiation therapy may be given to your pelvic lymph nodes as well as to your prostate. There are two ways to give radiation:

External beam radiation therapy

For prostate cancer, radiation is often given using a machine outside the body. This method is called EBRT (external beam radiation therapy). To receive EBRT, you first must have a simulation session. For simulation, imaging scans are used to help target the tumor with radiation.

Using the scans, your treatment team will plan the best radiation dose, number and shape of radiation beams, and number of treatment sessions. Beams are shaped with computer software and hardware added to the radiation machine. Radiation beams are aimed at the tumor with help from ink marks on the skin or marker seeds in the tumor.

During treatment, you will lie on a table in the same position as done for simulation. Devices may be used to keep you from moving so that the radiation targets the tumor. You will be alone while the technician operates the machine from a nearby room. He or she will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises. One session often takes less than 10 minutes. EBRT is given 5 days a week for about 8 to 9 weeks, although there is growing interest in shortening the length of treatment.

There are multiple types of EBRT. For prostate cancer, 3D-CRT (three-dimensional conformal radiation therapy) or <u>IMRT</u> (intensity-modulated radiation therapy) may be used. In <u>3D-CRT</u>, the radiation beams match the shape of your tumor to avoid healthy tissues. IMRT is a more precise type of 3D-CRT that may be used especially for more aggressive prostate cancer. The radiation beam is divided into smaller beams, and the strength of each beam can vary.

The <u>prostate</u> can slightly shift within the body. Tumors may also change shape and size between and during treatment visits. <u>IGRT</u> (image-**g**uided **r**adiation therapy) can improve how well 3D-CRT and IMRT target the tumor. IGRT uses a machine that delivers radiation and also takes pictures of the tumor. Pictures can be taken right before or during treatment. These pictures are compared to the ones taken during simulation. If needed, changes will be made to your body position or the radiation beams.

Often, <u>ADT</u> (androgen deprivation therapy) is used with <u>EBRT</u>. ADT is described later in this chapter. Many studies have shown that adding ADT to EBRT improves treatment outcomes when prostate cancers are more aggressive. ADT has <u>side effects</u> so it shouldn't be used unless needed. Some men require short-term (4 to 6 months) ADT while others are on ADT for 24 to 36 months.

Proton beams. 3D-CRT and IMRT are x-ray–based treatments. They use photon radiation beams. Photon beams are a stream of particles that have no mass or electric charge.

In recent years, some cancer centers have built radiation machines that use proton beams. Proton beams are a stream of positively charged particles that emit energy within a short distance. Some doctors think that proton treatment is better than x-ray–based treatment. One benefit would be less severe side effects. To date, research hasn't shown that proton treatment is any better or worse for treating cancer or causing side effects. Well-designed research on IMRT and proton treatment is ongoing. Thus, NCCN experts state that proton treatment can be an option if received at cancer centers with the proper equipment and experience.

SBRT. (Stereotactic body radiotherapy) is a newer treatment. It treats cancer with very precise, highdose beams. Receiving SBRT is much like getting other EBRTs except treatment is finished in about 5 visits. Research thus far has shown that SBRT and IMRT are alike in treating cancer and causing side effects. However, well-designed research of SBRT to assess long-term results is needed. Thus, NCCN experts recommend that treatment with SBRT be carefully decided. If chosen, it should be received only at cancer centers with the proper equipment and experience.

Brachytherapy

<u>Brachytherapy</u> is another standard radiation therapy for prostate cancer. This treatment involves placing radioactive seeds inside your prostate. Brachytherapy is also called <u>interstitial radiation</u>—a seed treatment. Brachytherapy may be used alone or combined with EBRT, ADT, or both.

The seeds are about the size of a grain of rice. They are inserted into your body through the <u>perineum</u> and guided into your prostate with imaging tests. Treatment planning is done beforehand to design the best course of treatment. You will be under general or spinal anesthesia when the seeds are placed. Brachytherapy can be given either as permanent LDR (low-dose rate) or temporary HDR (high-dose rate) therapy.

LDR brachytherapy uses thin needles to place 40 to 100 seeds into your prostate. Placement of the seeds is done as an outpatient procedure. The seeds usually consist of either radioactive iodine or palladium. They will remain in your <u>prostate</u> to give low doses of radiation for weeks or months. The radiation travels a very short distance. This allows for a large amount of radiation within a small area while sparing nearby healthy tissue. Over time, the seeds will stop radiating.

For <u>LDR brachytherapy</u>, seed placement is harder if you have a very large or small prostate, your urine flow is blocked, or you've had <u>TURP</u> (transurethral resection of the **p**rostate). Moreover, your chances of <u>side effects</u> are higher. If your prostate is large, you may be given <u>ADT</u> before LDR brachytherapy to shrink it. After the seeds are implanted, your doctor should measure the radiation dose for quality assurance.

<u>HDR brachytherapy</u> uses seeds made of iridium-194 that are contained inside soft catheters. The catheters are removed after radiation has been given. This treatment requires staying in the hospital for 1 to 2 days. HDR brachytherapy may be given along with <u>EBRT</u>.

Side effects of radiation therapy

Similar to surgical treatment, a common side effect of EBRT and brachytherapy is <u>erectile dysfunction</u>. Unlike surgery, erectile dysfunction may develop several years after radiation therapy. Although not as common as erectile dysfunction, other sexual changes may include difficulty achieving orgasm, thicker semen, <u>dry orgasm</u>, discolored semen, and a decreased sperm count. These less common side effects often stop after a short period of time.

Urinary problems right after EBRT may include frequent urination, a burning feeling while urinating, blood in urine (hematuria), and feeling the need to rush to a bathroom or you'll leak urine (<u>urge</u> <u>incontinence</u>). After brachytherapy, you may have burning with urination, a slow or weak urinary



stream, <u>urinary retention</u>, <u>overflow incontinence</u>, and hematuria. These side effects go away. Several years later, radiation injury to the bladder can cause <u>urinary</u> <u>incontinence</u>, although this isn't common for either EBRT or brachytherapy. However, your risk after brachytherapy is higher if you have had a TURP.

Despite the best treatment planning and delivery, your rectum will be exposed to some radiation during EBRT or brachytherapy. You may have rectal pain, diarrhea, blood in the stool, and inflammation of the colon. These side effects will go away over several months. Several years later, radiation injury to the rectum can cause rectal bleeding and irritation but these symptoms are rare.

EBRT may cause changes in your skin. Your treated skin will look and feel as if it has been sunburned. It will likely become red and may also become dry and sore and feel painful when touched. You may also feel extremely tired despite sleep (<u>fatigue</u>) and not feel hungry. Exercise may help reduce fatigue.

Not all side effects of radiation therapy are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

Cryosurgery

<u>Cryosurgery</u> is a treatment option if radiation therapy fails. Cryosurgery treats prostate tumors by freezing them. Very thin needles will be inserted through your <u>perineum</u> into your prostate. Imaging tests will be used to place the needles. Argon gas will flow through the needles and freeze your prostate to below-zero temperatures. Freezing kills the cancer cells. Your <u>urethra</u> will be spared by use of a catheter filled with warm liquid. This treatment is often done as an outpatient procedure.

The full range of <u>side effects</u> from cryotherapy is unknown. More research is needed. Known shortterm side effects include <u>urinary retention</u>, painful swelling, and "pins and needles" feeling in the penis (penile paresthesia). Long-term side effects include <u>erectile dysfunction</u>, <u>stress incontinence</u>, <u>fistulas</u>, and blockage of the urethra with rectal scar tissue.

Hormone therapy

Prostate cancer cells need hormones called androgens to grow. The main male androgen is <u>testosterone</u>. <u>Hormone therapy</u> will stop your body from making testosterone or will stop the action of testosterone. It can slow tumor growth or shrink the tumor for a period of time.

The types of hormone therapy are:

- **Bilateral orchiectomy** is the surgical removal of both testicles. They are removed since they make most of the testosterone in the body.
- LHRH (luteinizing hormone-releasing hormone) agonists are drugs used to stop the testicles from making testosterone. They are either injected into a muscle or implanted under the skin every 1, 3, 4, 6, or 12 months. <u>LHRH agonists</u> include goserelin acetate,

histrelin acetate, leuprolide acetate, and triptorelin palmoate. **See Chart 4.1** for a list of drugs used to treat prostate cancer.

- LHRH antagonists are drugs used to stop the testicles from making testosterone. They are injected under the skin usually every month. Degarelix is an LHRH antagonist.
- Antiandrogens are drugs that block receptors on cancer cells from receiving testosterone. Antiandrogens include bicalutamide, flutamide, nilutamide, and enzalutamide.
- Estrogens can stop the adrenal glands and other tissues from making testosterone. DES (diethylstilbestrol) is an estrogen.
- **Corticosteroids** can stop the adrenal glands and other tissues from making testosterone.
- Androgen synthesis inhibitors are drugs that block the making of androgen at different sites. Ketoconazole is an antifungal drug that stops the adrenal glands and other tissues from making testosterone. Abiraterone acetate works similarly but is more potent and less toxic.

The term "hormone therapy" can be confusing because of the many names it is called. Some people refer to all hormone therapy as androgen suppression therapy or <u>ADT</u>. However, to be exact, only <u>orchiectomy</u> and <u>LHRH agonists</u> and <u>antagonists</u> are ADTs.

Sometimes, antiandrogens are used with LHRH agonists or following an orchiectomy. This type of treatment is called <u>CAB</u> (**c**ombined **a**ndrogen **b**lockade). However, CAB is no better than castration alone for <u>metastases</u>. Moreover, it may lead to higher costs and worse side effects.

Finasteride or dutasteride used with CAB is called <u>triple androgen blockade</u>. The benefit of triple androgen blockade is probably small if any benefit exists.

If you will be on long-term <u>ADT</u>, your doctor may consider <u>intermittent treatment</u> to reduce <u>side effects</u>. Intermittent treatment is alternating periods of time on

and off treatment. It can provide similar cancer control to continuous <u>hormone therapy</u>.

Chart 4.1 Drug treatment for prostate cancer

Generic name	Brand name (sold as)	Type of treatment	
Abiraterone acetate	Zytiga™	Hormone therapy	
Bicalutamide	Casodex®	Hormone therapy	
Cabazitaxel	Jevtana®	Chemotherapy	
Degarelix	Firmagon®	Hormone therapy	
Diethylstilbestrol	-	Hormone therapy	
Docetaxel	Taxotere®	Chemotherapy	
Enzalutamide	Xtandi®	Hormone therapy	
Flutamide	-	Hormone therapy	
Goserelin acetate	Zoladex®	Hormone therapy	
Histrelin acetate	Vantas®	Hormone therapy	
Ketoconazole	Nizoral®	Hormone therapy	
Leuprolide acetate	Eligard [®] , Lupron Depot [®] , Lupron [®]	Hormone therapy	
Mitoxantrone hydrochloride	Novantrone®	Chemotherapy	
Nilutamide	Nilandron	Hormone therapy	
Prednisone	-	Hormone therapy	
Radium-223	Xofigo	Radiopharmaceutical	
Sipuleucel-T	Provenge®	Immunotherapy	
Triptorelin pamoate	Trelstar®	Hormone therapy	

Side effects of hormone therapy

<u>Hormone therapy</u> has multiple <u>side effects</u>. It can be hard to know whether you will get a side effect. Many factors play a role. Such factors include your age, your health before treatment, how long or often you take treatment, and so forth.

