



# Prostate Cancer Advanced Stage

Presented with support from:





Available online at NCCN.org/patients



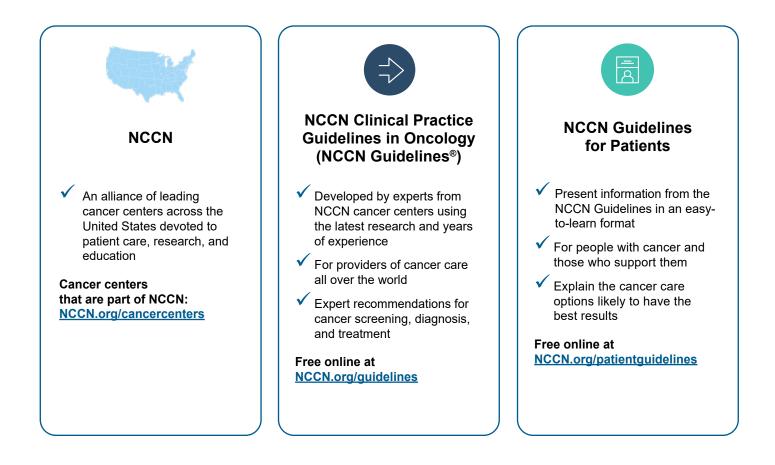


Step-by-step guides to the cancer care options likely to have the best results
 Based on treatment guidelines used by health care providers worldwide
 Designed to help you discuss cancer treatment with your doctors



National Comprehensive Cancer Network®

# NCCN Guidelines for Patients<sup>®</sup> are developed by the National Comprehensive Cancer Network<sup>®</sup> (NCCN<sup>®</sup>)



# These NCCN Guidelines for Patients are based on the NCCN Guidelines<sup>®</sup> for Prostate Cancer, Version 4.2022 — May 10, 2022.

© 2022 National Comprehensive Cancer Network, Inc. All rights reserved. NCCN Guidelines for Patients and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. No one, including doctors or patients, may use the NCCN Guidelines for Patients for any commercial purpose and may not claim, represent, or imply that the NCCN Guidelines for Patients that have been modified in any manner are derived from, based on, related to, or arise out of the NCCN Guidelines for Patients. The NCCN Guidelines are a work in progress that may be redefined as often as new significant data become available. NCCN makes no warranties of any kind whatsoever regarding its content, use, or application and disclaims any responsibility for its application or use in any way. NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

National Comprehensive Cancer Network (NCCN) / NCCN Foundation 3025 Chemical Road, Suite 100 Plymouth Meeting, PA 19462 215.690.0300



# NCCN Guidelines for Patients are supported by funding from the NCCN Foundation<sup>®</sup>

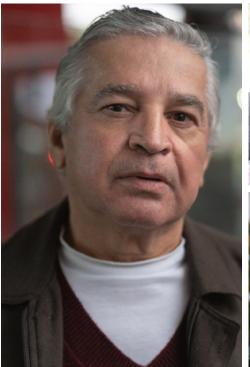
To make a gift or learn more, please visit <u>NCCNFoundation.org/donate</u> or e-mail <u>PatientGuidelines@NCCN.org</u>.















# Contents

- 6 Prostate cancer basics
- 14 Tests for prostate cancer
- 24 Determining the diagnosis
- 33 Risk assessment
- 38 Prostate cancer treatments
- 55 If cancer returns
- 61 Non-metastatic prostate cancer
- 66 Metastatic prostate cancer
- 71 Making treatment decisions
- 81 Words to know
- 84 NCCN Contributors
- 85 NCCN Cancer Centers
- 86 Index

# 1 Prostate cancer basics

7	What is prostate cancer?
8	What causes prostate cancer?
10	Are there different types of prostate cancer?
12	What are symptoms of prostate cancer?
12	Can prostate cancer be cured?
13	Key points



The prostate is a gland located deep inside the lower abdomen. Anyone with a prostate has a chance of getting prostate cancer. This chapter offers an overview of this common cancer.

# What is prostate cancer?

Prostate cancer develops in a small gland called the prostate. The prostate gland is part of the male reproductive system. The prostate is located deep inside the lower part of the trunk of the body, just below the bladder.

Prostate cancer develops when cells in the gland start to grow out of control.

# What is cancer?

Cancer is a disease where cells—the building blocks of the body—grow out of control. This can end up harming the body. There are many types of cells in the body, so there are many types of cancers.

Cancer cells don't behave like normal cells. Normal cells have certain rules. Cancer cells don't follow these rules.

- Cancer cells develop genetic errors (mutations) that allow them to multiply and make many more cancer cells. The cancer cells crowd out and overpower normal cells. Cancer cells take away energy and nutrients that normal cells need.
- Normal cells live for a while and then die. Cancer cells avoid normal cell death. They survive much longer than normal cells do.
- Cancer cells can spread to other areas of the body. They can replace many normal cells and cause organs to stop working well.
- Treatment may get rid of cancer at first but sometimes the cancer comes back later.
- Cancer can stop responding to treatment that worked before.

Scientists have learned a great deal about cancer. As a result, today's treatments work better than treatments in the past. Also, many people with cancer have more treatment choices now than they had before.

## What causes prostate cancer?

Doctors don't know exactly what causes prostate cells to grow out of control (become cancerous). But several factors are linked to a higher risk of prostate cancer. These are called risk factors. A risk factor is anything that increases your chance of getting cancer.

Risk factors don't necessarily cause prostate cancer, but people with prostate cancer usually have one or more of these risk factors:

- Age The biggest risk factor for prostate cancer is age. Prostate cancer is diagnosed most often in those aged 65 years and above. Your chances of getting prostate cancer increase as you become older.
- Family history Your family health history is information about the diseases and health conditions in your family. A family history reflects a pattern of certain diseases among family members. Males who have a close family member (a brother or father) with prostate cancer have a greater chance of getting it themselves. Those with a family history of certain other cancers (breast, ovarian, colon, pancreatic, and other cancers) are also at a higher risk for prostate cancer.
- Genetic factors Genetic testing can find specific inherited genetic abnormalities (mutations) known to be linked with prostate cancer or other cancers. For instance, a man with an inherited genetic abnormality in the BRCA2 gene likely has a higher risk of prostate cancer. Inherited mutations are passed down a generation from either parent. Genetic abnormalities that aren't inherited can occur, too.

- Race Black males are more likely than White males to develop prostate cancer. Prostate cancer in Black males is also more likely to occur at an earlier age and be more aggressive and more advanced when diagnosed. Lack of equal access to health care is a major factor contributing to these differences.
- Diet and lifestyle Eating food that's high in fat, such as meat and dairy products, has been linked with an increased risk for prostate cancer. Smoking may also increase the risks of developing prostate cancer and of dying from it. Eating more fruits and vegetables may reduce this risk. Exercise also likely decreases the likelihood of dying from prostate cancer.

These risk factors aside, anyone with a prostate has a risk of getting prostate cancer. Prostate cancer is the most common cancer in American males besides skin cancer.

## The prostate enlarges with age

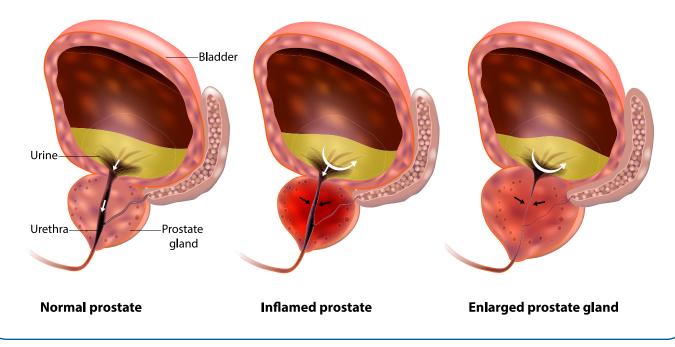
A young man's prostate is said to be the size of a walnut or a ping-pong ball and weigh about the same as an AA battery. As you grow older, your prostate gradually grows larger, possibly reaching the size of a lemon or an orange.

Having an enlarged prostate is a condition called benign prostatic hyperplasia (BPH). Benign means it's not cancerous. An enlarged prostate doesn't cause prostate cancer or increase your risk of getting it. However, it's common to have an enlarged prostate and prostate cancer at the same time. Notably, an enlarged prostate can cause the same symptoms as those caused by prostate cancer.

Doctors aren't sure what causes the prostate to grow as men get older. A common theory is that levels of hormones (like testosterone) change with age, which affects the size of the prostate.

In many individuals, the prostate grows large enough to squeeze the urethra—a tube that passes through the prostate. The urethra allows urine to flow out of the bladder. This squeezing can narrow the urethra, which slows down or stops the flow of urine when you try to pee.

Although prostate cancer usually doesn't cause any symptoms, it also can slow the flow of urine if it grows large enough. That's why it's important to get these problems checked out.



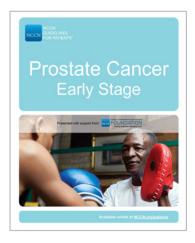
# Are there different types of prostate cancer?

Prostate cancer can be grouped into earlystage cancer or advanced-stage cancer.

#### Early stage

Prostate cancer usually grows slowly and stays in the prostate. Early stage means the cancer has not spread beyond the prostate. Cancer that is contained entirely within the prostate is called localized prostate cancer.

A book about early-stage prostate cancer, NCCN Guidelines for Patients: Prostate Cancer, Early Stage, can be found at NCCN.org/patientguidelines.



#### Advanced stage

This book is all about advanced-stage (metastatic) prostate cancer.

Advanced stage means that the cancer has spread beyond the prostate to other areas in the body. This spreading is called metastasis or metastatic cancer.

Cancer cells can use the bloodstream like a highway to travel to distant areas in the body. Cancer cells can also spread through the lymphatic system. The lymphatic system is a network of organs and vessels that fights infections and circulates a clear fluid called lymph throughout the body. Lymph nodes are a normal and important part of this system. Lymph nodes are small, disease-fighting clusters that filter the lymph fluid to remove germs. Lymph vessels and nodes are found everywhere in the body.

Prostate cancer can metastasize to the lymph nodes, bones, liver, lungs, and other organs.

Some men have advanced-stage prostate cancer when they're first diagnosed. Others develop advanced-stage cancer after having treatment for early-stage cancer.

Sometimes prostate cancer is found without even looking for it. It might be discovered by chance during medical testing for another health issue. This is called an incidental finding.

## Where does the prostate fit in?

The prostate is located deep inside the lower body. It makes semen and is important for sexual reproduction.

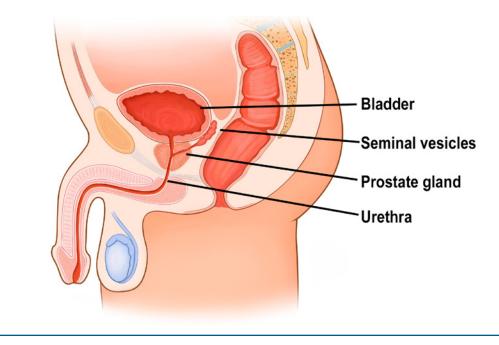
**Prostate:** A gland in the male reproductive system. A gland is an organ that makes fluids or chemicals the body needs. The prostate gland makes a liquid that nourishes and helps transmit semen.

**Semen:** A fluid made up of liquids from the prostate and the seminal vesicles as well as sperm from the testicles. During ejaculation, semen is released from the body through the urethra and out through the penis.

**Urethra:** A tube that carries urine from the bladder and out of the body. The prostate wraps around the urethra just beneath the bladder.

**Seminal vesicles:** Two glands that make another part of the fluid that becomes semen. The seminal vesicles are located above the prostate and behind the bladder.

Bladder: An organ that holds urine.



# What are symptoms of prostate cancer?

A symptom is a feeling or problem that can be a sign of a disease or condition. Prostate cancer often grows slowly and shows no symptoms for a long time. You don't have to have symptoms to have prostate cancer. This is true in the early stages of the disease and even advanced prostate cancer may have few or mild symptoms.