Side effects differ between the types of hormone therapy. In general, <u>ADT</u> may reduce your desire for sex and cause <u>erectile dysfunction</u>. These sexual side effects don't seem to lessen with time. The longer you take ADT, the more your risk for thinning and weakening bones (osteoporosis), bone fractures, weight gain, loss of muscle mass, diabetes, and heart disease increases. Other side effects of ADT include hot flashes, mood changes, and <u>fatigue</u>.

A side effect specific to <u>orchiectomy</u> is the loss of your testicles. Implants that look like testicles can be inserted into your scrotum. Your testicles won't be removed with <u>LHRH agonists</u> but these drugs will shrink your testicles over time.

Side effects of antiandrogens are like those of ADT. When an antiandrogen is used with a LHRH agonist, diarrhea is a major side effect. Other side effects include nausea, liver problems, breast growth and tenderness, and tiredness. Estrogens also increase risk for breast growth and tenderness as well as blood clots. Ketoconazole can cause low cortisol levels and cause health problems when taken with other drugs.

Abiraterone with prednisone is a newer hormone therapy. While taking abiraterone, you should be tested for high blood pressure (hypertension), low potassium (hypokalemia), fluid buildup (edema), and problems with your adrenal glands, heart, and liver. You could also have hot flashes, fatigue, diarrhea, vomiting, constipation, coughing, shortness of breath, joint or muscle pain, and lung or urinary infections.



Enzalutamide is also a newer hormone therapy. A rare but severe side effect of enzalutamide is seizures. Common side effects include fatigue, hot flashes, diarrhea, headaches, pain, not feeling hungry, constipation, lung infections, swelling, shortness of breath, weight loss, headache, high blood pressure, dizziness, and a feeling that things are spinning around (vertigo). The chance that you may fall is greater when taking enzalutamide.

Not all of the side effects of hormone therapy are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. Part 6.1 describes some ways to reduce risks of hormone therapy, but your treatment team can tell you more.

Immunotherapy

Sipuleucel-T is a drug that uses your white blood cells to destroy prostate cancer cells. In a lab, your white blood cells from a blood sample will be changed by a protein so they will recognize and destroy prostate cancer cells. Common side effects of this drug include chills, fever, nausea, and headache. These effects don't appear to last for long. Serious heart problems rarely occur.

Chemotherapy

Chemotherapy, or 'chemo,' is the use of drugs to kill cancer cells. Some chemotherapy drugs kill cancer cells by damaging their DNA or disrupting the making of DNA. Other drugs interfere with cell parts that are needed for making new cells.

Docetaxel and cabazitaxel are chemotherapy drugs used to treat advanced prostate cancer. They may improve survival, delay or relieve symptoms, and reduce tumor growth and <u>PSA</u> levels. Mitoxantrone hydrochloride may relieve symptoms caused by advanced cancer. Read Part 7 for more details on chemotherapy.

These chemotherapy drugs are liquids that are injected into a vein. The drugs travel in the bloodstream to treat cancer throughout the body. Chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle.

Docetaxel is an option for some men who are taking <u>ADT</u> for the first time. In this case, six 3-week cycles are recommended. <u>Side effects</u> may include <u>fatigue</u>, weakness or numbness in the toes or fingers (neuropathy), inflammation of the mouth (stomatitis), diarrhea, and low counts of neutrophils (neutropenia) with or without fever. Neutrophils are a type of white blood cell. Docetaxel is also used to treat <u>metastases</u> after ADT fails to stop cancer growth. Three-week cycles are also recommended. The number of cycles you receive should be based on how much the drug is helping and the severity of side effects.

Cabazitaxel is an option if docetaxel fails to work. However, the benefits of cabazitaxel are small and the side effects can be severe. You may have a severe allergic reaction within a few minutes of receiving cabazitaxel. Severe stomach and intestinal problems, illness from too few white blood cells, and kidney failure may occur. Common side effects are fatigue, neuropathy, hematuria, back pain, bruising, shortness of breath, cough, joint pain, and hair loss. You should not take cabazitaxel if your liver, kidney, or bone marrow is not working well or if you have severe neuropathy.

Not all of the side effects of chemotherapy are listed here. Please ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better.

Radiopharmaceuticals

<u>Radiopharmaceuticals</u> are drugs that contain a radioactive substance. Radium-223 is a radiopharmaceutical that is injected into the body to treat prostate cancer that has spread to the bone. It may improve survival time. It may also delay bone problems and the need for radiation to treat pain.

Since the chemical makeup of radium-223 is similar to calcium, it travels to bone damaged by cancer. Once it reaches the bone, it delivers radiation that kills the nearby cancer cells. The radiation doesn't travel far so healthy tissue is spared.

Radium-223 may lower blood cells counts. Thus, you may get infections and bruises and have unusual bleeding or fatigue. Since radium-223 leaves the body through the gut, other common side effects are nausea, diarrhea, and vomiting.

89Sr (strontium-89) and 153Sm (Samarium-153) also are radiopharmaceuticals. They haven't been shown to extend life. However, they may relieve pain caused by cancer metastases in the bone. They also may cause a decrease in the number of blood cells.

Clinical trials

New tests and treatments aren't offered to the public as soon as they're made. They need to be studied. A clinical trial is a type of research that studies a test or treatment. Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow's standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help men with prostate cancer.

New tests and treatments go through a series of clinical trials to make sure they're safe and work. Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials have four phases. Examples of the four phases for treatment are:

- **Phase I trials** aim to find the best dose of a new drug with the fewest <u>side effects</u>.
- **Phase II trials** assess if a drug works for a specific type of cancer.
- **Phase III trials** compare a new drug to the standard treatment.
- Phase IV trials test new drugs approved by the U.S. FDA (Food and Drug Adminstration) in many patients with different types of cancer.

Joining a clinical trial has benefits. First, you'll have access to the most current cancer care. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other patients with cancer.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may not help. Another downside may be that paperwork or more trips to the hospital are needed. To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial are often alike in terms of their cancer and general health. This is to know that any progress is because of the treatment and not because of differences between patients. To join, you'll need to review and sign a paper called an informed consent form. This form describes the study in detail, including the risks and benefits.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you're getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 8.

Treatments needing more research

The treatments described so far are those approved by NCCN experts. These treatments have been proven in clinical trials to be safe and work well. You may have heard about other treatments. Some treatments that are of great interest but need more research are addressed next.

Cryosurgery as initial treatment

<u>Cryosurgery</u> is a treatment option following failure of radiation therapy. It is not recommended as an initial treatment at this time. More research is needed to compare cryosurgery to prostatectomy and radiation therapy.

High intensity focused ultrasound

HIFU (high intensity focused ultrasound) is a treatment that is gaining interest. This treatment kills cancer using a machine that emits strong sound waves. It only treats a confined area of cancer. HIFU isn't recommended by NCCN experts at this time unless it's part of a clinical trial.

Vascular-targeted photodynamic

VTP (vascular-targeted photodynamic) destroys blood vessels of prostate tumors. It consists of a drug that is first injected into your vein. Then, the drug is activated by light. The light is emitted from tiny laser fibers that are inserted into your <u>prostate</u>. VTP isn't recommended by NCCN experts at this time unless it's part of a clinical trial.

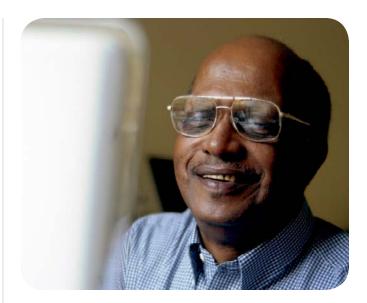
Complementary and alternative medicine

CAM (complementary and alternative medicine) is a group of treatments that aren't often given by doctors. There is much interest today in CAM for cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are treatments given along with usual medical treatments. While CAMs aren't known to kill cancer cells, they may improve your comfort and well-being. Two examples are acupuncture for pain management and yoga for relaxation.

Alternative medicine is used in place of usual medicine. Some alternative medicines are sold as cures even though they haven't been proven to work. If there was good proof that CAMs or other treatments cured cancer, they would be included in this book.

It is important to tell your treatment team if you are using any CAMs. They can tell you which CAMs may be helpful and which CAMs may limit how well medical treatments work.



Review

- · A radical prostatectomy removes the prostate and the seminal vesicles.
- · A PLND removes lymph nodes near the prostate.
- · Radiation from a machine or "seeds" are used to kill cancer cells or stop new cancer cells from being made.
- · Cryosurgery kills cancer cells by freezing them.
- Hormone therapy treats prostate cancer by either stopping testosterone from being made or stopping the action of testosterone.

- · Immunotherapy activates your body's disease-fighting system to destroy prostate cancer cells.
- · Chemotherapy drugs stop the growth process of cells.
- · Radiopharmaceuticals are radioactive drugs used to treat cancer in the bones.
- · Clinical trials give people access to new tests and treatments.
- · More research on cryosurgery, HIFU, VTP, and CAM is needed.



National Comprehensive Cancer Network[®]

5 Treatment guide: Initial treatment



5 Treatment guide: Initial treatment

Part 5 is a guide to the initial treatment options for men with prostate cancer. Groups based on the <u>prognosis</u> of the cancer are used to recommend treatment options. There are six <u>risk</u> <u>groups</u>. These risk groups have been tested and were found to predict treatment outcomes well. They provide a better basis for treatment recommendations than just using the stage of cancer. These groups are defined as follows:

44 5.1 Very low risk

Includes men with a T1c tumor, PSA level less than 10 ng/mL, PSA density less than 0.15 ng/mL/g, <u>Gleason</u> <u>score</u> 6 or less, and cancer in fewer than three <u>biopsy</u> cores and in half or less of any core.

46 **5.2 Low risk**

Includes men with a T1a, T1b, T1c, or T2a tumor, PSA level less than 10 ng/mL, and Gleason score 6 or less.

48 5.3 Intermediate risk

Includes men with a T2b or T2c tumor, PSA level between 10 and 20 ng/mL, or Gleason score 7. If you meet two or all three conditions, your risk is high.

50 5.4 High risk

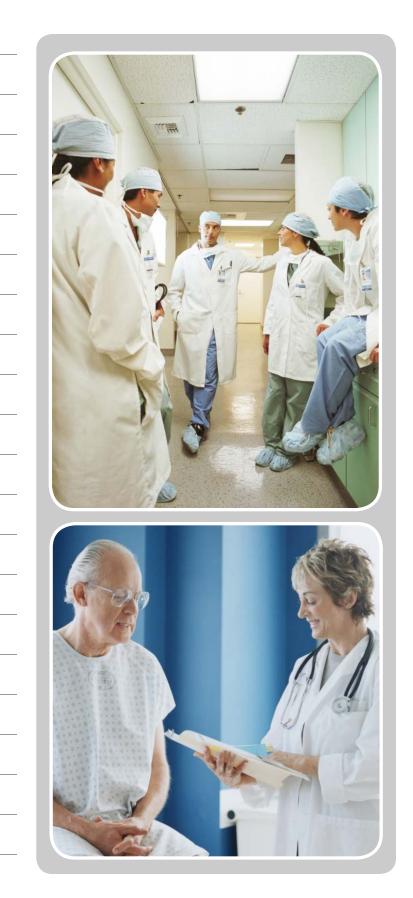
Includes men with a T3a tumor, a PSA level greater than 20 ng/mL, or a Gleason score between 8 and 10. If you meet two or all three conditions, your risk is very high.

52 5.5 Very high risk

Includes men with a T3b or T4 tumor, primary <u>Gleason</u> <u>grade</u> 5, or more than 4 biopsy cores with Gleason scores between 8 and 10.

54 5.6 Metastatic disease Includes men with N1 or M1 disease.





5.1 Very low risk

Chart 5.1 Primary treatment

Expected years to live	Treatment options	
<10 years	Observation	
10–20 years	 Active surveillance PSA no more often than every 6 months, DRE no more often than every 12 months, and Prostate biopsy no more often than every 12 months 	
≥20 years	 Active surveillance PSA no more often than every 6 months, DRE no more often than every 12 months, and Prostate biopsy no more often than every 12 months 	
	 Radiation therapy EBRT, or LDR brachytherapy 	
	 Surgical treatment Radical prostatectomy, or Radical prostatectomy + PLND if ≥2% risk of cancer in lymph nodes 	

Chart 5.1 lists the treatment options for men at very low risk of <u>recurrence</u>. The criteria for very low risk include a T1c tumor. This tumor can't be felt with a <u>DRE</u> but is found because of high <u>PSA</u> levels.

NCCN experts are concerned about over-treatment of this early cancer. As a result, they recommend starting <u>observation</u> after diagnosis if you're expected to live less than 10 years since the cancer may never cause any problems. Observation consists of testing on a regular basis so that <u>supportive care</u> with <u>ADT</u> can be given if symptoms from the cancer are likely to start. Tests during observation include PSA and DRE. <u>Active surveillance</u> is an option if you are likely to live more than 10 years. Active surveillance consists of testing on a regular basis so that treatment can be started when needed. Treatment is given when there is still an excellent chance for a cure. This option may be of interest if you're younger and want to avoid treatment <u>side effects</u> until treatment is clearly (if ever) needed. If older, treating the cancer may not be an urgent concern in light of other more serious health problems.

In general, PSA testing should occur no more often than every 6 months. DRE should occur no more often than every 12 months. Doctors don't agree on the need for and frequency of repeat biopsies. Some doctors do repeat biopsies each year and others do them based on test results. Examples of such test results include a rise in <u>PSA</u> level or change in <u>DRE</u>.

A decision to do a repeat <u>biopsy</u> should balance the potential benefits and risks. Risks include infection and other <u>side effects</u>. If 10 or more cores were removed, the next biopsy may be done within 18 to 24 months of diagnosis. If you're likely to live less than 10 years or are older than 75 years of age, repeat prostate biopsies are rarely needed.

There is debate over which events during <u>active</u> <u>surveillance</u> should signal the start of treatment. The decision to start treatment should be based on your doctor's judgment and your personal wishes. NCCN experts suggest the following triggering events:

- Cancer from the repeat biopsy has a <u>Gleason</u> <u>grade</u> of 4 or 5, or
- There is a larger amount of cancer within biopsy samples or a greater number of biopsy samples have cancer.

Besides active surveillance, there are two other options if you're likely to live more than 20 years. You may want treatment now since, in time, the cancer may grow outside your <u>prostate</u>, cause symptoms, or both. If you want treatment now, radiation therapy is an option. Very-low-risk cancers may be treated with <u>LDR brachytherapy</u> alone. They can also be treated with <u>EBRT</u> to the prostate and maybe the <u>seminal</u> <u>vesicles</u> but not to the pelvic <u>lymph nodes</u>.

The third option is to have a <u>radical prostatectomy</u>. If you choose a prostatectomy, you may also have a <u>PLND</u> if your risk is 2% or higher for having cancer in the pelvic lymph nodes. Your doctor will determine your risk using a <u>nomogram</u>, which was described in Part 3.

5.2 Low risk

Chart 5.2.1 Primary treatment

Expected years to live	Treatment options
<10 years	Observation
≥10 years	 Active surveillance PSA no more often than every 6 months, DRE no more often than every 12 months, and Prostate biopsy no more often than every 12 months
	 Radiation therapy EBRT, or LDR brachytherapy
	 Surgical treatment Radical prostatectomy, or Radical prostatectomy + PLND if ≥2% risk of cancer in lymph nodes

Chart 5.2.2 Adjuvant treatment after prostatectomy

Surgical results	Treatment options
No high-risk features or cancer in lymph nodes	Observation
High-risk features but no cancer in lymph nodes	EBRT, orObservation
Cancer in lymph nodes	 ADT ± EBRT, or Observation

Chart 5.2.1 lists the treatment options for men at low risk of <u>recurrence</u>. The criteria for low risk include T1 and T2a tumors. Treatment options are based on how many years a man is expected to live.

If you're likely to live less than 10 years, starting <u>observation</u> after diagnosis is recommended since the

cancer may never cause any problems. Observation consists of testing on a regular basis so that <u>supportive care</u> with <u>ADT</u> can be given if symptoms from the cancer are likely to start. Tests during observation include <u>PSA</u> and <u>DRE</u>. Low risk

Active surveillance is an option if you are likely to live 10 or more years. Active surveillance consists of testing on a regular basis so that treatment can be started when needed. Treatment is given when there is still an excellent chance for a cure.

In general, <u>PSA</u> testing should occur no more often than every 6 months. DRE should occur no more often than every 12 months. Doctors don't agree on the need for and frequency of repeat biopsies. Some doctors do repeat biopsies each year and others do them based on test results. Examples of such test results include a rise in PSA level or change in DRE.

A decision to do a repeat biopsy should balance the potential benefits and risks. Risks include infection and other side effects. If 10 or more cores were removed, the next biopsy may be done within 18 to 24 months of diagnosis. If you're likely to live less than 10 years or are older than 75 years of age, repeat prostate biopsies are rarely needed.

There is debate over which events during active surveillance should signal the start of treatment. The decision to start treatment should be based on your doctor's judgment and your personal wishes. NCCN experts suggest the following triggering events:

- The cancer from the repeat biopsy has a Gleason grade of 4 or 5, or
- There is a larger amount of cancer within biopsy samples or a greater number of biopsy samples have cancer.

Besides active surveillance, there are two other options if you're likely to live more than 10 years. You may want treatment now since, in time, the cancer may grow outside your prostate, cause symptoms, or both. If you want treatment now, radiation therapy is an option. Low-risk cancers may be treated with LDR brachytherapy alone. They can also be treated with EBRT to the prostate and maybe the seminal vesicles but not to the pelvic lymph nodes.

The third option is to have a radical prostatectomy. If you choose a prostatectomy, you may also have a PLND if your risk is 2% or higher for having cancer in the pelvic lymph nodes. Your doctor will determine your risk using a nomogram, which was described in Part 3.

The tissue that will be removed from your body during the operation will be sent to a pathologist for testing. The pathologist will assess how far the cancer has spread within the tissue. After the operation, your PSA level will also be tested.

Chart 5.2.2 lists options for adjuvant treatment after a prostatectomy. Options are based on the presence of high-risk features and cancer in the lymph nodes. High-risk features suggest that not all of the cancer was removed by the operation. High-risk features include:

- Cancer in <u>surgical margins</u>
- Cancer outside the prostatic capsule
- Cancer in the seminal vesicle(s)
- Detectable PSA levels

If test results find no high-risk features or cancer in the lymph nodes, no more treatment is needed. You may start observation. The options for when there are high-risk features but no cancer in the lymph nodes are EBRT or observation. EBRT will target areas where the cancer cells have likely spread. Treatment will be started after you've healed from the operation.

There are two treatment options if cancer is found in lymph nodes. The first option is to start ADT now. EBRT may be given with ADT. ADT can be given on an intermittent schedule to reduce its side effects. However, the benefits of ADT in this case are unclear. For adjuvant ADT, an LHRH antagonist or LHRH agonist is recommended. If your PSA levels are undetectable, a second option is to start observation and then have treatment if the levels rise.

5.3 Intermediate risk

Chart 5.3.1 Primary treatment

Expected years to live	Treatment options
	Observation
<10 years	 Radiation therapy EBRT ± brachytherapy ± ADT for 4–6 months, or LDR brachytherapy alone for low-volume disease
≥10 years	 Surgical treatment Radical prostatectomy, or Radical prostatectomy + PLND if ≥2% risk of cancer in lymph nodes
	 Radiation therapy EBRT ± brachytherapy ± ADT for 4–6 months, or LDR brachytherapy alone for low-volume disease

Chart 5.3.2 Adjuvant treatment after prostatectomy

Surgical results	Treatment options
No high-risk features or cancer in lymph nodes	Observation
High-risk features but no cancer in lymph nodes	EBRT, orObservation
Cancer in lymph nodes	 ADT ± EBRT, or Observation

Chart 5.3.1 lists the treatment options for men in the intermediate <u>risk group</u>. The criteria for intermediate risk include T2b and T2c tumors. Treatment options are based on how many years a man is expected to live.

Observation instead of treatment is an option for men expected to live less than 10 years. In this case, the cancer is unlikely to cause problems. Observation consists of testing on a regular basis so that <u>supportive care</u> with <u>ADT</u> can be given if symptoms from the cancer are likely to start. Tests during observation include <u>PSA</u> and <u>DRE</u>. For all men with intermediate risk, a treatment option is radiation therapy. Research has shown that <u>EBRT</u> alone often controls intermediate-risk prostate cancer. <u>LDR</u> or <u>HDR brachytherapy</u> can be used with EBRT for intermediate-risk cancers but will likely cause more <u>side effects</u>. <u>LDR brachytherapy</u> alone may be given if test results suggest the cancer hasn't spread far.

Your doctor may want to add a short course of <u>ADT</u> to radiation therapy. Research has shown that adding ADT can extend life. For ADT, an <u>LHRH antagonist</u> or <u>LHRH agonist</u> may be used. However, doctors often use <u>CAB</u>. If you will receive ADT, it will be given before, during, and after radiation therapy.

If you are expected to live 10 or more years, a <u>radical</u> <u>prostatectomy</u> is a third option. You may also have a <u>PLND</u> if your risk is 2% or higher for having cancer in the pelvic <u>lymph nodes</u>. Your doctor will determine your risk using a <u>nomogram</u>, which was described in Part 3.