Some symptoms that may occur include:

- Urinating (peeing) frequently, especially at night
- > Weak or intermittent urine stream
- > Trouble urinating or straining to urinate
- > Trouble holding in urine
- Feeling like your bladder hasn't fully emptied
- > Blood in the urine or semen
- Erectile dysfunction (difficulty getting an erection)
- > Dull pain in the groin or pelvis
- > Burning or pain while urinating
- Unexplained weight loss
- > Bone, hip, or back pain
- > Weakness of the knees or legs
- > Feeling dizzy or lightheaded

#### It's important to know that prostate cancer has many of the same symptoms as a condition called enlarged prostate (also called benign prostatic hyperplasia, or BPH). It's difficult to tell the difference between the two conditions based on symptoms alone, and BPH is much more common than prostate cancer. Be sure to tell your doctor about any symptoms you have because you may need specific testing.

# Can prostate cancer be cured?

Advanced-stage prostate cancer isn't curable, but treatment can slow down its growth, reduce its symptoms, and prolong your life. Treatments for advanced prostate cancer include hormone therapy, chemotherapy, immunotherapy, surgery, radiation therapy, radiopharmaceuticals, and targeted therapy.

Prostate cancer in the advanced stage can be fatal. But in the past few decades, better detection and treatments have been reducing the number of fatalities from prostate cancer in men of all races and ethnicities. Many patients with advanced-stage prostate cancer continue to live with the cancer and, in the end, may die from something else.

#### Key points

# Key points

- Prostate cancer develops when cells in the prostate gland grow out of control.
- Age is the biggest risk factor for prostate cancer. As you age, your chances of developing prostate cancer increase.
- The majority of prostate cancers are diagnosed in males over the age of 65.
- Males who have a close family member (brother, father) with prostate cancer have a greater chance of getting it themselves.
- All males are at risk for prostate cancer but Black males are at greater risk.
- Advanced-stage prostate cancer has spread beyond the prostate to other areas in the body. This spread is called metastasis.
- Cancer cells can spread to other body parts through blood or lymph.
- You don't have to have symptoms to have prostate cancer.
- Advanced-stage prostate cancer isn't curable, but treatment can slow it down, reduce its symptoms, and improve longevity.
- Advanced-stage prostate cancer can be difficult to treat. Seek out a medical center that specializes in prostate cancer.
- Better detection and treatments for prostate cancer have reduced the number of fatalities in men of all races and ethnicities.

Advanced prostate cancer can be difficult to treat. Seek out a medical center that specializes in the diagnosis and treatment of prostate cancer.

# 2 Tests for prostate cancer

- 15 Screening tests
- 17 General health tests
- 17 Blood and urine tests
- **17 Diagnostic tests**
- 23 Key points



If you haven't been diagnosed yet, testing is necessary to find out if you have prostate cancer and whether it has spread. Testing can also help your doctors plan how to treat it.

Doctors use a variety of tests to find out if you have cancer and determine how advanced the cancer is. Tests are used to plan treatment and check how well treatment is working. This chapter will help you know what tests you may have and what to expect during testing. Bring someone with you to listen, ask questions, and write down the answers.

For people who are suspected of having prostate cancer, testing begins with screening tests, followed by tests of their general health, and then diagnostic tests.

People who are already diagnosed with prostate cancer won't need screening tests, but they will need other tests.

# Screening tests

A screening test looks for disease before you have any symptoms. The goal of screening is to detect disease early when there's a better chance of stopping it.

Screening tests aren't diagnostic, which means they can't tell you for sure whether or not you have the disease. Rather, screening tests indicate that you may need a diagnostic test.

The two screening tests for prostate cancer are a digital rectal exam and a prostatespecific antigen (PSA) test.

# **Tips for testing**

Results from blood tests, imaging studies, and biopsies will be used to determine your treatment plan. It's important you understand what these tests mean. Ask questions and keep copies of your test results. Online patient portals are a handy way to access your test results.

#### Remember these tips for testing:

- Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don't be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician informed of any changes.

#### **Digital rectal exam**

Don't be fooled by the name—no high-tech electronics are used in a digital rectal exam. For this test, the word "digital" means "finger." To put it bluntly, the doctor will stick a finger up your butt (rectum) to check your prostate. The doctor will wear gloves and use a lubricant to make it easier.

A digital rectal exam (also called a prostate exam) may sound like a crude and unpleasant form of testing. But it's the simplest and most direct way for the doctor to feel the size and texture of your prostate. If the doctor finds an irregular or hardened part of the prostate, it could be a sign of a tumor.

The digital rectal exam is usually paired with a PSA test and other factors—your age, race, family history, and more—to determine whether you need further testing, such as imaging or a biopsy.

#### **PSA** test

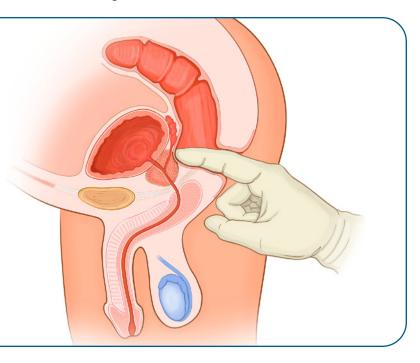
This test measures the amount of prostatespecific antigen (PSA) in your blood. PSA is a protein made inside the prostate. Its job is to help semen transport sperm.

Both normal prostate cells and prostate cancer cells make PSA. If there's something wrong with the prostate—like prostate cancer—these cells may make more PSA. An unusually high amount of PSA in the blood may be a sign of prostate cancer. However, other conditions such as an enlarged prostate or a urinary tract infection—can also cause high levels of PSA. This means that a PSA test by itself can't provide a diagnosis of prostate cancer. That's why a PSA test is often paired with a digital rectal exam or imaging, or both, to decide whether you need a biopsy.

If a person has a high PSA level but no other symptoms of prostate cancer, a second PSA test may be performed. This is done to doublecheck the result before undergoing additional testing.

#### **Digital rectal exam**

A digital rectal exam is a procedure in which your doctor will insert a finger into your rectum to feel your prostate. An irregular or hardened part of the prostate could be a sign of a tumor.



# General health tests

#### **Health history**

Your doctors need to have all of your health information. They'll ask you about any health problems and treatments you've had in your life. Be prepared to talk about any illness or injury you've had and when it happened.

Bring a list of old and new medicines and any over-the-counter medicines, herbals (such as saw palmetto), or supplements you take. Tell your doctor about any symptoms you have.

#### **Family history**

Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history.

It's important to ask members from both your mother's and father's side of the family about all cancers, not just prostate cancer. Ask family members about other health issues like heart disease and diabetes, at what age they were diagnosed, and if anyone died of cancer.

Share this information and any changes to your family history with your doctor.

# Blood and urine tests

For a blood test, a needle is inserted into a vein in your arm to remove a sample of blood. The sample is examined in a lab where cells, proteins, and other components in the blood are tested for signs of disease or other conditions.

Sometimes, men with a higher PSA level have additional blood or urine testing. These tests, sometimes referred to as biomarker tests, can be used in addition to PSA to help decide whether a biopsy is needed. Biomarker tests such as PHI, SelectMDx, 4Kscore, MPS, IsoPSA, and ExoDx are options to consider for those with a high PSA level.

# **Diagnostic tests**

If the digital rectal exam, PSA test, and other factors (like family history, race, or age) suggest you have prostate cancer, you'll be offered diagnostic testing. Talk with your doctor about whether a biopsy or imaging should be the next test you take.

#### **Biopsy**

A biopsy is a procedure that removes cells or a small piece of tissue from your body. These are tested in a laboratory to find cancer. A biopsy is the only test that can confirm (diagnose) prostate cancer.

The most common biopsy for prostate cancer is a core needle biopsy. This procedure is usually performed by a urologist using an ultrasound probe inserted in the rectum to see the prostate. A urologist is a doctor who's an expert in treating diseases of the urinary system and the male reproductive organs.

For this procedure, you'll lie on a table on your side with your knees bent. Once the lubricated probe is inserted into your rectum, it will release high-energy sound waves that will bounce off of internal tissues. A computer will convert these sound waves into a sonogram, which shows a video image of the prostate.

The urologist will then insert a hollow needle into the prostate gland using the ultrasound image to guide it. The needle will be inserted either through the rectum or through the perineum (the skin between the anus and scrotum). When the doctor removes the needle, it will pull out a small sample of prostate tissue called a core.

Your doctor will take several core samples from different parts of the prostate. Sometimes these will be removed from a specific area in the prostate based on the findings of an MRI.

Your biopsy samples will then be sent to a lab for testing. At the lab, a pathologist will examine the samples under a microscope. A pathologist is a doctor who's an expert at examining cells and tissue to find disease. If the pathologist finds cancer cells in the samples, further testing can identify your cancer risk. Additional tests can indicate whether the cancer will grow and spread quickly. Or the results may suggest that the cancer will grow very slowly and not spread outside of the prostate. This information helps plan the best treatment for your type of cancer.

#### **Genetic tests**

A genetic test is used to find abnormal changes (mutations) in your genes. Genes are small segments of DNA inside every cell. Genes provide the instructions to tell the cell how to make proteins, which are the building blocks of tissues.

Once in a while, a gene will have or develop an abnormal change (mutation). A mutation is when something is different in your genes compared to most other people's genes. Sometimes an abnormal change can cause a gene to make the wrong type of protein or make no protein at all. This abnormality can affect the cell, which may in turn cause a disease such as cancer.

Mutations can be passed down in families, in which case they occur in every cell in your body. Or, mutations can occur spontaneously in just some of your cells, such as in cancer cells. In other words, they may be present before you're born (called an inherited or germline mutation) or occur on their own later in life (called an acquired or somatic mutation).

The two basic types of genetic tests used for prostate cancer care are germline testing and molecular biomarker testing:

#### Germline testing

Sometimes, mutations in genes inherited from your parents can increase the risk for different cancers. You can pass these genes on to your children. Other family members might also carry these mutations. If you have a family history of cancer or other features, your doctor might suggest genetic testing to find out if you have an inherited cancer risk.

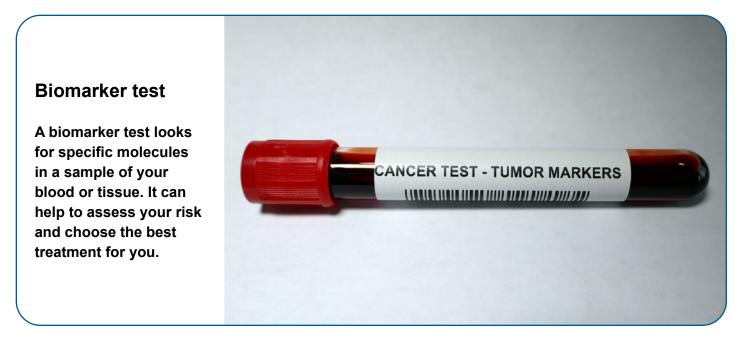
The goal of this type of genetic testing is to look for germline (inherited) mutations that occur in every cell in your body. Genetic germline testing is done using a sample of your blood, urine, or saliva.

For prostate cancer, germline testing looks for mutations in these genes: *BRCA1, BRCA2, ATM, CHEK2, MLH1, MSH2, MSH6, PALB2, PMS2,* and others. Some mutations can put you at risk for more than one type of cancer. Germline mutations in genes like *BRCA1* or *BRCA2* are also related to breast, ovarian, and pancreatic cancer. Germline mutations in *MSH2, MSH6, MLH1,* and *PMS2* are also linked to colorectal and uterine cancers.

If a germline mutation is suspected based on your family's or your own health history, you should seek genetic counseling. A genetic counselor is an expert who has special training in genetic diseases and can help you decide whether you would like to undergo germline testing. A genetic counselor will also help you interpret the results of these tests.

Germline testing is recommended for those with any of the following:

- A family history of prostate cancer, breast cancer, ovarian cancer, intestinal cancer, and certain other cancers
- High-risk, very-high-risk, regional, or metastatic prostate cancer regardless of family history
- > Ashkenazi Jewish ancestry
- > Having any other cancer



Talk to your medical providers and/or a genetic counselor about your family history of cancer.

#### Molecular biomarker testing

In biomarker testing, a sample of your blood or tissue is tested to look at its molecular components. This information is used to help choose the best treatment for you. Biomarker testing can be considered for those with localized, regional, or metastatic prostate cancer. Biomarker testing is sometimes called gene profiling or molecular tumor testing.