The tissue that will be removed from your body during the operation will be sent to a <u>pathologist</u> for testing. The pathologist will assess how far the cancer has spread within the tissue. After the operation, your <u>PSA</u> level will also be tested.

Chart 5.3.2 lists options for adjuvant treatment after a prostatectomy. Recommendations for adjuvant treatment are based on the presence of high-risk features and cancer in the lymph nodes. High-risk features suggest that not all of the cancer was removed by the operation. High-risk features include:

- Cancer in surgical margins,
- Cancer outside the prostatic capsule,
- Cancer in the seminal vesicle(s), and
- Detectable PSA levels.

If test results find no high-risk features or cancer in the lymph nodes, no more treatment is needed. You may start <u>observation</u>. The options for when there are high-risk features but no cancer in the lymph nodes are EBRT or <u>observation</u>. EBRT will target areas where the cancer cells have likely spread. Treatment will be started after you've healed from the operation.

There are two treatment options if cancer is found in lymph nodes. The first option is to start <u>ADT</u> now. EBRT may be added to ADT. ADT can be given on an intermittent schedule to reduce its <u>side effects</u>. However, the benefits of ADT in this case are unclear. For adjuvant ADT after prostatectomy, an <u>LHRH</u> <u>antagonist</u> or <u>LHRH agonist</u> is recommended. If your PSA levels are undetectable, a second option is to start observation and then have treatment if the levels rise.

5.4 High risk

Chart 5.4.1 Primary treatment

Treatment options

- Radiation therapy ± ADT
 - EBRT + ADT for 2–3 years, or
 - EBRT+ brachytherapy ± ADT for 2–3 years
- · Surgical treatment
 - Radical prostatectomy + PLND

Chart 5.4.2 Adjuvant treatment

Treatment results	Treatment options
After radiation therapy	
If on ADT	Continue to complete 2–3 years of ADT
After surgical treatment	
No high-risk features or cancer in lymph nodes	Observation
High-risk features but no cancer in lymph nodes	EBRT, orObservation
Cancer in lymph nodes	 ADT ± EBRT, or Observation

Chart 5.4.1 lists the treatment options for men in the high-<u>risk group</u>. The criteria for high risk include T3a tumors. For high-risk cancers, research supports treatment unless you're likely to live less than 5 years when <u>observation</u> is the best choice.

There are three treatment options for high-risk tumors. The preferred treatment is <u>EBRT</u> to the

<u>prostate</u> and pelvic <u>lymph nodes</u> and long-term <u>ADT</u>. The second treatment option is EBRT plus <u>HDR</u> <u>brachytherapy</u> and maybe ADT.

For ADT, an <u>LHRH antagonist</u> or <u>LHRH agonist</u> may be used. However, doctors often use <u>CAB</u>. If you will receive ADT, it will be given before, during, and after radiation therapy for a total of 2 to 3 years. A third option is a <u>radical prostatectomy</u> with <u>PLND</u>. The tissue that will be removed from your body will be sent to a <u>pathologist</u> for testing. The pathologist will assess how far the cancer has spread within the tissue. Your <u>PSA</u> level will also be tested.

Chart 5.4.2 lists options for adjuvant treatment. If you had radiation therapy, you may have started <u>ADT</u>. ADT is recommended for 2 to 3 years, so you will need to keep taking these drugs after radiation therapy has ended.

Options for adjuvant treatment after a prostatectomy are based on the presence of high-risk features and cancer in the <u>lymph nodes</u>. High-risk features suggest that not all of the cancer was removed by the operation. High-risk features include:

- Cancer in surgical margins,
- · Cancer outside the prostatic capsule,
- · Cancer in the seminal vesicle(s), and
- Detectable PSA levels.

If test results find no high-risk features or cancer in the lymph nodes, no more treatment is needed. You may start <u>observation</u>. The options for when there are high-risk features but no cancer in the lymph nodes are <u>EBRT</u> or observation. EBRT will target areas where the cancer cells have likely spread. Treatment will be started after you've healed from the operation.

There are two treatment options if cancer is found in lymph nodes. The first option is to start ADT now. EBRT may be added to ADT. ADT can be given on an intermittent schedule to reduce its <u>side effects</u>. However, the benefits of ADT in this case are unclear. For adjuvant ADT, an <u>LHRH antagonist</u> or <u>LHRH</u> <u>agonist</u> is recommended. If your PSA levels are undetectable, a second option is to start observation and then have treatment if the levels rise.

5.5 Very high risk

Chart 5.5.1 Primary treatment

Treatment options

- Radiation therapy ± ADT
 - EBRT + ADT for 2–3 years, or
 - EBRT+ brachytherapy ± ADT for 2–3 years
- Surgical treatment
 - · Radical prostatectomy and PLND if the cancer isn't fixed to nearby organs
- · ADT when a cure is not possible

Chart 5.5.2 Adjuvant treatment

Treatment options	Treatment options
After radiation therapy	
If on ADT	Continue to complete 2–3 years of ADT
After surgical treatment	
No high-risk features or cancer in lymph nodes	Observation
High-risk features but no cancer in lymph nodes	EBRT, orObservation
Cancer in lymph nodes	 ADT ± EBRT, or Observation

Chart 5.5.1 lists the treatment options for men at very high risk of <u>recurrence</u>. Men at very high risk include those with T3b and T4 tumors, primary <u>Gleason grade</u> 5, or more than 4 <u>biopsy</u> cores with <u>Gleason scores</u> between 8 and 10. There are four treatment options for very-high-risk tumors. The preferred treatment is <u>EBRT</u> to the <u>prostate</u> and pelvic <u>lymph nodes</u> and long-term <u>ADT</u>. The second treatment option is EBRT plus <u>HDR brachytherapy</u> and maybe ADT. For ADT given with radiation, an <u>LHRH antagonist</u> or <u>LHRH agonist</u> may be used. However, doctors often use <u>CAB</u>. If you will receive <u>ADT</u>, it will be given before, during, and after radiation therapy for 2 to 3 years.

If the tumor isn't fixed to nearby organs, a third option is a <u>radical prostatectomy</u> with <u>PLND</u>. When a tumor isn't fixed, it is more likely to be fully removed. In this case, an operation may be able to cure the cancer. The tissue that will be removed from your body will be sent to a <u>pathologist</u> for testing. The pathologist will assess how far the cancer has spread within the tissue. Your <u>PSA</u> level will also be tested.

If you have a very-high-risk cancer that can't be cured, ADT can be used. The goal of ADT is to control the growth of the cancer. Recommendations for ADT include an <u>LHRH antagonist</u> or <u>LHRH agonist</u>. If these drugs don't suppress your <u>testosterone</u> level, your doctor may want you to take <u>CAB</u>.

Chart 5.5.2 lists options for adjuvant treatment. If you had radiation therapy, you may have started ADT. ADT is recommended for 2 to 3 years, so you will need to keep taking these drugs after radiation therapy has ended.

Options for adjuvant treatment after a prostatectomy are based on the presence of high-risk features

and cancer in the <u>lymph nodes</u>. High-risk features suggest that not all of the cancer was removed by the operation. High-risk features include:

- · Cancer in surgical margins,
- Cancer outside the prostatic capsule,
- Cancer in the seminal vesicle(s), and
- Detectable PSA levels.

If test results find no high-risk features or cancer in the lymph nodes, no more treatment is needed. You may start <u>observation</u>. The options for when there are high-risk features but no cancer in the lymph nodes are <u>EBRT</u> or observation. EBRT will target areas where the cancer cells have likely spread. Treatment will be started after you've healed from the operation.

There are two treatment options if cancer is found in lymph nodes. The first option is to start ADT now. Radiation therapy may be added to ADT. ADT can be given on an intermittent schedule to reduce its <u>side</u> <u>effects</u>. However, the benefits of ADT in this case are unclear. For adjuvant ADT, an LHRH antagonist or LHRH agonist is recommended. If your PSA levels are undetectable, a second option is to start observation and then have treatment if the levels rise.

5.6 Metastatic disease

Chart 5.6 Primary treatment

TNM scores	Treatment options
	Observation
Any T, N1, M0	 ADT Orchiectomy LHRH agonist ± antiandrogen for ≥7 days to prevent testosterone flare LHRH agonist + antiandrogen LHRH antagonist
	 Radiation therapy + ADT EBRT + ADT for 2–3 years
Any T, Any N, M1	 ADT Orchiectomy LHRH agonist ± antiandrogen for ≥7 days to prevent testosterone flare LHRH agonist + antiandrogen LHRH antagonist Continuous ADT and docetaxel for castration-sensitive, high-volume M1 disease

Chart 5.6 lists the treatment options for men with <u>metastatic</u> disease. Metastatic disease refers to cancer that has spread to nearby <u>lymph nodes</u>, a distant site, or both. The growth of these cancers can be controlled with treatment.

If the cancer has only spread to nearby lymph nodes (N1, M0), the options are <u>observation</u>, <u>ADT</u>, and <u>EBRT</u> with long-term ADT. When ADT is given with EBRT, an <u>LHRH antagonist</u> or <u>LHRH agonist</u> may be used. However, doctors often use <u>CAB</u>. ADT is given before, during, and after EBRT.

ADT is also recommended for men with distant metastases. ADT can consist of surgical castration with a bilateral <u>orchiectomy</u> or medical castration with an LHRH antagonist or agonist. Both methods for castration work equally well.

Some metastases can be seen with imaging tests. When these overt metastases are treated with LHRH agonists, there can be an increase in <u>testosterone</u> for several weeks. This increase is called a "<u>flare</u>." Flare can cause pain if there are bone metastases, but the pain doesn't mean the cancer is growing. Flare can also cause paralysis if metastases are located in weight-bearing bones (legs or spine). To prevent the <u>flare</u>, an antiandrogen can be given for 7 or more days, starting before or along with the <u>LHRH agonist</u>.

Another option for first-line <u>ADT</u> is long-term use of an antiandrogen with an LHRH agonist. This is a form of <u>CAB</u>. However, CAB is no better than castration alone for <u>metastases</u>. Moreover, it may lead to higher costs and worse <u>side effects</u>.

A new option for some men is continuous ADT with docetaxel. Prednisone is not given with these drugs. ADT with docetaxel is only an option if you have castration-sensitive, high-volume M1 disease. Castration-sensitive disease is prostate cancer growth that is controlled when <u>testosterone</u> levels are lowered. High-volume disease is defined as 1) metastases in internal organs (<u>visceral disease</u>); 2) four or more bone metastases with at least one spinal metastasis above the pelvis; or 3) both.



Review

- One option for men with very low- and lowrisk cancers is not to start treatment since the cancer might never cause problems. Otherwise, radiation therapy and surgical treatment are options.
- For intermediate-risk cancer, not starting treatment is an option if you are likely to live less than 10 years. Another option is radiation therapy. If you are likely to live 10 or more years, radiation therapy and surgical treatment are options. Short-term ADT may be given with EBRT.
- Treatment is recommended for high-risk, very-high-risk, and metastatic disease.
 Local treatment is an option when cure is likely. Sometimes long-term ADT is added to radiation therapy. ADT alone is an option when the cancer can be controlled but not cured.



6 Treatment guide: Monitoring

NCCN Guidelines for Patients® Prostate Cancer, Version 1.2015

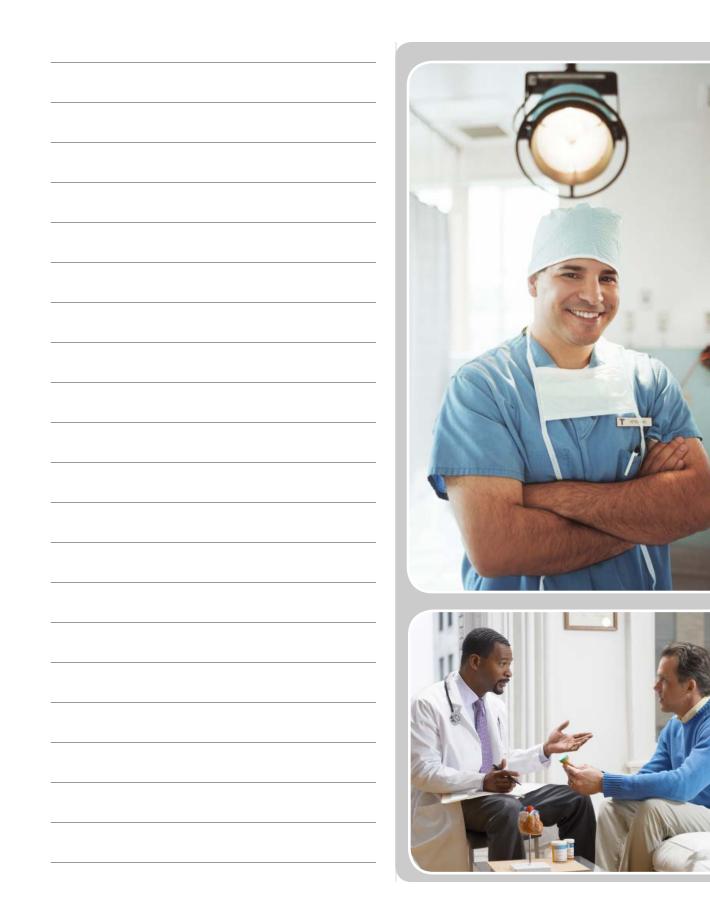
6 Treatment guide: Monitoring

Part 6 is a guide to monitoring after initial treatment. If you are taking <u>ADT</u>, Part 6.1 is important to read. Some health risks of ADT are discussed. Monitoring also includes assessing if initial treatment was successful. The tests used to assess the results of initial treatment are detailed in Part 6.2. Parts 6.3 and 6.4 list treatment options if local treatments don't succeed in treating the cancer.

60 6.1 Reducing ADT risks

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6.1 Reducing ADT risks

Chart 6.1 Reducing ADT risks

Risk	Treatment options
Osteoporosis	 Calcium (1200 mg every day) and vitamin D3 (800–1000 IU every day) if older than 50 years Denosumab (60 mg every 6 months), zoledronic acid (5 mg every year), or alendronate (70 mg every week) if at high risk for bone fracture
Diabetes	Follow guidelines for general population
Heart (cardiovascular) disease	Follow guidelines for general population

Chart 6.1 lists some risks of <u>ADT</u> and ways to reduce them. One known risk of ADT is the thinning and weakening of bones (osteoporosis). Calcium 1200 mg (milligram) and vitamin D3 800 to 1000 IU (international unit) taken every day may help prevent or control osteoporosis. Both are recommended if you are older than 50 years old. Your blood should be tested to ensure the proper levels.

If you are at high risk for bone fracture, there are drugs that may strengthen your bones. Before treatment, you should receive a <u>DEXA</u> (dual energy **x**-ray **a**bsorptiometry) scan to measure your bone density. Denosumab (120 mg every 6 months), zoledronic acid (5 mg every year), or alendronate (70 mg every week) are recommended. Denosumab is injected under the skin. Zoledronic acid is injected into a vein. Alendronate is a pill that is swallowed. One year after treatment has started, another DEXA scan is recommended.

Denosumab, zoledronic acid, and alendronate have possible <u>side effects</u>. They have been linked to

osteonecrosis—bone tissue death—of the jaw. Other side effects are hypocalcemia and arthralgias. You may be at higher risk of jaw osteonecrosis if you already have dental problems. Thus, it's important to get a dental exam and dental treatment before starting any of these drugs.

Diabetes and cardiovascular disease are common in older men. ADT increases the risk for these diseases. Thus, screening and treatment to reduce your risk for these diseases are recommended.

ADT and other <u>hormone therapies</u> will increase your risk for other health conditions as discussed in Part 4. These risks included <u>erectile dysfunction</u>, <u>fatigue</u>, hot flashes, breast tenderness and growth, diarrhea, weight gain, liver injury, and so forth. There are ways to prevent or treat many of these side effects. Examples include exercise for fatigue, antidepressant drugs for hot flashes, and radiation to prevent breast growth. Talk to your treatment team about ways to manage risks of hormone therapy.

6.2 Testing initial treatment results

Chart 6.2 Testing initial treatment results

Risk group	Test name	Testing schedule
Very-low low-, intermediate-, high-, and very-high-risk cancers treated for cure	PSA	 Every 6–12 months for 5 years If normal results, then PSA every year
	DRE	Every year unless PSA is undetectable
Very-high-risk and metastatic disease not treated for cure	Physical exam	Every 3–6 months
	PSA	Every 3–6 months

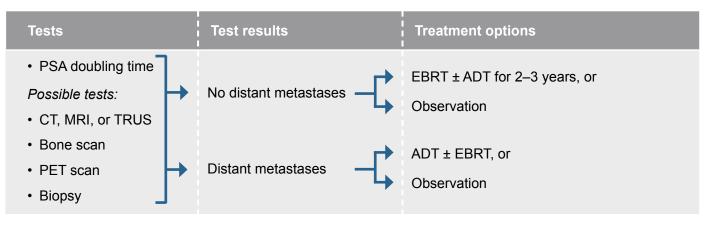
Chart 6.2 lists the tests used to assess the results of initial treatment. For many men, the goal of initial treatment is to cure the cancer. A cure is possible when the cancer has not spread far. The cancer may have been cured if tests find no signs of cancer after treatment. An undetectable <u>PSA</u> level after treatment is a good sign. However, prostate cancer returns in some men after having no signs of cancer for a period of time.

<u>DRE</u> and PSA testing done on a regular basis may catch a <u>recurrence</u> early. A DRE can find a recurrence near the <u>prostate</u>. An increase in the PSA level can be a sign of recurrence either near the prostate or in other areas. Besides PSA level, your doctor will assess the <u>PSA doubling time</u> and <u>velocity</u>. If the goal of your initial treatment was to cure the cancer, PSA testing every 6 to 12 months for 5 years is recommended. However, PSA testing every 3 months may be needed if you have a high risk of recurrence. If PSA levels remain normal during the 5 years, then PSA testing is recommended every year. A DRE can also help to find a recurrence of prostate cancer early as well as cancer in the rectum or colon.

If your initial treatment controls but doesn't cure the cancer, you should be checked often by a doctor. In addition to PSA testing, a complete physical exam is recommended. A physical exam may tell if the cancer is still growing despite undergoing treatment.

6.3 Treatment after prostatectomy





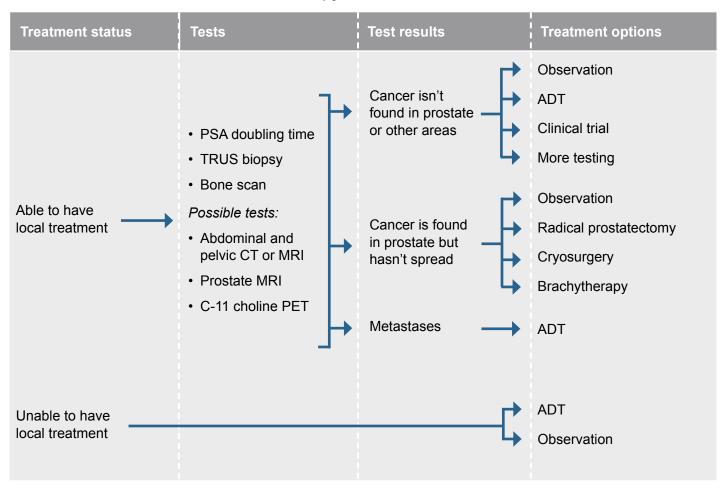
After a radical prostatectomy, your <u>PSA</u> level should fall to near zero since the whole prostate was removed. If this doesn't happen, it may be a sign of <u>persistent cancer</u>. Persistent cancer is cancer that was not completely removed or destroyed by initial treatment. If tests find that your PSA level increases twice in a row after falling to near zero, the cancer may have returned (<u>recurrence</u>).

Chart 6.3 displays the tests and treatment options when PSA scores or a <u>DRE</u> suggest there's cancer. Since high PSA levels don't always mean persistent or recurrent cancer, tests that find distant <u>metastases</u> may be done. A fast PSA doubling time is a sign of aggressive cancer with possible spread to the bone. A <u>CT, MRI</u>, or <u>TRUS</u> is used to look for cancer spread to <u>lymph nodes</u> or other organs. A bone scan shows if the cancer has spread to the bone. It is usually done when there are symptoms of bone metastases or when your PSA level is rising quickly. If imaging tests suggest there's cancer near to where the prostate was, a <u>biopsy</u> can be used to confirm if cancer is present. If there is little reason to suspect distant metastases, <u>EBRT</u> with or without long-term <u>ADT</u> is recommended. However, <u>observation</u> may be a better choice depending on your overall health and personal wishes. For ADT, an <u>LHRH antagonist</u> or <u>LHRH</u> <u>agonist</u> may be used, but doctors often use <u>CAB</u>. If you will receive ADT, it will be given before, during, and after radiation therapy.

For known or highly suspected distant metastases, ADT is the main treatment. Radiation therapy may also be used to treat the metastatic site. However, observation may be a better choice depending on your overall health and personal wishes.

6.4 Treatment after radiation therapy

Chart 6.4 Treatment after radiation therapy



After radiation therapy, <u>PSA</u> levels usually fall to 0.3 ng/mL or below. If your PSA increases by at least 2 ng/mL after falling to low levels, the cancer may have returned. There are other changes in PSA that may be a sign of <u>recurrence</u>. Thus, your doctor may assess if the cancer has returned before the PSA level increases by 2 ng/mL. Signs of cancer also may be found by a <u>DRE</u>.