The main reason to have a molecular biomarker test is to help assess whether you have lower or higher risk prostate cancer. A molecular biomarker test can flag those who have higher risk prostate cancer, which may give them a head start on treatment.

Molecular biomarker testing is discussed further in Chapter 4.

#### **Imaging tests**

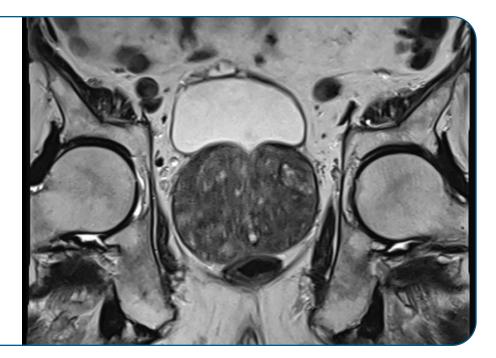
An imaging test takes pictures (images) of the insides of your body. The images can reveal cancer, including its size, location, and other features. The images may show where the cancer started (primary tumor) and whether the cancer has spread (metastasized).

After your scan, your images will be studied by a radiologist. A radiologist is a doctor who's an expert in reading imaging tests. The radiologist will send the results to your doctor. This information helps your doctor plan the next steps of your care. Your doctor will discuss the results with you. Be sure to ask any questions you may have.

Imaging methods for detecting prostate cancer include ultrasound, MRI, CT, PET, or a combination of these. If your PSA, digital rectal exam, and biopsy results suggest that the cancer has spread, your doctor may recommend one or more of the following imaging tests:

#### **MRI scan**

In the MRI image shown here, the large, dark object shaped like a tomato is an enlarged prostate.



#### CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. CT takes many x-rays of the same body part from different angles. The computer combines all the x-ray pictures to make a single detailed image.

CT scans are good at seeing lymph nodes and the area around the prostate. To look for cancer that has spread beyond the prostate, a CT scan of your abdomen and/or pelvis may be used. The pelvis is the area of the lower abdomen located between the hip bones; it contains the prostate, bladder, and rectum.

A CT scanner is a large machine that has a tunnel in the middle. During the test, you'll lie on a table that moves slowly through the tunnel. Pillows or straps may be used to help keep you still during the test. Tell your team if you get nervous in small spaces. You may be given a sedative (medicine) to help you relax.

You may also be given contrast (sometimes called contrast dye) before the CT scan. Contrast is used to make blood vessels, organs, and other tissues stand out more clearly in the images. Contrast is injected into the bloodstream and flushed out in urine. Let your doctor know if you've had a reaction to contrast before.

For the scan, you'll be alone but a technician will operate the machine in a nearby room. The technician will be able to see, hear, and speak with you at all times. As the machine takes pictures, you may hear buzzing, clicking, or whirring sounds. A CT scan is done in about 30 seconds, but the entire process takes 20 to 30 minutes.

#### MRI scan

Magnetic resonance imaging (MRI) uses radio waves and powerful magnets to take pictures of the inside of the body. Like a CT scan, an MRI may use contrast to make the images clearer. Also like a CT scan, the MRI scanner is a large machine with a tunnel in the middle. It also makes a lot of loud noises. Unlike a CT scan, MRI doesn't use radiation (x-rays).

An MRI is used to get a more detailed view of the cancer within the prostate. It's also used to see if cancer has spread to nearby lymph nodes or to the bones in your pelvis. The entire process lasts about 1 and a half hours, though the MRI scan itself takes about 45 to 60 minutes.

Because an MRI uses magnets, don't bring any metal objects (jewelry, cell phone, wristwatch, belts with metal buckles) into the imaging room.

#### PET scan

A positron emission tomography (PET) scan highlights cells in your body that may be cancerous. A PET scan can show even small amounts of cancer. It's used after you've been diagnosed to determine the extent of your cancer or to see if it has metastasized. PET imaging can also show how well treatment is working. A PET scan requires injecting a radioactive substance called a tracer into your bloodstream. It takes about an hour for the tracer to circulate throughout your body. The tracer targets your cancer cells, which show up as bright spots on the scan. Afterward, the radiotracer is passed out of your body in your urine.

Like a CT and MRI, a PET scanner is a large, donut-shaped machine with a tunnel in the middle. A PET scan appointment can take 1 to 2 hours, including about 30 minutes of actual scanning time.

#### PET/CT and PET/MRI

Because PET uses a different imaging method, it's often combined with other types of imaging, such as CT or MRI, to provide an even more detailed image. These combined methods are called PET/CT or PET/MRI scans. Like all imaging tests, PET/CT and PET/MRI are not perfect and can sometimes miss areas of cancer.

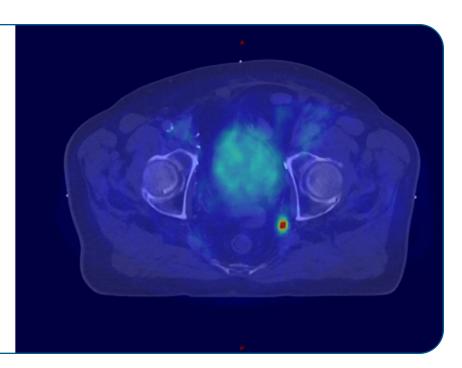
#### Bone scan

A bone scan can detect whether cancer has spread to your bones. A bone scan may be used if you have bone pain, have a high risk for bone metastases, or have changes in certain test results. Bone scans may also be used to monitor treatment.

Like a PET scan, a bone scan uses a radioactive tracer to make pictures of the inside of bones. A special camera will take pictures of the tracer in your bones. Areas of bone damage absorb more tracer than healthy bone. Bone damage can be caused by cancer, cancer treatment, or other health problems. These areas show up as bright spots on the pictures.

#### PET/CT scan of metastatic prostate cancer

This image combines PET and CT scans to show a crosssection of a patient's pelvis. The greenish circle identifies cancer in the prostate, while the intense red dot indicates cancer that has spread to a pelvic lymph node.



# Key points

- Tests are used to plan treatment and check how well treatment is working.
- A digital rectal exam is the simplest way for your doctor to check the size and texture of your prostate.
- A high level of prostate-specific antigen (PSA) in the blood may be a sign of prostate cancer.
- A biopsy is used to confirm (diagnose) prostate cancer. It's a procedure that removes samples of cells or tissue to find cancer.
- A genetic test is used to find abnormal changes (mutations) in your genes.
- Your doctor might refer you for genetic counseling and testing to find out if you have an inherited risk for cancer.
- A blood or tissue sample of your tumor might be tested to look at its molecular components (biomarker testing).
- Imaging tests may be used to see if the cancer has spread beyond the prostate.

# **3** Determining the diagnosis

25	Digital rectal exam	

- 26 PSA
- 26 Prostate biopsy
- 29 Gleason score
- 30 Grade groups
- 31 Tumor stage
- 31 Key points



#### **3** Determining the diagnosis

#### Digital rectal exam

It's important to know the risk of your cancer getting worse. Doctors look at several key characteristics to find out your risk group. This chapter explains each of these characteristics.

Both doctors and patients want to know the risk for the cancer to spread. So doctors look at the clinical characteristics of your cancer, such as your PSA level, biopsy results, and other test results (which we'll talk about in this chapter).

From this information, doctors can classify your disease into one of 5 different risk groups:

- Very low risk
- Low risk
- Intermediate risk
- High risk
- Very high risk

Why do you need to know your risk group? Because your prognosis is based on your risk group. A prognosis predicts the likely course and outcome of a disease.

Your prognosis guides your treatment options. For example, patients with lower risk generally get minimal treatment or no treatment at all. Patients with higher risk usually get more aggressive treatment.

But before we get into treatment, let's talk about the clinical characteristics that make up each of the 5 risk groups. These characteristics come from the results of tests described in the previous chapter plus tests described in this chapter.

## Diagnosis vs. prognosis

What's the difference between your diagnosis and your prognosis? These two words sound alike but they're very different.

**Diagnosis** means identifying an illness based on tests. Your diagnosis names what illness you have.

**Prognosis** is the likely course and outcome of a disease based on tests and your response to treatment. Your prognosis predicts how your illness will turn out.

Let's take a look at the following tests to see how they contribute to each risk group:

## Digital rectal exam

A digital rectal exam is used to screen for cancer, rate the tumor size, and assess how your cancer is responding to treatment. For a digital rectal exam, your doctor will insert a lubricated, gloved finger into your rectum. Your doctor will feel your prostate for abnormal size or hardness, either of which may be a sign of a tumor.

Not all parts of the prostate can be felt during this exam, though. So other tests, like PSA level and imaging, are used to get a more complete picture of your prostate health.

# PSA

A simple blood test will tell you how much prostate-specific antigen (PSA) is in your bloodstream. PSA level (also called total PSA) is measured in nanograms of PSA per milliliter (ng/mL) of blood. The higher the level of PSA in the blood, the greater the risk that the cancer poses. However, PSA levels can vary due to age, race, and other factors.

PSA level doesn't tell the whole story, though. There are other ways that PSA can be interpreted, such as PSA density and PSA recurrence.

#### **PSA** density

Males with larger prostates tend to have higher PSA levels. But that doesn't mean they have a greater likelihood for prostate cancer. To adjust for this, doctors can calculate the PSA density.

PSA density is the amount of PSA compared to the size of the prostate. PSA density is calculated by dividing a patient's PSA level by his prostate size. The size of the prostate is measured by transrectal ultrasound (TRUS) or MRI scan. A higher PSA density (above 0.15 ng/mL<sup>2</sup>, for example) indicates a greater likelihood of cancer. PSA density also accounts for males with small and very small prostates, who could have prostate cancer even with low PSAs.

#### **PSA recurrence**

When PSA level rises after surgery or radiation therapy, it's called PSA recurrence. This rise in PSA could mean that the cancer has returned (recurrence) or that the treatment didn't reduce the amount of cancer in the body (persistence).

# Prostate biopsy

A biopsy removes a sample of tissue that's tested for cancer. Rising PSA levels and an abnormal digital rectal exam are signs of possible prostate cancer. However, the only way to know for sure if you have prostate cancer is to remove tissue from your body and test it for cancer cells.

For a prostate biopsy, a sample of tissue is removed using a hollow needle. You may need to stop taking some medicines, such as aspirin or blood thinners, a week before the procedure.

It's common for patients to have more than one biopsy. You'll have one biopsy to determine your diagnosis and possibly another biopsy in a year or two (called a confirmatory biopsy) to see if the results of both biopsies are the same.

There are two surgical methods for prostate cancer biopsies: transrectal and transperineal.

#### **Transrectal biopsy**

For a transrectal biopsy, a sample of tissue is removed by going into the rectum (transrectal) and, from there, into the prostate.

This can be done in the urologist's office. You'll be awake for the procedure but receive anesthesia to prevent any pain. You'll lie on your side with your knees curled up. A probe will be inserted into your rectum. The probe has a spring-loaded hollow needle. Your doctor will trigger the needle to go through the rectal wall and into your prostate. The needle will remove tissue samples—called cores—about the width of a toothpick and the length of a dime.

#### Prostate biopsy

At least 12 or more core samples are taken from different parts of the prostate. Checking different areas provides a more complete evaluation of cancer throughout the gland.

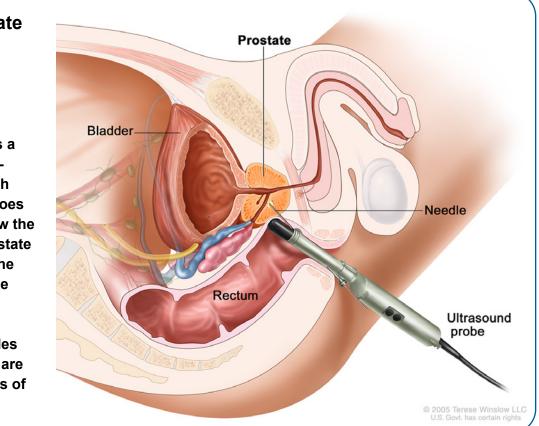
To ensure the best samples are removed, doctors use imaging methods (ultrasound, MRI, or sometimes both) to view the prostate gland and guide the needle.

Transrectal biopsies aren't perfect tests. They sometimes miss cancer sites in the prostate. They can also cause complications. A complication is an unwanted and unplanned result from an operation. Complications of a transrectal biopsy include bleeding from the rectum or blood in the urine, stool, or semen. This usually goes away after a few days or, with semen, after a few weeks. Fever is a sign of a more serious complication, and it's caused by an infection. To prevent this, you'll be given an antibiotic medicine to take the day of the biopsy and for a few days after it. Even with antibiotics, infection is still a serious risk with transrectal biopsy. Difficulty peeing is another uncommon but potentially serious complication. Speak to your doctor if you have either of these problems.

A transrectal biopsy, including preparation and recovery, may take several hours, though the procedure itself takes only about 20 minutes.

#### **Transperineal biopsy**

For a transperineal biopsy, a needle is inserted into the prostate through the perineum. The



# Transrectal prostate biopsy

A biopsy is the only way to be certain that someone has cancer. This illustration shows a transrectal ultrasoundguided biopsy, in which an ultrasound probe goes into the rectum to allow the doctor to view the prostate gland. A needle from the probe goes through the wall of the rectum and into the prostate. The needle removes samples of prostate tissue that are tested in a lab for signs of cancer.

#### **3** Determining the diagnosis

#### Prostate biopsy

perineum is the area in the crotch between the testicles and the anus.

For this biopsy, you'll lie on your back with your legs raised or you'll lie on your side with your knees curled up. Depending on the center, you'll be given general anesthesia that will put you to sleep for the procedure or you'll be awake for the procedure and have local anesthesia to numb your genital and prostate area.

After cleansing the perineum, the doctor will insert a long biopsy needle through the skin and into the prostate to draw out samples of tissue. The doctor may make multiple needle punctures in the perineum to remove multiple core samples. Or the doctor may use a technique that removes multiple samples but requires only a few punctures through the skin.

Ultrasound, MRI, or a combination of both imaging methods are used to guide this procedure. The ultrasound or MRI probe must be inserted into the rectum to scan the prostate.

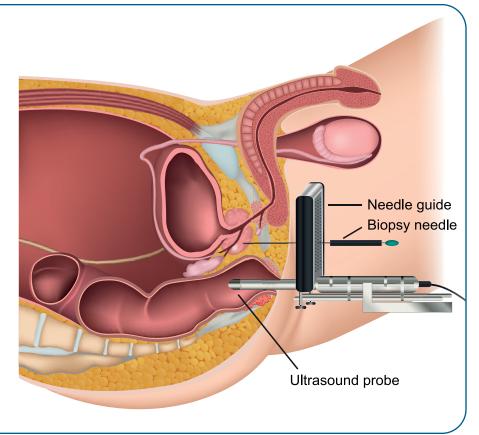
The transperineal procedure takes about 20 to 40 minutes.

#### **Pathology report**

Your biopsy samples will be sent to a lab where a pathologist will examine them under a microscope and test them for cancer. The pathologist will find out how many of the core samples contain cancer and will also measure

# Transperineal prostate biopsy

This illustration shows a transperineal biopsy, in which a needle is inserted through the perineum and into the prostate. An ultrasound probe, which goes into the rectum, helps the doctor guide the needle into the prostate.



#### **3** Determining the diagnosis

#### Gleason score

the percentage of cancer in each core. With this information, the pathologist can estimate the amount of cancer in the prostate and can sometimes tell whether the cancer has spread outside of the prostate. Also, by knowing where each core sample was taken, the pathologist can figure out whether the cancer is concentrated in a certain section of the prostate.

The pathologist will put these results into a report. Ask your doctor to review the report with you.

### **Gleason score**

After studying your biopsy sample under a microscope, the pathologist will give it a Gleason score. A Gleason score represents how much your biopsy sample looks like normal prostate tissue. It also describes how aggressive your prostate cancer is—how quickly it will grow and whether it will spread. A Gleason score is another factor that doctors use to determine risk and plan treatment.

For a Gleason score, the pathologist assigns a number, ranging from 3 to 5, based on the "pattern" of cancer cells in the biopsy sample. Cancer with a cell pattern that looks more like normal and healthy cells has a lower number. Cancer with a cell pattern that looks more abnormal has a higher number.

Prostate cancers often contain more than one pattern of cancer cells. To account for this, a Gleason score is made up of two numbers. The pathologist gives one number to the pattern of cancer cells that take up the largest area in the tumor. The second number is given

#### Your pathology report

Lab results used for diagnosis are put into a pathology report. This report will be sent to your doctor. It's used to plan your treatment.

Ask for a copy of the report. Ask your doctor to review your results with you. Take notes and ask questions.

to the cell pattern that accounts for the secondlargest area.

Add these two numbers together and you get a Gleason score. For example:

pattern 3 + pattern 4 = Gleason score of 7

Most prostate cancers have a Gleason score between 6 and 10. A Gleason score of 6 is low-grade cancer, 7 is intermediate-grade, and 8 to 10 is high-grade. A higher Gleason score means the cancer is more likely to grow and spread quickly than a cancer with a lower Gleason score.

To double-check your Gleason score, you can ask for a second pathologist to review your biopsy.

#### Grade groups

## Grade groups

Gleason scores can be organized into Grade Groups to make them simpler to understand. There are five Grade Groups, numbered 1 to 5. The higher the Grade Group, the more aggressive the cancer. Compare this to a Gleason score, which ranges from 6 to 10, where 6 is the lowest score. This can be confusing because 6 seems like it would be a medium score, not a low score. So in the Grade Group system, a cancer with the lowest Gleason score of 6 has a Grade Group of 1. The Grade Group system also takes into account that Grade Group 2 and Grade Group 3 both have a Gleason score of 7. The difference is that the cancer in Grade Group 3 is more serious. Why? Because the first number of the Gleason score in Grade Group 3 (4+3) is higher than the first number in Grade Group 2 (3+4). Remember, the first number is given to the cancer pattern that makes up the largest area of the tumor. See Guide 1.

#### Guide 1 What does your Gleason score tell you?

Gleason patterns	Gleason score	Grade Group	Risk	Prognosis	
3+3	6	1	Low risk	<b>Low-grade cancer</b> is less aggressive and likely to grow and spread very slowly. If the cancer is small, many years may pass before it becomes a problem. Low-grade cancer may never need treatment.	
3+4	7	2	Favorable intermediate risk	<b>Intermediate-grade cancer</b> is moderately aggressive and likely to grow and spread at a modest pace. If the cancer is small, several	
4+3	7	3	Unfavorable intermediate risk	years may pass before it becomes a problem. To prevent problems, treatment may be needed.	
4+4, 3+5, 5+3	8	4	High risk	<b>High-grade cancer</b> is very aggressive and likely to grow and spread quickly. If the cancer is small, a few years may pass before the cancer becomes a life-threatening problem. To prevent problems, treatment is needed now.	
4+5, 5+4, 5+5	9 or 10	5	Very high risk		

# **Tumor stage**

The tumor, node, metastasis (TNM) system is used to "stage" prostate cancer. Staging is a way to describe how much cancer is in your body and how far it has spread. Knowing your stage is important for predicting the course of your disease and for making a treatment plan.

In this system, the letters T, N, and M stand for different areas of cancer growth:

- T (tumor) Describes the size of the main (primary) tumor and if it has grown outside the prostate
- N (node) Identifies whether cancer has spread to nearby lymph nodes
- M (metastasis) Indicates if cancer has spread to distant parts of the body (metastasized)

Based on test results, your doctor will assign a number to each letter. The higher the number, the larger the tumor or the more the cancer has spread. These scores are combined to assign a stage to the cancer.

# Summary

If you've read this chapter from the beginning, you'll recall that it all started with a discussion of risk—the risk that your cancer might grow. All the elements described in this chapter (digital rectal exam, prostate-specific antigen level, biopsy results, Gleason score, Grade Group, and tumor stage) are put together to come up with your initial level of risk.

In the next chapter, we'll talk about risk assessment and what that means for you.

# Key points

- Clinical characteristics of your cancer digital rectal exam, PSA level, biopsy results, Gleason score, Grade Group, and tumor stage—are used to classify your disease into risk groups.
- Patients with lower risk generally get minimal or no treatment. Patients with higher risk usually get more aggressive treatment.
- For a digital rectal exam, the doctor feels the prostate for abnormal size or hardness, either of which may be a sign of cancer.
- PSA levels can vary due to age, race, and other factors.
- The only way to know for sure if you have prostate cancer is to remove tissue from your body and test it for cancer cells. This is called a biopsy.
- A Gleason score describes how aggressive your prostate cancer is.
- Gleason scores are organized into Grade Groups, which are simpler to understand.
- The TNM system is used to stage prostate cancer.
- Cancer staging describes how much cancer is in the body and where it's located.

## How to understand the TNM system

Tumors come in all shapes and sizes. This makes it tough to be able to compare one tumor to another. So cancer experts created a system that can describe any tumor. Each letter is matched with a number that explains the extent (or "stage") of the cancer.

#### T = Tumor

T stands for tumor, and the numbers 0 through 4 refer to its size and growth:

- **T0** means that no tumor can be detected.
- **T1** tumors can't be felt during a digital rectal exam and aren't found on imaging tests, although a biopsy shows cancer is present.
- **T2** tumors can be felt during a digital rectal exam. They also may be seen on an imaging test. T2 tumors are found only in the prostate gland.
- **T3** tumors have broken through the outside layer of the prostate gland. They may reach the connective tissue around the prostate or the neck of the bladder.
- **T4** tumors have grown outside the prostate

into nearby structures such as the bladder, rectum, pelvic muscles, or pelvic wall.

#### N = Node

N is for node, as in lymph node. There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful substances. The number 0 or 1 after the letter N tells whether the cancer has or hasn't spread to the lymph nodes near the prostate:

- **N0** means cancer hasn't spread to any lymph nodes.
- **N1** means cancer has spread to lymph nodes near the prostate (regional lymph nodes).

#### M = Metastasis

When prostate cancer metastasizes, it tends to spread to the bones, liver, lungs, distant lymph nodes, and other organs:

- **M0** means the cancer hasn't spread to distant parts of the body.
- **M1** means the cancer has spread to distant parts of the body (metastasized).

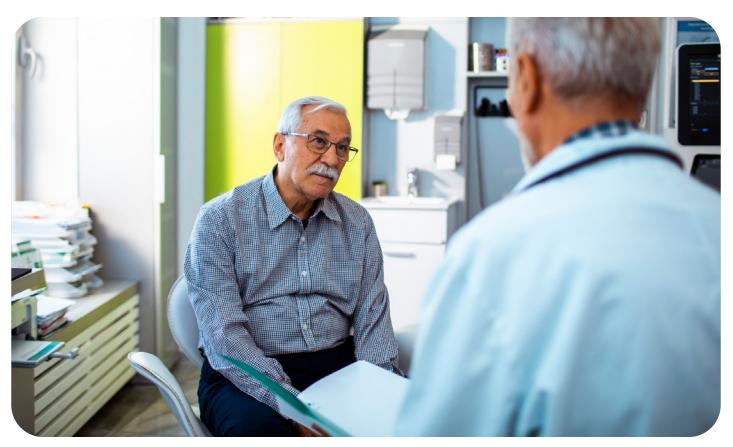
#### How to read a TNM score

Let's say your prostate cancer is given a TNM stage of **T4**, **N1**, **M0**. This says that the tumor has grown outside the prostate gland (T4) and has spread to nearby lymph nodes (N1), but has not spread to distant parts of the body (M0).

Why know your TNM score? For one, it lets you know the extent of your cancer. It also helps characterize your risk group. Your risk group suggests the most appropriate treatment for you.

# **4** Risk assessment

34	Risk groups
34	Life expectancy
36	Nomograms
36	Molecular tumor tests
37	Key points



A risk assessment estimates the chances of future problems or difficulties. In the case of prostate cancer, a risk assessment helps to plan the best treatment for you.

After being told you have cancer, your next thought may be, "How soon can I start treatment to fight it?" Figuring out when to be treated or which treatment to use requires an assessment of your risks.

A risk assessment involves identifying potential problems and then considering what would happen if those problems occurred.

Doctors use these tools to make a risk assessment:

- Risk group
- Life expectancy
- Nomograms
- Molecular testing

# Risk groups

Doctors use risk groups to help choose treatment options and to predict the likelihood that the cancer will recur after initial treatment.