Chart 6.4 displays the tests and treatment options when PSA scores or a DRE suggest there's cancer. More testing is recommended if you may be able to have local treatment. Local treatment is an option if: 1) the clinical stage was T1 or T2; 2) initial tests found no <u>lymph node metastases</u> or weren't done; 3) you're likely to live at least another 10 years; and 4) your current PSA level is below 10. If you don't meet these criteria or have metastases, the treatment options are <u>ADT</u> or observation. To confirm that local treatment is right for you, your doctors will assess where the cancer has grown. A fast <u>PSA doubling time</u> suggests spread beyond the prostate. A <u>TRUS</u> <u>biopsy</u> of the prostate along with a bone scan should also be done. Possible other tests include a <u>CT</u> or <u>MRI</u> scan of your abdomen and pelvis or a prostate MRI.

Sometimes the prostate biopsy and imaging tests find no cancer despite rising PSA levels. One option in this situation is to continue <u>observation</u> until cancer growth is confirmed. Another option is to start <u>ADT</u>. When to start ADT should be influenced by <u>PSA velocity</u>, your anxiety as well as your doctor's concern about cancer growth, and your feelings about <u>side effects</u>. A third option is to enroll in a clinical trial. A fourth option is to have more tests to try to find the source of the rising PSA level. These tests can include another biopsy, <u>MR spectroscopy</u>, or a prostate MRI. There are four options if cancer has returned in the prostate but has unlikely spread to distant sites. The first option is to continue observation until further cancer growth is found. Another option is radical prostatectomy. Be aware that the side effects of prostatectomy following radiation therapy are worse than when it used as initial treatment. Other options for local treatment include <u>cryotherapy</u> and <u>brachytherapy</u>. Which treatment you will receive needs to be based on your chances of further cancer growth, treatment being a success, and the risks of the treatment.

Review

- ADT can increase your chances of osteoporosis, diabetes, and heart disease.
 Take steps to prevent or decrease the severity of these health problems.
- The results of initial treatment should be checked on a regular basis.
- If local treatments don't succeed, there are more options for treating the cancer.



7 Treatment guide: Advanced cancer

NCCN Guidelines for Patients® Prostate Cancer, Version 1.2015

7 Treatment guide: Advanced cancer

Part 7 is a guide to treatment for advanced disease. Advanced disease can't be cured by surgical treatment or radiation therapy. Instead, there are treatments that can control cancer growth for long periods of time. Part 7.1 lists options for first-time treatment.

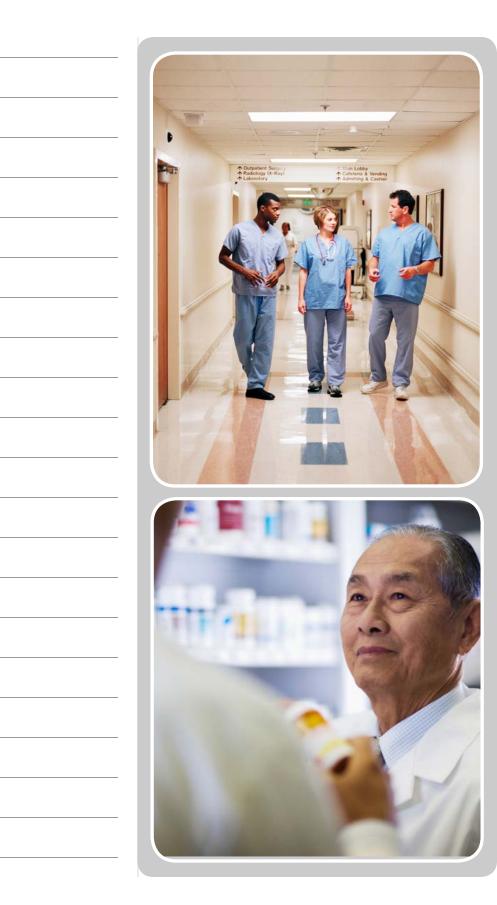
Prostate cancer that grows when <u>hormone</u> <u>therapy</u> has lowered <u>testosterone</u> is called CRPC (castration-recurrent prostate cancer). CRPC may occur because androgen receptors in the cancer cells become active again. Changes in androgen receptors, called mutations, allow cancer cells to receive signals from unusual sources that activate growth. One unusual source is antiandrogens. Activation of androgen receptors may also occur because the cancer cells or nearby cells start to make testosterone. Part 7.2 lists options for CRPC without metastases. Part 7.3 lists options for when there are metastases.

72 7.1 First-time treatment

- 74 7.2 Treatment for CRPC without metastases
- 76 7.3 Treatment for CRPC with metastases

80 Review





7.1 First-time treatment

Chart 7.1 ADT and more

Treatment options

- Orchiectomy
- LHRH agonist ± antiandrogen for ≥7 days to prevent testosterone flare
- LHRH agonist + antiandrogen
- LHRH antagonist
- Continuous ADT and docetaxel for castration-sensitive, high-volume M1 cancer
- Observation for M0 cancer only

Chart 7.1 lists options for men who will be treated for the first time for advanced cancer. For these men, options include surgical or medical castration. Surgical castration is done with a bilateral <u>orchiectomy</u>. Medical castration is done using an <u>LHRH antagonist</u> or <u>agonist</u>. Both castration methods work equally well.

Some <u>metastases</u> can be seen with imaging tests. When these overt metastases are treated with <u>LHRH</u> <u>agonists</u>, there can be an increase in <u>testosterone</u> for several weeks. This increase is called a "<u>flare</u>." Flare can cause pain if there are bone metastases, but the pain doesn't mean the cancer is growing. Flare can also cause paralysis if metastases are located in weight-bearing bones (legs or spine). To prevent the flare, an antiandrogen can be given for 7 or more days, starting before or along with the LHRH agonist.

Another option is long-term use of an antiandrogen with an LHRH agonist. This is one form of <u>CAB</u>. However, CAB is no better than castration alone for metastases. Moreover, it may lead to higher costs and worse <u>side effects</u>. For advanced cancer, the risks for side effects can be reduced by intermittent use of <u>ADT</u>. <u>Intermittent</u> <u>treatment</u> improves quality of life without affecting survival. It often begins with continuous treatment that is stopped after about 1 year. ADT is resumed when a certain <u>PSA</u> level is reached or symptoms appear. PSA levels that trigger restarting treatment usually are 10, 20, or 40 ng/mL.

A new option for some men is continuous ADT with docetaxel. Prednisone is not given with these drugs. ADT with docetaxel is only an option if you have castration-sensitive, high-volume M1 cancer. Castration-sensitive disease is cancer growth that is controlled when testosterone levels are low. Highvolume cancer is defined as 1) metastases in internal organs (visceral disease); 2) four or more bone metastases with at least one spinal metastasis above the pelvis; or 3) both.

Besides treatment, <u>observation</u> is an option for men with metastases (M0). Observation consists of testing on a regular basis so that <u>supportive care</u> with ADT can be given if symptoms from the cancer are likely to start. Tests during observation include PSA and <u>DRE</u>. While on <u>hormone therapy</u>, your doctor will monitor treatment results. A rising <u>PSA</u> level suggests the cancer is growing. This increase is called a biochemical relapse. If PSA levels are rising, your <u>testosterone</u> levels should be tested to see if they are at castrate levels (less than 50 ng/dL). If the levels aren't very low, the dose of your treatment will likely be increased. If the levels are very low, you may receive imaging tests to look for <u>metastases</u>.

7.2 Treatment for CRPC without metastases

Chart 7.2 CRPC without metastases

Treatment options

- Clinical trial (preferred)
- Observation
- · Secondary hormone therapy
 - Antiandrogen
 - Antiandrogen withdrawal
 - Ketoconazole
 - · Corticosteroids
 - DES or other estrogen

Despite that the cancer has returned during <u>hormone</u> <u>therapy</u>, it is important to keep taking it. To treat the cancer, your <u>testosterone</u> levels need to stay at castrate levels. To do so, your doctor may keep you on your current treatment or may switch the type of hormone therapy you are using.

Chart 7.2 lists treatments for CRPC with no <u>metastases</u>. There are three options. Joining a clinical trial is the preferred option. A clinical trial is a type of research that studies how well a treatment works. Because of clinical trials, the treatments in this book are now widely used to help men with prostate cancer.

The second option is <u>observation</u>. Instead of changing your treatment, you may want to continue observation until the proof for cancer growth is stronger. This is especially true if the <u>PSA doubling</u> <u>time</u> was 10 months or longer. The third option is secondary hormone therapy, especially if the PSA doubling time is less than 10 months. Secondary hormone therapy may help control cancer growth if the androgen receptors are active. However, secondary therapies haven't been shown to extend life when given before chemotherapy.

If your first hormone therapy was surgical or medical castration, starting <u>CAB</u> may help. Adding an antiandrogen may lower testosterone levels. Ketoconazole, steroids, DES, and other estrogens may also lower testosterone levels. If you're already on CAB, stopping your use of the antiandrogen known as antiandrogen withdrawal—may help if the cancer cells are using the antiandrogen to grow. This effect is called the antiandrogen withdrawal response and usually last several months.

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7.3 Treatment for CRPC with metastases

First-line treatment

Chart 7.3.1 First-line immunotherapy

Treatment conditions

Sipuleucel-T is an option if these statements describe you:

- The cancer is causing few or no symptoms,
- · There are no liver metastases,
- · You are expected to live more than 6 months, and
- You are in good health other than having cancer

Options if no metastases in internal organs	Options if metastases in internal organs
 Enzalutamide Abiraterone acetate with prednisone Docetaxel with prednisone Radium-223 for bone metastases causing symptoms Clinical trial Secondary hormone therapy Antiandrogen Antiandrogen withdrawal Ketoconazole Corticosteroids 	 Docetaxel with prednisone Enzalutamide Abiraterone acetate with prednisone Alternative chemotherapy (mitoxantrone) Clinical trial

Chart 7.3.2 Other first-line treatment

Part 7.3 addresses treatment for CRPC with <u>metastases</u>. Despite that the cancer has returned during <u>hormone therapy</u>, it is important to keep taking it. To treat the cancer, your <u>testosterone</u> levels need to stay at castrate levels. To do so, your doctor may keep you on your current treatment or may switch the type of hormone therapy you are using. You should keep taking hormone therapy even if given other types of treatment, such as <u>immunotherapy</u>.

Prostate cancer often spreads to the bones. When prostate cancer invades your bones, they are at risk for injury and disease. Such problems include bone fractures, bone pain, and spinal cord compression. Denosumab every 4 weeks or zoledronic acid every 3 to 4 weeks may help to prevent or delay these problems.

If you have painful bone metastases, radiation therapy may help to lessen the pain. <u>EBRT</u> may be used when pain is limited to a specific area or your bones are about to fracture. <u>Radiopharmaceuticals</u> 89Sr (strontium) or 153Sm (samarium) may relieve pain from widely spread bone <u>metastases</u> that isn't responding to other treatments. Be aware that these treatments can cause your bone marrow to make fewer blood cells, which could prevent you from being treated with chemotherapy.

Radiation therapy used to relieve pain is called <u>supportive care</u>. Supportive care (also called palliative care) doesn't aim to treat cancer but aims to improve quality of life. Ask your treatment team for a supportive care plan to address any symptoms you have and other areas of need.