As you read in Chapter 3, results from several different tests are put together to determine each risk group:

- Digital rectal exam Is a tumor detectable by touch?
- PSA level What's the likelihood of prostate cancer?
- > Biopsy *Is cancer present?*

- Gleason score, Grade Group How quickly will the cancer grow?
- TNM score How far has the cancer spread?

Based on the results of these tests, you'll be placed into an initial risk group. Your risk group helps determine which treatment options may be best for you. Using these tests together to create risk groups is more reliable than using any test by itself to choose treatment options. See Guide 2 and Guide 3.

# Life expectancy

Life expectancy is the average lifespan of a person. It's measured in years. An estimate of your life expectancy is an important factor in deciding which tests and treatments you'll need.

It's important to be aware that life expectancy is only an estimate based on large numbers of people. That means life expectancy can be applied to a big population or a broad age range, but it's not as easy to make a precise estimate of the lifespan of an individual patient.

Sometimes, patients in certain risk groups should wait until symptoms appear before having tests or starting treatment. Prostate cancer often grows slowly. There may be no benefit to having additional tests or undergoing treatment if you don't have any symptoms or if you have other more life-threatening health conditions.

## Life expectancy

## Guide 2

Prostate cancer risk groups

	PSA level	Grade Group	TNM score (tumor stage)	Biopsy
Very low risk Includes all of these	Less than 10 ng/mL	1	T1c	Cancer in 1 to 2 biopsy cores with no more than half of each core showing cancer
Low risk Includes all of these	Less than 10 ng/mL	1	T1 to T2a	More than 2 biopsy cores show cancer, but less than half of all cores show cancer
Favorable intermediate risk Includes at least one	10 to 20 ng/ mL	1 or 2	T2b or T2c	Less than half of biopsy cores show cancer
Unfavorable intermediate risk Includes at least one	10 to 20 ng/ mL	3	T2b or T2c	More than half of biopsy cores show cancer
High risk Includes only one	More than 20 ng/mL	4 or 5	T3a	More than half of the biopsy cores show cancer, but less than 4 cores are Grade Group 4 or 5
Very high risk Includes one of these or at least two from High risk	More than 20 ng/mL	5	T3b to T4	More than 4 biopsy cores are Grade Group 4 or 5

### Guide 3 T Guide

In Guide 2, the TNM score includes letters after the tumor stage. These letters give more information about the amount of cancer and its location in the prostate.

	<b>T1a</b> – Cancer found in 5 percent (5%) or less of the removed tissue.
T1	<b>T1b</b> – Cancer found in more than 5 percent (5%) of the removed tissue.
	T1c – Cancer found in one or both sides of the prostate.
	<b>T2a</b> – Cancer is found in half or less than half of one side of the prostate.
Т2	<b>T2b</b> – Cancer is found in more than half of one side of the prostate, but it isn't in both sides.
	<b>T2c</b> – Cancer has grown into both sides of the prostate.
т2	<b>T3a</b> – Cancer has grown outside the prostate, but not into the seminal vesicle(s).
T3 -	<b>T3b</b> – Cancer has grown outside the prostate and into the seminal vesicle(s).

## Nomograms

A nomogram predicts the course your cancer will take (your prognosis). A nomogram uses math to compare you and your prostate cancer to hundreds or thousands of other patients who have been treated for prostate cancer.

To use a nomogram, your doctor will input information about you and the characteristics of your cancer—your age, PSA level, Gleason score, or other details—and the nomogram will calculate the likely result of a certain treatment or outcome.

For comparison, risk groups are used to consider the many treatment options for prostate cancer while nomograms can provide information that is more specific to you. Both are used, along with other risk assessment tools, to plan treatment.

## Molecular tumor tests

Molecules are very tiny particles found in the cells of your body. Special tests are now used to measure certain molecules and biomarkers. A biomarker is something found in your body that can be measured to assess your health. One type of cancer biomarker is a molecule from the tumor.

Molecular tests use samples of blood or tissue that were removed during biopsy. Results from these and other tests may help choose a treatment plan that's right for you. Another reason you might have a molecular test is to see how well your body is responding to prostate cancer treatment. Importantly, molecular tests can identify localized lower risk prostate cancer that doesn't need treatment right away. These patients can be spared aggressive treatment along with its complications and side effects.

A molecular tumor test is also known as a molecular assay or analysis. A few of the more common molecular tests for prostate cancer are named Decipher, Oncotype DX, and Prolaris.

If your doctor recommends molecular testing, it would be in addition to standard tests such as PSA, Gleason score, and imaging. If you have any questions about why you're having a test or what it means, ask your care team.



# Taking supplements?

It's important to bring a list of old and new medicines to your doctor's office when you begin testing. It's also important to tell your treatment team if you're using any complementary medicines, especially supplements, vitamins, or herbs. Some of these can interfere with your cancer tests or treatment. This may reduce the effectiveness of treatment or cause more side effects.

## Key points

# Key points

- A risk assessment identifies potential problems and then considers what would happen if those problems occurred.
- Your risk assessment is based on information about your risk group, life expectancy, nomograms, and sometimes molecular tumor tests.
- Doctors use risk groups to help choose treatment options and to predict the likelihood that cancer will recur after initial treatment.
- Results from several different tests are put together to determine your risk group.
- Life expectancy is the number of years you will likely live. Life expectancy is used to choose the best treatment for you.
- A nomogram predicts the course your cancer will take, called a prognosis.
- A biomarker is something found in your body that can be measured to assess your health.
- Molecular tests provide information for your prognosis. They also help with choosing the best treatment options.



# We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

NCCN.org/patients/feedback

# **5** Prostate cancer treatments

00	
39	Treatment team

- 40 Hormone therapy
- 42 Chemotherapy
- 44 Immunotherapy
- 44 Biomarker-targeted therapy
- 44 Bone-targeted therapy
- 45 Radiopharmaceuticals
- 46 Surgery
- 48 Radiation therapy

- 50 Observation
- 50 Supportive care
- 51 Clinical trials
- 54 Key points



NCCN Guidelines for Patients<sup>®</sup> Advanced-Stage Prostate Cancer, 2022 There's more than one treatment for prostate cancer. This chapter describes treatment options and what to expect. Discuss with your doctor which treatment might be best for you.

# **Treatment team**

Treating prostate cancer takes a team approach. Some members of your care team will be with you throughout your cancer treatment, while others will only be there for parts of it. Your team should communicate and work together to bring the best knowledge from each specialty. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team may include a dozen or more health care providers:

- Your primary care doctor handles medical care not related to your cancer. Your primary doctor can help you express your thoughts about treatments to your cancer care team.
- A pathologist interprets tests on cells, tissues, and organs removed during a biopsy or surgery.
- A diagnostic radiologist reads the results of x-rays and other imaging tests.
- A urologist is an expert in the male and female urinary systems and the male reproductive organs.
- A urologic oncologist is a surgeon who diagnoses and treats cancers of the urinary tract and the male reproductive organs.

- > A radiation oncologist prescribes and plans radiation therapy to treat cancer.
- A medical oncologist treats cancer using systemic therapies such as hormone therapy and chemotherapy. A medical oncologist will often coordinate your care with other team members. If not, ask who will coordinate your care.
- A nuclear medicine doctor treats cancers using intravenous forms of radiation medicines (radiopharmaceuticals).
- An anesthesiologist gives anesthesia, a medicine so you don't feel pain during surgery or procedures.
- Advanced practice providers are an important part of any team. These are registered nurse practitioners and physician assistants who monitor your health and provide care.
- Residents and fellows are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- Oncology nurses provide your handson care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects.
- Nutritionists can provide guidance on what foods or diet are most suitable for your particular condition.
- Psychologists and psychiatrists are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.

 Genetic counselors are experts who can help interpret how your family history may impact your treatment.

**TIP:** It's important to see both a **radiation oncologist** and a **urologist** to discuss the treatment approach that's right for you.

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know who to contact with questions or concerns.

Prostate cancer is a complex disease with many treatment options. Treatments for advanced-stage prostate cancer include hormone therapy, chemotherapy, immunotherapy, surgery, radiation therapy, and targeted therapy.

Treatment can be local, systemic, or a combination of both.

- Systemic therapies attack cancer cells throughout the body. Systemic therapy includes hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals, as well as other treatments designed to maintain or improve your quality of life.
- Local therapies target specific areas or parts of the body that contain cancer cells. In prostate cancer, local treatments include surgery and radiation therapy.

Then again, your treatment plan may include no direct therapy but instead include observation only.

# Hormone therapy

Hormone therapy is a systemic (whole-body) treatment that adds, blocks, or removes hormones. Hormones are natural chemicals made by glands in the body. Their job is to activate cells or organs.

Male hormones are called androgens. The main androgen is testosterone. Most of the testosterone in the body is made by the testicles. Testosterone also helps prostate cancer to grow.

A type of hormone therapy called androgen deprivation therapy (ADT) can stop your body from making testosterone or block cancer cells from using testosterone. Reducing the amount of testosterone in your body can shrink the tumor or slow tumor growth for a period of time.

Hormone therapy is a common treatment for advanced-stage prostate cancer. It's sometimes given with radiation therapy, chemotherapy, corticosteroids, or other hormone therapies.

You might hear the term "castration" used with prostate cancer treatment. This term describes a drastic reduction of testosterone. Castration can be a short-term reversible treatment using drugs or it can be permanent surgical removal of one or both testicles (orchiectomy). Though orchiectomy is a surgical procedure, it's still considered hormone therapy because it removes the primary testosterone source (the testicles).

Surgical removal of the testicles is much less common nowadays because systemic drug therapy is often just as effective at blocking testosterone. Most LHRH agonists and LHRH antagonists are injections. These may be given monthly or 2, 3, or 4 times a year. Anti-androgens, corticosteroids, and androgen synthesis inhibitors are available as pills and taken 1 to 3 times a day, depending on the medication. See Guide 4. **Palliative ADT.** Palliative ADT is given to relieve (palliate) symptoms of prostate cancer. Palliative ADT can be given to those who have a shorter life expectancy or metastatic prostate cancer. Palliative ADT can also be given to those who begin to develop symptoms during observation.

## Guide 4 Hormone therapy drugs for prostate cancer

Hormone therapy	Generic name	Brand name
<b>LHRH agonists</b> prevent the release of luteinizing hormone-releasing hormone (LHRH), which causes the testicles to stop making testosterone.	<ul> <li>Goserelin</li> <li>Histrelin</li> <li>Leuprolide</li> <li>Triptorelin</li> </ul>	<ul> <li>Zoladex</li> <li>Vantas</li> <li>Lupron, Eligard</li> <li>Trelstar</li> </ul>
<b>LHRH antagonists</b> block or stop the pituitary gland (located in the brain) from making LHRH. This causes the testicles to stop making testosterone.	<ul><li>Degarelix</li><li>Relugolix</li></ul>	<ul><li>Firmagon</li><li>Orgovyx</li></ul>
Anti-androgens block receptors on prostate cancer cells from receiving testosterone.	<ul> <li>Apalutamide</li> <li>Bicalutamide</li> <li>Darolutamide</li> <li>Enzalutamide</li> <li>Flutamide</li> <li>Nilutamide</li> </ul>	<ul> <li>Erleada</li> <li>Casodex</li> <li>Nubeqa</li> <li>Xtandi</li> <li>Eulexin</li> <li>Nilandron</li> </ul>
<b>Corticosteroids</b> ("steroids") are synthetic hormones made in a lab that can stop the adrenal glands and other tissues from making testosterone.	<ul> <li>Dexamethasone</li> <li>Hydrocortisone</li> <li>Methylprednisolone</li> <li>Prednisone</li> </ul>	Corticosteroids are all available generically
Androgen synthesis inhibitors block androgen production.	<ul><li>Abiraterone</li><li>Ketoconazole</li></ul>	<ul> <li>Zytiga, Yonsa</li> <li>Available generically</li> </ul>

### Chemotherapy

### Side effects of hormone therapy

Hormone therapy has significant side effects. Many factors affect your risk for side effects including your age, your health before treatment, how long or often you have treatment, and other considerations.

Side effects differ among the types of hormone therapy. In general, ADT may reduce your desire for sex and cause erectile dysfunction. If you will be on long-term ADT, your doctor may consider intermittent treatment to reduce side effects. Intermittent treatment means alternating periods of time when you are on and off ADT treatment. It can provide similar cancer control to continuous hormone therapy but it gives your body a break from the side effects of treatment.

The longer you take ADT, the greater your risk for thinning and weakening bones (osteoporosis), bone fractures, weight gain, loss of muscle mass, diabetes, and heart disease. Other side effects of ADT include hot flashes, mood changes, fatigue, weight gain, change in testicle size, and tenderness and growth of your breasts.

LHRH agonists can cause a surge in testosterone for a few weeks before dropping to castration level. This increase is called a testosterone flare. A testosterone flare can cause bone pain and urinary problems. But these symptoms will go away after the first few weeks of treatment. You might be given a medicine to prevent flare.

Before ADT, you may receive a test to measure your bone density. Your doctor may recommend medications you can take if your bone density is low. Calcium and vitamin D supplements taken every day may help prevent or control osteoporosis for those on ADT.

Talk to your doctor about the other risks of ADT treatment for prostate cancer. ADT increases the risk for diabetes and cardiovascular disease. If you already have either of these conditions, ADT can cause them to get worse. Ask your doctor about monitoring your blood pressure and cholesterol levels. Also, let your primary care physician know you're being treated with ADT.

Ask your care team about how to manage the side effects of hormone therapy. They have ways to lessen or soothe some of these problems.

# Chemotherapy

Chemotherapy is a systemic drug therapy that damages rapidly dividing cells throughout the body. Cancer cells divide and multiply rapidly, which makes them a good target for chemotherapy. Chemotherapy can harm healthy cells, too. That's how chemotherapy can cause side effects.

## Docetaxel

Docetaxel is a chemotherapy medicine used along with hormone therapy in patients with advanced prostate cancer. Docetaxel is an option for some who are taking ADT for the first time. Docetaxel is also used to treat metastases after ADT fails to stop cancer growth. Though docetaxel can't cure prostate cancer, it can help people live longer as well as reduce their pain and other symptoms.

#### Cabazitaxel

Cabazitaxel is a chemotherapy option if docetaxel isn't effective. Cabazitaxel can't cure prostate cancer but it can help people live longer and improve pain and other symptoms.

### **Mitoxantrone**

Mitoxantrone is used to relieve pain and decrease the need for pain medications. It's an option for men who aren't able to tolerate other therapies.

## **Cisplatin and carboplatin**

Cisplatin and carboplatin are chemotherapy drugs made from platinum. These are sometimes used for patients with very advanced or aggressive cancer. Usually, either cisplatin or carboplatin is combined with another chemotherapy medicine such as cabazitaxel or docetaxel.

## Guide 5

Non-hormone systemic therapies for prostate cancer

Type of therapy	Generic name	Brand name
Chemotherapies	<ul> <li>Docetaxel</li> <li>Cabazitaxel</li> <li>Mitoxantrone</li> <li>Cisplatin</li> <li>Carboplatin</li> </ul>	<ul> <li>Taxotere</li> <li>Jevtana</li> <li>Novantrone</li> <li>Platinol</li> <li>Paraplatin</li> </ul>
Immunotherapies	<ul><li>Sipuleucel-T</li><li>Pembrolizumab</li></ul>	<ul><li>Provenge</li><li>Keytruda</li></ul>
Biomarker-targeted therapies	• Rucaparib • Olaparib	• Rubraca • Lynparza
Bone-targeted therapies	<ul><li>Denosumab</li><li>Zoledronic acid</li><li>Alendronate</li></ul>	• Prolia, Xgeva • Zometa • Fosamax
Radiopharmaceuticals	<ul><li>Lutetium-177</li><li>Radium-223</li></ul>	<ul><li>Pluvicto</li><li>Xofigo</li></ul>

## Immunotherapy

## Immunotherapy

The immune system is the body's natural defense against infection and disease. Immunotherapy is a type of systemic therapy that boosts the ability of your immune system to find and destroy cancer cells. Immunotherapy is usually given alone for treating prostate cancer.

Immunotherapy drugs include sipuleucel-T and pembrolizumab.

## Sipuleucel-T

Sipuleucel-T is an immunotherapy that supercharges your own immune cells to destroy prostate cancer cells. This drug is known as a "cancer vaccine." First, immune cells are collected from your body and sent to a lab. The immune cells are then activated to identify and target prostate cancer cells. Lastly, the immune cells are injected back into your body where they attack cancer cells.

## Pembrolizumab

Pembrolizumab is type of immunotherapy called a monoclonal antibody. In people with prostate cancer who have specific genetic mutations, pembrolizumab can restore the immune system's ability to detect and destroy cancer cells.

## **Biomarker-targeted therapy**

This treatment targets specific biomarkers that are found through molecular tumor testing. Biomarkers that these therapies target include mutations in *BRCA1*, *BRCA2*, and other genes. Because biomarkers differ between people, a treatment that helps one person may not help another.

Biomarker-targeted therapies include:

- rucaparib
- olaparib

# Bone-targeted therapy

Medicines that target bones can help to relieve bone pain or reduce the risk of bone problems. Some medicines work by slowing or stopping bone breakdown, while others help increase bone thickness.

Some treatments for prostate cancer, like hormone therapy, can cause bone loss (osteoporosis). This could increase your risk for fractures.

Also, cancer that spreads to your bones puts them at risk for injury and disease. Such problems include osteoporosis, fractures, bone pain, and squeezing (compression) of the spinal cord.

Drugs to prevent bone loss and fractures include:

- Denosumab
- Zoledronic acid
- Alendronate

If you're at risk for osteoporosis, you may have a bone mineral density test. This is a special x-ray scan that measures how much calcium and other minerals are in your bones. Bone mineral density tests look for osteoporosis and help predict your risk for bone fractures. You should have a follow-up bone mineral density test after 1 year of hormone therapy.

You might also have blood tests to monitor kidney function and calcium levels. Your doctor may recommend you start taking calcium and vitamin D supplements to help protect your bones.

**TIP:** Tell your dentist if you're taking bone-targeted therapies. Some of these medicines might affect your teeth and jaws. Osteonecrosis, or bone tissue death of the jaw, is a rare but serious side effect of denosumab and zoledronic acid.

# Radiopharmaceuticals

A radiopharmaceutical is a medicine that contains a radioactive substance. This radioactive substance releases radiation to kill cancer cells. The radiation doesn't travel far from cancer cells so nearby healthy tissue remains mostly unharmed.

Radiopharmaceuticals are injected into a vein (intravenous injection). Because radiopharmaceuticals leave the body through the gut, common side effects are nausea, diarrhea, and vomiting.

## Lutetium-177

Lutetium-177 (Lu-177) targets and attaches itself to prostate cancer cells anywhere in the body. The cancer cells absorb the radiation from the drug and die. The cancer cells must be the kind that have prostatespecific membrane antigen (PSMA) on their cell surface. PSMA-PET imaging is required before getting lutetium-177 to confirm that the treatment could work. Also, lutetium-177 isn't given until both hormone therapy and chemotherapy have been tried.

## Radium-223

Radium-223 is used to treat prostate cancer that has metastasized in the bone but hasn't spread to other organs. Radium-223 collects in bones and gives off radiation that can kill prostate cancer cells. You'll need to have blood tests before each dose. A bone-targeting therapy, either denosumab or zoledronic acid, should be given with radium-223.

Radium-223 is also used as palliative, bonetargeted therapy to reduce pain from bone metastases.

## Surgery

# Surgery

Surgery is a local procedure to remove cancer from the body. The tumor will be removed along with some normal-looking prostate tissue around its edge called the surgical margin.

- A positive margin is when cancer cells are found along the edge of the tissue that the surgeon removes.
- A negative margin is when no cancer cells are found around the edge of the tissue that the surgeon removes. A negative margin is the better result because it means that all of the tumor in that area has likely been removed.

Surgery may be used as the main (primary) treatment for localized prostate cancer. Or, surgery may be only one part of a treatment plan.

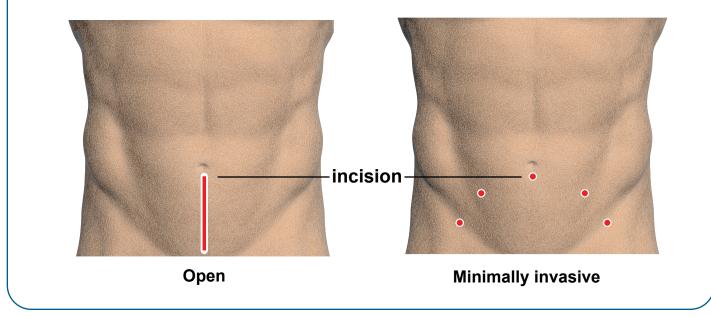
The type of surgery you receive depends on the size and location of the tumor. It also depends on whether cancer is found in any surrounding organs and tissues.

## **Radical prostatectomy**

Prostatectomy means removing the prostate gland through surgery. A radical prostatectomy removes not only the entire prostate but also the surrounding tissue and seminal vesicles. Pelvic lymph nodes may also be removed.

## Open vs. minimally invasive prostatectomy

A prostatectomy is an operation that removes the whole prostate. Open surgery removes the prostate through one large cut or incision. Minimally invasive surgery uses several small incisions or cuts instead of one large cut.



NCCN Guidelines for Patients<sup>®</sup> Advanced-Stage Prostate Cancer, 2022

#### Surgery

A radical prostatectomy is often used when all of the following are true:

- > The tumor is found only in the prostate.
- The tumor can be removed completely with surgery.
- You have a life expectancy of 10 or more years.
- You have no other serious health conditions.

A radical prostatectomy is complex and requires a great deal of skill. Surgeons who are experienced in this type of surgery often have better results.

There are two surgical methods for radical prostatectomy:

- Open surgery removes the prostate through one large cut or incision. The large incision lets your doctor directly view and access the tumor to remove it. When the incision runs from your belly button down to the base of your penis, it's called radical retropubic prostatectomy. When the cut is made in the perineum (the area between your scrotum and anus), it's called a radical perineal prostatectomy.
- Minimally invasive surgery has become more common than open surgery. Minimally invasive surgery uses several small incisions or cuts instead of one large cut. The surgeon uses robotic arms to precisely insert small tools through each incision to perform the surgery. This is called robot-assisted radical prostatectomy. One of the tools, called an endoscope, has a light and a video camera at the end. The camera gives the

surgeon a magnified view of your prostate and the nearby tissues inside your body. Other surgical tools are used to remove the tumor.

Either open surgery or minimally invasive surgery can be used for a radical prostatectomy. Patients who receive minimally invasive surgery often have shorter hospital stays, less blood loss, fewer surgical complications, and faster recovery time.

The major side effects from robotic-assisted radical prostatectomy—incontinence and erectile dysfunction—occur about as often with open surgery.

#### Side effects of surgery

Radical prostatectomy frequently causes two side effects:

#### Urinary incontinence

You'll likely lose the ability to hold your pee after a radical prostatectomy. This is called urinary incontinence and it's usually temporary. Most patients gradually recover control of their bladder in a few weeks or months.

Immediately after the procedure, a catheter will be inserted into your urethra to allow you to empty your bladder and your urethra to heal. The catheter will stay in place for 1 to 2 weeks after surgery. You'll be shown how to care for it while at home. If the catheter is removed too early, you may lose control of your bladder or be unable to urinate due to scar tissue.

Physical therapy for pelvic floor strengthening (Kegel exercises) can stop urinary incontinence. If incontinence continues to be a problem, another surgical procedure can be done to improve it.

#### **Erectile dysfunction**

Erectile dysfunction means having difficulty or being unable to have an erection of the penis. This happens a lot after prostate surgery but it's also usually temporary. There's a higher risk for erectile dysfunction if:

- You are older
- You have erectile problems before surgery
- Your cavernous nerves are damaged or removed during surgery

The cavernous nerves control the ability to have erections. These nerves run alongside the prostate. Doctors do their best to avoid these nerves when performing a prostatectomy but damage to the nerves during surgery is sometimes unavoidable.

Removing your prostate and seminal vesicles will cause you to have dry orgasms. This means there will be no semen and you'll be unable to have children (infertility).