Chart 7.3.1 lists a newer treatment option for CRPC with metastases. Sipuleucel-T is an <u>immunotherapy</u> drug that was tested among men with metastatic CRPC. Research found that men who took sipuleucel-T lived, on average, 4 months longer than men not taking this drug. Your results may be the same, better, or worse. Sipuleucel-T is only recommended for men who meet the conditions listed in the chart. Sipuleucel-T has not been tested among men with metastases to the internal organs (visceral disease).

For treatments other than sipuleucel-T, a drop in <u>PSA</u> levels or improvement in imaging tests occurs if treatment is working. Be aware that these signs don't occur during sipuleucel-T. Thus, don't be discouraged if your test results don't improve.

Chart 7.3.2 lists other options if sipuleucel-T is not right for you. Options for metastatic CRPC that isn't in the internal organs are listed in the left column. In the right column, options are listed for when there is visceral disease. Some options in the two columns overlap. However, the order of options differ based what's best for that group.

Enzalutamide and abiraterone acetate are newer <u>hormone therapies</u>. Enzalutamide is a antiandrogen that may work better than other antiandrogens. In a clinical trial, it lowered PSA levels and extended life by an average of about 5 months. Abiraterone acetate is taken on an empty stomach with prednisone. This drug has been shown to slow cancer growth. Enzalutamide and abiraterone acetate have only been tested among men with few or no cancer symptoms.

Chemotherapy with hormone therapy is another treatment option. Docetaxel with prednisone on an every-3-week schedule is the preferred treatment option if the cancer is causing symptoms. It is not often used when the cancer isn't causing symptoms. However, your doctor may suggest it if the cancer is growing fast or may have spread to your liver.

If your PSA level rises while taking docetaxel, it doesn't mean without doubt that the treatment has failed. Your doctor may suggest that you keep taking docetaxel until it is clear that the cancer has grown or <u>side effects</u> are too severe. If docetaxel's side effects are too severe, you may be given mitoxantrone. Mitoxantrone is a chemotherapy drug. It may improve your quality of life, but it isn't likely to increase how long you will live.

New research supports use of radium-223 if the cancer has metastasized to the bone but not to the internal organs. In clinical trials, radium-223 was shown to extend the lives of men by an average of about 4 months. Your results may be the same, better, or worse. Radium-223 also reduced the pain caused by the bone metastases and the use of pain medication.

Joining a clinical trial is another option. A clinical trial is a type of research that studies how well a treatment works. Because of clinical trials, the treatments in this book are now widely used to help men with prostate cancer.

Treatment after first-line

Chart 7.3.3 Treatment after enzalutamide or abiraterone

Options if no metastases in internal organs	Options if metastases in internal organs
 Docetaxel with prednisone Abiraterone acetate or enzalutamide Radium-223 if mostly bone metastases Sipuleucel-T (see Chart 7.3.1) Clinical trial Secondary hormone therapy Antiandrogen Antiandrogen withdrawal Ketoconazole Corticosteroids DES or other estrogen Best supportive care 	 Docetaxel with prednisone Clinical trial Abiraterone acetate or enzalutamide Secondary hormone therapy Antiandrogen Antiandrogen withdrawal Ketoconazole Corticosteroids DES or other estrogen Best supportive care

Chart 7.3.4 Treatment after docetaxel

Options if no metastases in internal organs	Options if metastases in internal organs
 Enzalutamide Abiraterone acetate with prednisone Radium-223 if mostly bone metastases Cabazitaxel with prednisone Sipuleucel-T (see Chart 7.3.1) Clinical trial Docetaxel rechallenge Alternative chemotherapy (mitoxantrone) Secondary hormone therapy Antiandrogen Antiandrogen withdrawal Ketoconazole Corticosteroids DES or other estrogen 	 Enzalutamide Abiraterone acetate with prednisone Cabazitaxel with prednisone Clinical trial Docetaxel rechallenge Alternative chemotherapy (mitoxantrone) Secondary hormone therapy Antiandrogen Antiandrogen withdrawal Ketoconazole Corticosteroids DES or other estrogen Best supportive care

Chart 7.3.2 continued

Secondary <u>hormone therapy</u> is an option for when there is no <u>visceral disease</u>. Compared to abiraterone acetate, these treatments have only minor benefits. If your first hormone therapy was surgical or medical castration, starting <u>CAB</u> or switching to a new antiandrogen may help. If you're already on CAB, stopping your use of the antiandrogen—known as antiandrogen withdrawal—may help if the cancer cells are using the antiandrogen to grow. This effect is called the antiandrogen withdrawal response and usually lasts several months. Ketoconazole and corticosteroids may help stop cancer growth by lowering <u>testosterone</u> levels.

Chart 7.3.3 lists treatment options following enzalutamide or abiraterone. Docetaxel with prednisone on an every-3-week schedule is preferred for cancer that is causing symptoms. Abiraterone acetate can be received if you took enzalutamide before and enzalutamide can be received if you took abiraterone acetate before.

Radium-223 is an option for <u>metastases</u> that occur mostly in the bones and not in the internal organs. Sipuleucel-T may also be used for CRPC that hasn't spread to internal organs. Read Chart 7.3.1 for more details.

Other options to consider are clinical trials and secondary hormone therapy. Joining a clinical trial is strongly supported. It may give you access to new treatments. Secondary hormone therapy may have minor benefits. All men with CRPC should receive best <u>supportive care</u>. **Chart 7.3.4** lists options if docetaxel fails. There is no strong agreement on what is the next best treatment. Abiraterone acetate with prednisone or enzalutamide has been shown to slightly prolong life when used after docetaxel. Similar results were found with cabazitaxel plus prednisone. However, cabazitaxel can cause severe <u>side effects</u> so close monitoring is needed. You shouldn't use cabazitaxel if you have liver problems.

Radium-223 is an option for metastases that occur mostly in the bones and not in the internal organs. Sipuleucel-T may also be used for CRPC that hasn't spread to internal organs. Read Chart 7.3.1 for more details.

After docetaxel fails, your doctor may want you to take docetaxel again. This is called docetaxel rechallenge. Whether you took docetaxel or not, other recommendations include chemotherapy and secondary hormone therapy. If you can't take a taxane-based chemotherapy like cabazitaxel, mitoxantrone is an option. Mitoxantrone and other chemotherapy drugs haven't extended the lives of men after docetaxel failure but may help you feel better by reducing symptoms.

Other options to consider are clinical trials and secondary hormone therapy. Joining a clinical trial is strongly supported. It may give you access to new treatments. Secondary hormone therapy may have minor benefits. All men with CRPC should receive best supportive care.

Review

- Advanced disease is often first treated with ADT.
- CRPC is prostate cancer that grows even though testosterone is at very low levels.
- A clinical trial, observation, and secondary hormone therapy are options for CRPC without metastases.
- Newer treatments for CRPC with metastases include sipuleucel-T, abiraterone acetate, enzalutamide, and radium-223. Chemotherapy with hormone therapy, clinical trials, and secondary hormone therapy are other options.
- All men with CRPC should receive supportive care.



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8 Making treatment decisions

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84	Questions to ask your doctors
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Having cancer is very stressful. While absorbing the fact that you have cancer, you have to learn about tests and treatments. In addition, the time you have to accept a treatment plan feels short. Parts 1 through 7 described the cancer and the test and treatment options recommended by NCCN experts. These options are based on science and agreement among NCCN experts. Part 8 aims to help you make decisions that are in line with your beliefs, wishes, and values.

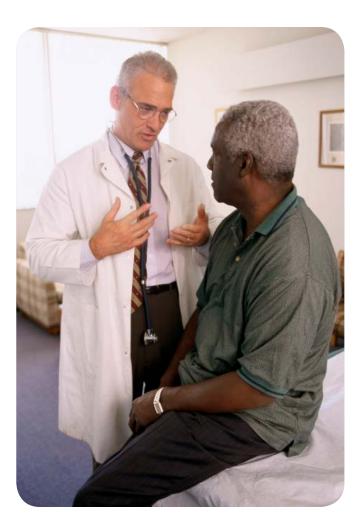
It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Your doctors will give you the information you need to make an informed choice. In early-stage disease, there are often multiple good options. It is good news to have multiple options.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. However, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.



Questions to ask your doctors

You will likely meet with experts from different fields of medicine. Strive to have helpful talks with each person. Prepare questions before your visit and ask questions if the person isn't clear. You can also record your talks and get copies of your medical records. It may be helpful to have your spouse, partner, or a friend with you at these visits. They can help to ask questions and remember what was said. Suggested questions to ask include:

What's my diagnosis and prognosis?

It's important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors can tell you which type of cancer you have. He or she can also give a <u>prognosis</u>. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

- 1. Where did the cancer start? In what type of cell?
- 2. Is this cancer common?
- 3. What is the cancer stage? Does this stage mean the cancer has spread far?
- 4. What is the grade of the cancer? Does this grade mean the cancer will grow and spread fast?
- 5. What other test results are important to know?
- 6. How often are these tests wrong?
- 7. Would you give me a copy of the pathology report and other test results?
- 8. Can the cancer be cured? If not, how well can treatment stop the cancer from growing?

What are my options?

There is no single treatment practice that is best for all men. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

- 1. What will happen if I do nothing?
- 2. Can I just carefully monitor the cancer?
- 3. Do you consult NCCN recommendations when considering options?
- 4. Are you suggesting options other than what NCCN recommends? If yes, why?
- 5. How do my age, health, and other factors affect my options?
- 6. Which option is proven to work best?
- 7. Which options lack scientific proof?
- 8. What are the benefits of each option? Does any option offer a cure? Are my chances any better for one option than another? Which option spares the most healthy tissue? Is any option less invasive? Less time-consuming? Less expensive?
- 9. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?

What does each option require of me?

Many men consider how each option will practically affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that is the least taxing may be important to you:

- 1. Will I have to go to the hospital or elsewhere? How often? How long is each visit?
- 2. How do I prepare for treatment?
- 3. Should I bring someone with me when I get treated?
- 4. Will the treatment hurt?
- 5. How much will the treatment cost me? What does my insurance cover?
- 6. Is home care after treatment needed? If yes, what type?
- 7. How soon will I be able to manage my own health?
- 8. When will I be able to return to my normal activities?

What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

- 1. Are you board certified? If yes, in what area?
- 2. How many patients like me have you treated?
- 3. How many procedures like the one you're suggesting have you done?
- 4. Is this treatment a major part of your practice?
- 5. How many of your patients have had complications?

Weighing your options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

2nd opinion

The time around a cancer diagnosis is very stressful. People with cancer often want to get treated as soon as possible. They want to make their cancer go away before it spreads farther. While cancer can't be ignored, there is time to think about and choose which option is best for you.

You may wish to have another doctor review your test results and suggest a treatment plan. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion on which option is best can help.