It may take several months to 2 years to restore the erectile function you had before the surgery. However, you may never regain the same "mojo" you once had. Treatment options for erectile dysfunction include pills (like Viagra and Cialis), injections of medication into the penis, vacuum constriction devices ("penis pump"), and surgical implants that produce an erection.

#### Pelvic lymph node dissection

Prostate cancer can metastasize to the lymph nodes within the pelvis. A pelvic lymph node dissection (PLND) is an operation to remove these lymph nodes. PLND is usually part of a radical prostatectomy.

# Radiation therapy

Radiation therapy uses high-energy radiation from x-rays, gamma rays, and other sources to kill cancer cells and shrink tumors. It's given in regular doses over a certain period of time.

Radiation can be used instead of surgery to cure cancer. Sometimes radiation therapy is given after surgery to help prevent your cancer from coming back. Also, if your PSA begins to rise after surgery, radiation therapy might be recommended to try to kill any cancer cells that could have been left behind. One advantage of radiation therapy is that it's less invasive than surgery.

There are two main types of radiation treatment: external treatment and internal treatment.

#### **External radiation**

External beam radiation therapy (EBRT) uses a machine outside of the body to aim radiation at the tumor(s). The radiation beam focuses directly on the cancer while trying to avoid healthy tissue. This tactic allows for safer, higher doses of radiation.

EBRT is also used as palliative treatment for painful bone metastases.

#### **Internal radiation**

Brachytherapy is an internal form of radiation therapy. In this treatment, radiation is delivered inside the body by placing a radioactive object into or next to the tumor. You might hear it called brachy (said "bray-key") for short.

Brachytherapy may be used alone or combined with EBRT, androgen deprivation therapy (ADT), or both. There are two types of brachytherapy:

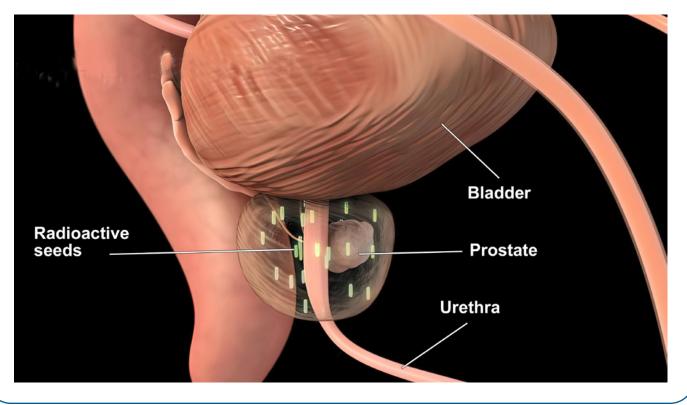
- Low dose-rate (LDR) brachytherapy uses tiny radioactive metal "seeds" that are implanted into your prostate. Each seed is about the size of a grain of rice. They're inserted into your body through the perineum. The seeds usually consist of either radioactive iodine or palladium. They'll stay in your prostate permanently and provide a low dose of radiation continuously for a few months while sparing nearby healthy tissue.
- High dose-rate (HDR) brachytherapy uses thin needles placed inside your prostate gland. These needles are then attached to tubes called catheters. Highdose radiation is delivered through the catheters. After treatment, the needles and catheters are removed.

### Side effects of radiation therapy

Common side effects of radiation therapy are urinary problems and bowel problems. Urinary problems include incontinence as

## **Brachytherapy radiation**

Low dose-rate (LDR) brachytherapy uses tiny radioactive metal "seeds" that are implanted into your prostate. Each seed is about the size of a grain of rice. They'll stay in your prostate permanently and provide a low dose of radiation continuously for a few months. This treatment strategy spares nearby healthy tissue from unnecessary radiation.



well as having to go more often, having to go suddenly, and a burning sensation when you go. Bowel problems can include diarrhea, pooping frequently, being unable to hold it in, and sometimes bleeding from the rectum.

Urinary and bowel problems usually go away after several weeks for most people, though not for all. Erectile dysfunction also sometimes occurs. Feeling very tired for a few weeks to months after treatment is also common.

# Observation

Observation means watching for symptoms without receiving treatment. (You might hear it called watch-and-wait or watchful waiting.)

Observation is generally for patients with localized and lower risk prostate cancer who don't have symptoms. If symptoms develop, then treatment is focused on palliative care or symptom relief instead of trying to cure the cancer. This allows patients to maintain a good quality of life without the burden of unnecessary treatment.

Observation is a less aggressive way to monitor patients. It doesn't require regular biopsies—just a PSA test and a physical once or twice a year.

Observation often applies to older or frail patients with shorter life expectancies. These patients commonly have one or more other illnesses or diseases that are more severe than their prostate cancer.

# Supportive care

Supportive care is treatment to relieve the symptoms of cancer, the side effects of cancer therapies, and other health issues related to the cancer such as nutrition and exercise. Supportive care also helps with psychological, social, and spiritual issues. Supportive care involves the whole person, not just their cancer.

Supportive care is given at any stage of disease, not just at the end of life.

Supportive care addresses many needs. It can help with making treatment decisions. It can also assist with coordinating care between health providers. Notably, supportive care can help prevent or treat physical and emotional symptoms.

Supportive care can also help with spiritual support, advance care planning (which means deciding what you would want if you become too sick to make medical decisions for yourself), and end-of-life concerns.

It's important to talk openly with your treatment team about supportive care.

# **Clinical trials**

Another avenue of treatment is a clinical trial. A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Clinical trials give people access to options that they couldn't usually receive otherwise. Talk to your doctor about whether a clinical trial may make sense for you.

## Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- Phase I trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- Phase II trials study how well the drug or approach works against a specific type of cancer.
- Phase III trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- Phase IV trials study the long-term safety and benefit of an FDA-approved treatment.

# It's normal to feel worried

Depression, anxiety, fear, and distress are very common feelings in people with cancer. These feelings can make it harder to deal with cancer and cancer treatment. They can hold you back even when you want to move forward.

Getting help when you're feeling worried or hopeless is an important part of cancer care. If you're feeling anxious or overwhelmed, ask your treatment team for help.

Read more about cancer and distress in *NCCN Guidelines for Patients: Distress During Cancer Care*, available at <u>NCCN.org/patientguidelines</u>.



## **Clinical trials**

#### Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in certain ways in order to compare how they respond to a specific treatment.

## **Informed consent**

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

#### Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you've already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.



## Worldwide

The U.S. National Library of Medicine (NLM) <u>clinicaltrials.gov</u>

Need help finding a clinical trial? NCI's Cancer Information Service (CIS) 1.800.4.CANCER (1.800.422.6237) cancer.gov/contact

## Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks aren't well understood by many with cancer.

#### Will I get a placebo?

Placebos (inactive versions of real medicines) are hardly ever used alone in cancer clinical trials. It's common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You'll be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

#### Are clinical trials free?

There's no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. However, you may have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. Depending on the trial, you may continue to receive standard cancer care. The standard therapy is billed to—and often covered by—insurance. You're responsible for copays and any costs for this care that aren't covered by your insurance. share with us.

## Take our survey

And help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments

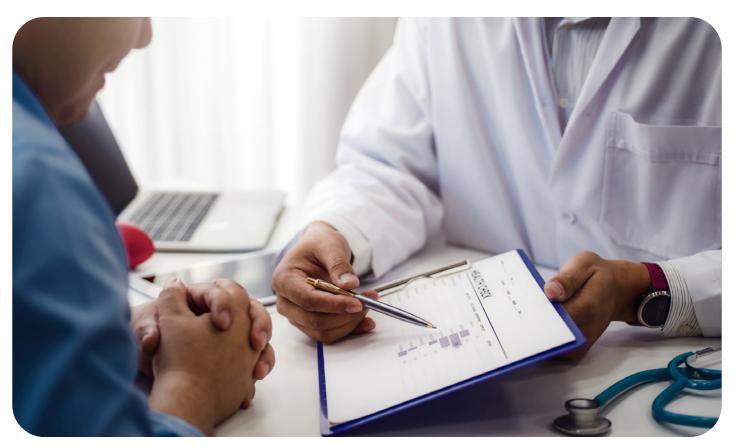
# Key points

- Prostate cancer cells use hormones to survive. Hormone therapy can stop your body from making hormones or block cancer cells from using hormones.
- Castration describes a drastic reduction of hormones. This can be done with either surgery or drugs.
- Androgen deprivation therapy is a hormone therapy that nearly eliminates the male hormones in the body.
- Chemotherapy uses drugs to destroy cancer cells throughout the body. It can also relieve symptoms in people with metastatic prostate cancer.
- Immunotherapy boosts the ability of your immune system to find and destroy cancer cells.
- Some bone-targeted therapies can increase bone thickness and reduce bone breakdown.
- A radiopharmaceutical is a drug that releases radiation to kill cancer cells.
- Radical prostatectomy surgery removes the whole prostate, the surrounding tissue, the seminal vesicles, and sometimes the lymph nodes in the pelvis.
- Side effects of a radical prostatectomy may include urinary incontinence and erectile dysfunction.
- Radiation therapy uses high-energy radiation to kill cancer cells and shrink tumors.

- Because prostate surgery and radiation therapy have similar long-term cure rates, it's important to see both a radiation oncologist and a urologist to discuss which treatment is right for you.
- Observation looks for signs of cancer in order to treat its symptoms.
- Supportive care is treatment to relieve the symptoms of cancer, the side effects of cancer therapies, and other health issues related to the cancer.
- Supportive care is given at any stage of disease, not just at the end of life.
- A clinical trial studies a treatment to see how safe it is and how well it works.
- Sometimes a clinical trial is the preferred treatment option for prostate cancer.

# 6 If cancer returns

56	Follow-up care
57	Recurrence or no recurrence?
57	Tests to confirm recurrence
58	Treatment for recurrence
59	After treatment
60	Key points



NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2022

## 6 If cancer returns

#### Follow-up care

After surgery or radiation therapy, PSA should fall to a very low level. But in some cases, it doesn't. In other cases, the PSA level does drop but later goes up again. Further treatment may halt recurring cancer.

You've just had treatment for your prostate cancer. Perhaps you had prostate surgery or radiation therapy, or both. Maybe you also had additional (adjuvant) hormone treatment or other therapy.

But what happens now? Are you cured? Or could the cancer come back (recurrence)? The only way to find out what's next is with regular follow-up visits.

Follow-up care

Follow-up care means seeing your doctor for regular visits after your treatment is over.

Follow-up care is important for finding any problems or symptoms that result from your cancer or cancer treatment. No one knows if, when, or how a person's cancer might come back. So it's important to keep going to your follow-up appointments to watch out for it.

During a follow-up visit, your doctor may ask you if you're having problems such as hormone-related symptoms, pain, sexual dysfunction, anxiety, or depression. Your doctor might also offer advice about exercise or weight management. Many men are able to live with prostate cancer and, in the end, may die from something else.

Most importantly, regular follow-up visits and tests are essential to look for any sign that the cancer may return.

Regular tests at follow-up visits often include:

#### PSA level

Checking your PSA level is a useful way to find out whether cancer may have come back. PSA should be at a nearly undetectable level after prostate surgery or radiation therapy.

After treatment, your doctor may check your PSA level once or twice every year at the start. In patients with higher risk, PSA may need to be tested as often as every 3 months at the beginning of follow-up care.

#### Digital rectal exam

If you've had surgery to remove your prostate, this won't apply to you. But those who haven't had a prostatectomy should have a digital rectal exam once each year. A prostate gland that has enlarged or hardened since therapy could be a sign of cancer recurrence.

Your doctor may decide to skip the digital rectal exam, though, if your PSA level continues to be undetectable after a few tests.

## Recurrence or no recurrence?

#### No recurrence

After their initial treatment, some patients with advanced-stage prostate cancer may never develop detectable cancer or symptoms of cancer in their lifetime. If your PSA level and prostate gland (if it hasn't been removed) have not changed since therapy, then there's a good chance the cancer hasn't returned.

More often, though, those with advanced-stage prostate cancer will likely see their cancer return at some point.

#### Recurrence

Recurrence means the cancer has come back after treatment. Cancer may come back in the same place or in a different area of the body.

Prostate cancer can also recur when a patient's PSA level is undetectable after initial treatment but then increases later on. This means the cancer may have returned even if there are no other signs of cancer.