Copies of the pathology report, a DVD of the imaging tests, and other test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

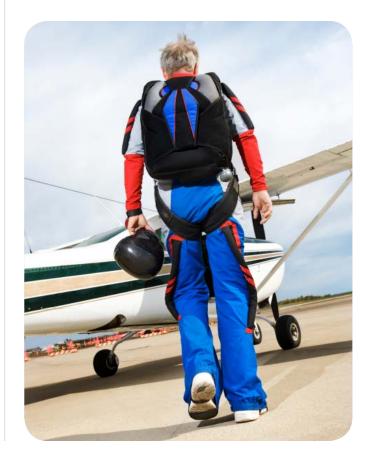
When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What's more, some health plans require a 2nd opinion. If your health plan doesn't cover the cost of a 2nd opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel more at peace about the treatment you accept to have. If the two opinions differ, think about getting a 3rd opinion. A 3rd opinion may help you decide between your options. Choosing your cancer treatment is a very important decision. It can affect your length and quality of life.

Decision aids

Decision aids are tools that help people make complex choices. For example, you may have to choose between two options that work equally as well. Sometimes making a decision is hard because there is a lack of science supporting a treatment.

Decision aids often focus on one decision point. In contrast, this book presents tests and treatment options at each point of care for large groups of patients. Well-designed decision aids include information that research has identified as what men need to make decisions. They also aim to help you think about what's important based on your values and preferences.



Support groups

Besides talking to health experts, it may help to talk to men who have walked in your shoes. Support groups often consist of men at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other men with prostate cancer.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others.

Websites

American Cancer Society www.cancer.org/cancer/prostatecancer/index

California Prostate Cancer Coalition (CPCC) prostatecalif.org

Decision Aids decisionaid.ohri.ca/AZinvent.php

www.prostatecancerdecision.org

Social Security's Life expectancy www.ssa.gov/OACT/STATS/table4c6.html

National Alliance of State Prostate Cancer Coalitions (NASPCC) www.naspcc.org

National Coalition for Cancer Survivorship www.canceradvocacy.org/toolbox

NCCN www.nccn.org/patients

Nomograms nomograms.mskcc.org/Prostate/index.aspx

Prostate Cancer Foundation www.pcf.org

Prostate Health Education Network (PHEN) prostatehealthed.org

Us TOO! www.ustoo.org

ZERO - The End of Prostate Cancer zerocancer.org

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make informed decisions.
- Getting a 2nd opinion, using decision aids, attending support groups, and comparing benefits and downsides may help you decide which treatment is best for you.



National Comprehensive Cancer Network®

Glossary

Dictionary Acronyms

NCCN Guidelines for Patients[®] Prostate Cancer, Version 1.2015

Dictionary

active surveillance

Delay of treatment with ongoing testing to watch for cancer growth.

androgen deprivation therapy (ADT) Treatment that stops the testicles from making testosterone.

biopsy

The removal of tissue or fluid samples from your body to test for disease.

brachytherapy The placement of radioactive objects near or in a tumor.

combined androgen blockade (CAB) Castration treatment used with an antiandrogen.

computed tomography (CT) A test that uses x-rays to view body parts.

cryosurgery Treatment that freezes tissue to kill cancer cells.

digital rectal exam (DRE)

An exam of the prostate by feeling it through the wall of the rectum.

dry orgasm Having an orgasm without ejaculation.

dual energy X-ray (DEXA) A test that measures bone strength.

epididymis The tube through which sperm travel after leaving the testicles.

epididymitis Swelling of the epididymis.

erectile dysfunction The inability to achieve erections sufficient for intercourse.

external beam radiation therapy (EBRT) Radiation therapy received from a machine outside the body.

extracapsular extension Cancer growth through the prostatic capsule.

fatigue

Severe tiredness despite getting enough sleep that limits one's ability to function.

fine-needle aspiration

Use of a thin needle to remove fluid or tissue from the body.

fistula

A passage between two organs that aren't normally connected.

flare

An increase in testosterone after starting castration treatment.

genes Information in cells for building new cells.

Gleason grade

A score from 1 (best) to 5 (worst) made by a pathologist based on the ability of prostate cells to form glands. The primary grade is the most common pattern, and the secondary grade is the second most common pattern. The two grades are summed to give a Gleason score.

Gleason score

The grading system for prostate cancer.

high-dose rate (HDR) brachytherapy

Radioactive objects are removed from the tumor after the radiation dose has been given.

hormone therapy

Treatment that stops the making or action of hormones in the body; androgen deprivation therapy.

image-guided radiation therapy (IGRT)

Radiation therapy that uses imaging tests during treatment to better target the tumor.

immunotherapy

Treatment that uses the immune system to fight disease.

intensity-modulated radiation therapy (IMRT)

Radiation therapy that uses small beams of different intensities.

intermittent treatment

Alternating periods of time on and off treatment.

interstitial radiation A type of radiation therapy that places radioactive objects in the tumor.

laparoscopic radical prostatectomy Removal of the prostate through several small cuts in the pelvis.

life expectancy The number of years a person is likely to live.

Iow-dose rate (LDR) brachytherapy Radioactive objects are inserted into the tumor and left to decay.

luteinizing hormone-releasing hormone (LHRH) agonist

A drug that acts in the brain to stop the testicles from making testosterone.

luteinizing hormone-releasing hormone (LHRH) antagonist

A drug that acts in the brain to stop the testicles from making testosterone.

lymph

A clear fluid containing white blood cells.

lymph node

A small clump of special immune cells. There are thousands of lymph nodes located throughout the body.

magnetic resonance imaging (MRI)

A test that uses a magnetic field and radio waves to view the parts of the body and how they are working.

magnetic resonance (MR) spectroscopy A test that measures chemicals in cells without removing tissue from the body.

medical oncologist A doctor who's an expert in drugs that treat cancer.

metastasis The growth of cancer beyond local tissue.

mutation An abnormal change in the coded instructions within cells.

nerve-sparing prostatectomy

One or both bundles of cavernous nerves aren't removed during a prostatectomy.

nomogram

A tool that uses clinical information to predict an outcome.

nuclear medicine specialist

A doctor who's an expert in tests that use radioactive substances.

observation

Testing on a regular basis so that supportive care can be given if cancer symptoms are likely to start.

open perineal prostatectomy

Removal of the prostate through one cut made between the scrotum and anus.

open retropubic prostatectomy

Removal of the prostate through one long cut from the belly button to the base of the penis.

orchiectomy

Surgical removal of one or both testicles from the body.

overflow incontinence Leakage of urine due to an overly full bladder.

pathologist A doctor who specializes in testing cells to identify disease.

pelvic lymph node dissection (PLND) Removal of the lymph nodes in the pelvis.

perineum The area in men between the scrotum and anus.

persistent cancer Cancer not completely removed or destroyed by treatment.

primary grade The most common pattern of prostate cells' ability to form into glands.

primary treatment The main treatment used to cure or control cancer.

prognosis A prediction of the pattern and outcome of a disease based on clinical information.

prostate

A male gland that makes fluid that protects sperm from the acid in the vagina.

prostate-specific antigen (PSA) A protein made by the prostate.

prostate-specific antigen (PSA) density Comparison of the level of PSA to the size of the prostate.

prostate-specific antigen (PSA) doubling time The time during which the level of PSA doubles.

prostate-specific antigen (PSA) level Number of nanograms per milliliter of PSA.

prostate-specific antigen (PSA) velocity How much the level of PSA changes over time.

radical perineal prostatectomy Removal of the prostate through the perineum.

radical retropubic prostatectomy Removal of the prostate through one incision in the lower abdomen.

radiologist A doctor who specializes in reading imaging tests.

radiopharmaceutical A drug that contains a radioactive substance.

recurrence The return of cancer after a disease-free period.

risk group Prediction of a person's chances for an event based on if he or she matches the criteria of a group.

robotic-assisted prostatectomy

A laparoscopic prostatectomy during which a surgeon uses a machine to operate.

secondary grade The second most common pattern of prostate cells' ability to form into glands.

seminal vesicles

A pair of male glands that makes fluid used by sperm for energy.

side effect

An unhealthy or unpleasant physical or emotional response to a test or treatment.

stress incontinence

Leakage of urine when pressure is exerted on the bladder from sneezing, coughing, exercise, and so forth.

supportive care

Treatment for symptoms of a disease.

surgical margin

Normal tissue around the edge of a tumor that is removed during an operation.

three-dimensional conformal radiation therapy (3D-CRT)

Radiation therapy that uses beams that match the shape of the tumor.

testosterone

A hormone that helps the sexual organs in men to work.

transrectal ultrasound (TRUS) A type of ultrasound that takes pictures of the prostate through the rectum.

transurethral resection of the prostate (TURP)

Surgical removal of some prostatic tissue through the urethra.

triple androgen blockade

Finasteride or dutasteride with combined androgen blockade.

urethra

A tube that expels urine from the body; it also expels semen in men.

urge incontinence The feeling of having to rush to urinate or you'll leak urine.

urinary incontinence Inability to control the release of urine from the bladder.

urinary retention Inability to empty the bladder.

urologist

A doctor who's an expert in the urinary system of men and women and in male sex organs.

visceral disease

Spread of cancer cells from the first tumor to internal organs.

Acronyms

3D-CRT three-dimensional conformal radiation therapy

ADT androgen deprivation therapy

AJCC American Joint Committee on Cancer

CAB combined androgen blockade

CAM complementary and alternative medicine

CRPC castration-recurrent prostate cancer

CT computed tomography

DES diethylstilbestrol

DEXA dual energy x-ray absorptiometry

DNA deoxyribonucleic acid

DRE digital rectal exam

EBRT external beam radiation therapy

HDR high-dose rate

HIFU high intensity focused ultrasound

IGRT image-guided radiation therapy

IMRT intensity-modulated radiation therapy

IU international unit

LDT low-dose rate

LHRH luteinizing hormone-releasing hormone

PSA prostate-specific antigen

mg milligram

MRI magnetic resonance imaging

PLND pelvic lymph node dissection

SBRT stereotactic body radiotherapy

TRUS transrectal ultrasound

TURP transurethral resection of the prostate

VTP vascular targeted photodynamic

NCCN Abbreviations and Acronyms

NCCN[®] National Comprehensive Cancer Network[®]

NCCN Patient Guidelines[®] NCCN Guidelines for Patients[®]

NCCN Guidelines[®] NCCN Clinical Practice Guidelines in Oncology[®]

NCCN Guidelines for Patients[®]

Patient-friendly translations of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)



- Acute Lymphoblastic Leukemia*
- Caring for Adolescents and Young Adults (AYA)
- Chronic Myelogenous Leukemia
- Colon Cancer*
- Esophageal Cancer

- Lung Cancer Screening*
- Malignant Pleural Mesothelioma*
- Melanoma*
- Multiple Myeloma*
- Non-Small Cell Lung Cancer*
- Ovarian Cancer

- Pancreatic Cancer*
- Prostate Cancer
- Soft Tissue Sarcoma*
- Stage 0 Breast Cancer*
- Stages I & II Breast Cancer*
- Stage III Breast Cancer*
- Stage IV Breast Cancer*

* Printed copies available.

Available online at NCCN.org/patientguidelines





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