Sometimes a person's PSA level remains at a detectable level even after prostate surgery or radiation therapy. When PSA doesn't fall to a very low level, it's called PSA persistence. Persistence means the cancer hasn't gone away after treatment. Other PSA changes might also be a sign of recurrence. PSA doubling time (PSADT) measures how long the PSA level takes to double. This reflects how fast cancer is growing. A fast PSADT (6 months or less, for example) suggests that cancer has spread beyond the prostate.

# Tests to confirm recurrence

If your PSA can be detected after treatment, your cancer may have returned. A rise in PSA level can indicate recurrence in or around the prostate, spread of cancer beyond the prostate, or both.

To confirm cancer recurrence, your doctor may recommend one or more of the following tests:

## PSADT

PSA doubling time indicates your risk level. If you have a fast PSADT, your doctor might recommend using a nomogram to predict your prognosis. Molecular testing and genetic counseling might also be helpful.

#### Imaging

Imaging can be used to look for cancer in and around the prostate or cancer that's far away from the prostate, such as in bones or other organs:

- Prostate MRI MRI can provide a detailed view of cancer within the prostate (if you haven't had surgery to remove it).
- Bone scan If patients develop symptoms or PSA levels increase rapidly, a bone scan is used to check for bone metastases.

If needed, other types of imaging can also look for metastases:

- Chest CT
- > CT or MRI of the abdomen and pelvis
- PET/CT or PET/MRI

#### **Biopsy**

The choice of biopsy will depend on what type of treatment you've had.

- Prostate bed biopsy If imaging suggests local cancer recurrence after prostate surgery, then you may need a biopsy from the area where the prostate was removed (prostate bed) to check for any cancer sites.
- Transrectal ultrasound biopsy If your PSA level rises rapidly after radiation therapy, then a biopsy of the prostate gland may be useful to locate any cancer.

#### Has the cancer spread?

Imaging and biopsies can show whether the cancer has spread (metastasized) beyond the prostate.

- If metastases are found, you have metastatic prostate cancer. See Chapter 9 to find out what can be done for it-
- If no metastases are found, continue reading to learn about treatment for recurrent non-metastatic prostate cancer.

## Treatment for recurrence

For patients with recurrent non-metastatic prostate cancer, those who had prostate surgery receive different treatment than those who had radiation therapy.

Read the section below that applies to you:

## **Recurrence after surgery**

Treatment options for cancer that recurs after radical prostatectomy are:

- External beam radiation therapy (EBRT) with or without androgen deprivation therapy (ADT)
- Observation

Now, go to After treatment on page 59.

#### **Recurrence after radiation**

Treatment for cancer that recurs after radiation therapy is based on whether you're a candidate for local therapy. Local therapy treats one part or area of the body, such as the prostate. Systemic therapy, such as ADT, affects the entire body.

Local therapy is based on whether a transrectal ultrasound (TRUS) biopsy finds recurrent cancer:

#### TRUS biopsy finds cancer

If TRUS biopsy finds cancer in or around the prostate, local treatment options are:

- Observation
- Radical prostatectomy with pelvic lymph node dissection (PLND)
- Cryotherapy
- High-intensity focused ultrasound (HIFU)
- Brachytherapy

#### TRUS biopsy doesn't find cancer

If TRUS biopsy does not find cancer in or around the prostate, then systemic treatment options are:

- Observation
- > ADT

Adding ADT to radiation therapy can help certain patients live longer. If you choose this option, ask your doctor about *intermittent* ADT, which may reduce treatment-related side effects.

Your choice of treatment depends on your risk as well as your previous treatment, age, personal preferences, and other factors. You'll have to weigh the potential advantages against the potential drawbacks. For example, having a radical prostatectomy after cancer recurrence may control the cancer for the long term. But it also often causes side effects of impotence and urinary incontinence.

# After treatment

As with your initial treatment, you'll need to go to follow-up visits after your secondary treatment. Tests and exams during followup visits can indicate whether the cancer is progressing.

#### No progression

Your most recent treatment may not get rid of the cancer but it could keep it from progressing. If there's no progression, you'll continue with regular follow-up visits. If you're on ADT, your doctor may ask you to continue taking it.

### Progression

If progression is suspected, then tests to confirm that cancer has grown or spread may include:

- Bone scan
- Chest CT
- > CT or MRI of abdomen and pelvis
- PET/CT or PET/MRI

If your PSA is rising but metastases **are not** found, read Chapter 8 to learn about nonmetastatic advanced prostate cancer.

If your PSA is rising and metastases **are** found, read Chapter 9 to learn what can be done about metastatic advanced prostate cancer.

# Key points

- Follow-up care is important for finding any problems or symptoms that result from your cancer or cancer treatment.
- Recurrence means that the cancer has returned after treatment. Cancer may come back in the same place or in a different area of the body.
- Persistence means that the treatment didn't reduce the amount of cancer in the body well enough.
- PSA level should be nearly undetectable after prostate surgery or radiation therapy.
- PSA recurrence happens when PSA levels rise after treatment with surgery or radiation therapy, even if there are no other signs of cancer.
- PSA doubling time (PSADT) indicates how fast cancer is growing.
- If your PSA level or imaging suggests recurrence, then a biopsy of the prostate gland, prostate bed, or other area may be useful to locate any cancer.
- Cancer that returns after prostate surgery is treated differently than cancer that returns after radiation therapy.
- Imaging and biopsies can show whether the cancer has spread (metastasized) beyond the prostate.

# 7 Non-metastatic prostate cancer

- 62 Are you on hormone therapy?
- 62 No, I haven't had ADT
- 63 Yes, I've had ADT
- 65 Key points



NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2022 The twin goals for treating nonmetastatic prostate cancer are halting the cancer and trying to prevent it from spreading elsewhere.

If your PSA is rising but metastases **are not** found, read this chapter.

If your PSA is rising and metastases **are** found, skip this chapter and go to Chapter 8.

# Are you on hormone therapy?

The aim of treating advanced-stage prostate cancer is to prevent or reduce the spread (metastasis) of cancer beyond the prostate. Androgen deprivation therapy (ADT) is the most common systemic treatment to accomplish this in advanced-stage prostate cancer. So if you've had treatment and tests show that your cancer is advancing—but it still hasn't metastasized—then your next steps depend on whether you've *had* or *not had* ADT.

- If you've had standalone ADT or you are on it now, go to Yes, I've had ADT on page 63.
- If you've not had standalone ADT and you are not on it now, then read the next section, No, I haven't had ADT.

Note: ADT given as short-term (adjunctive) therapy, such as hormone therapy given during radiation therapy, *does not count* in this case. If this describes you, then read the next section, *No, I haven't had ADT*.

# No, I haven't had ADT

If you're not taking ADT and your prostate cancer progresses or gets worse after initial treatment, it's called castration-naïve prostate cancer. "Castration-naïve" simply means that you haven't had treatment to bring your hormones down to castration level.

Treatment options for patients with castrationnaïve prostate cancer include:

- Observation Observation is the preferred option for castration-naïve prostate cancer without symptoms or metastases. Observation avoids unnecessary testing and the side effects of treatment.
- ADT ADT is the main treatment to lower your hormones to castration level for castration-naïve prostate cancer. This helps to prevent the spread of cancer. Compared with observation, ADT may be more appropriate for patients with a faster PSA doubling time and/or a higher Grade Group.

#### **Testing for progression**

If you're on ADT, you'll still need to have regular tests to look for signs that your cancer may be progressing. Testing also watches out for the many side effects of ADT.

Tests to detect progression include:

- Physical exam with PSA test every 3 to 6 months
- > Imaging if cancer symptoms occur
- Imaging to monitor ADT treatment

#### No progression

If there's no progression, then your doctor will maintain your current treatment and continue monitoring your cancer. Your doctor will also continue giving you tests to see if cancer might be getting worse. If your cancer isn't getting worse, it may be a sign that the current treatment is keeping your cancer stable.

#### Progression

If your cancer shows signs of advancing, your doctor will test you for metastases:

**No metastases found** – If your cancer has progressed but imaging doesn't show any metastases, then you still have non-metastatic prostate cancer. Even though your cancer has returned, it's important to continue taking ADT to keep testosterone at castration level (less than 50 ng/dL). You'll also continue to see your doctor for regular visits.

If this describes you, you can skip ahead to Chapter 9.

**Metastases found** – If your cancer has progressed and also metastasized, your treatment may depend on the location of the metastasis. Treatment options include ADT with:

- Secondary hormone therapy
- Chemotherapy

Either ADT alone or observation is recommended for patients with metastatic disease, no symptoms, and a shorter life expectancy (5 years or less).

If progression continues, read more about metastatic cancer treatment in Chapter 8.

Though most men with advanced prostate cancer stop responding to ADT at some point, additional hormone therapy may still work.

# Yes, I've had ADT

ADT is the main treatment for advanced prostate cancer, but it eventually becomes less effective in most patients.

If you're on ADT and tests such as PSA indicate your cancer is progressing, it's called castration-resistant prostate cancer. Many early-stage prostate cancers need testosterone to grow, but this isn't true for castration-resistant prostate cancer. "Castration-resistant" means that your cancer isn't improving despite using ADT to bring your hormones down to castration level.

Though most men with advanced prostate cancer stop responding to ADT at some point, another hormone therapy can still work. As a result, you'll continue with ADT but add another type of hormone therapy to it. This is called secondary hormone therapy. Treatment is based on whether your PSA is rising slowly or quickly. Your doctor will find out by calculating your PSA doubling time (PSADT).

- PSADT of more than 10 months. If your PSA level takes more than 10 months to double in number, then your cancer is progressing fairly slowly. The preferred option is to continue with ADT while being under observation. Observation may also be a better option for older patients.
- PSADT of 10 months or less. If your PSA takes 10 months or less to double, then you probably need more aggressive treatment. In addition to continuing ADT, secondary hormone therapy options include one of three anti-androgen drugs (apalutamide, darolutamide, or enzalutamide) or another type of hormone therapy.

## **Testing for progression**

While you're on ADT, you'll continue to have regular testing to look for signs that your cancer may still be progressing or has started to progress again. Testing also watches out for the many side effects of ADT.

Tests to detect progression include:

- Physical exam with PSA test every 3 to 6 months
- > Imaging if cancer symptoms occur
- Imaging to monitor ADT treatment

#### No progression

If there's no progression, you'll stay on your current treatment unless changes begin to occur. Your doctor will also continue giving you tests. If your cancer doesn't get worse, your current treatment may be keeping your cancer stable. If this describes you, you can now skip ahead to Chapter 9.

#### Progression

If your PSA level increases despite ADT and secondary hormone therapy, then you'll have imaging tests to see whether the cancer is metastasizing. Next steps are based on whether or not metastases develop:

**Metastases found** – If your cancer has spread beyond the prostate, then go to Chapter 8 to read about metastatic cancer.

**No metastases found** – If your cancer has progressed but imaging doesn't show any metastases, then you'll continue on your current hormone therapy or your doctor may recommend another one. You'll also continue to see doctor for regular visits. If this describes you, you can skip ahead to Chapter 9.

# Key points

- Castration-naïve prostate cancer means that you haven't had treatment to bring your hormones down to castration level.
- Observation is the preferred option for patients with castration-naïve prostate cancer without symptoms or metastases.
- Compared with observation, ADT may be an appropriate option for patients with more aggressive castration-naïve prostate cancer.
- After treatment, it's important to stay on ADT to keep your testosterone at castration level (less than 50 ng/dL).
- ADT will eventually stop being effective for most men with advanced prostate cancer. However, additional hormone therapy can still work.
- Castration-resistant prostate cancer is when your cancer isn't improving even with treatment to bring your hormones down to castration level.
- Treatment for non-metastatic castrationresistant prostate cancer is based on your PSA doubling time (PSADT).



## Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response

8 Metastatic prostate cancer

67	Treatment
69	Testing for progression
70	Survivorship
70	Key points



NCCN Guidelines for Patients<sup>®</sup> Advanced-Stage Prostate Cancer, 2022

#### Treatment

When prostate cancer spreads to other parts of the body, then whole-body (systemic) therapy is needed. This chapter explains the systemic treatment options for metastatic prostate cancer.

Metastatic prostate cancer is when the cancer has spread (metastasized) beyond the prostate to other parts of your body. You may have metastatic cancer when you're first diagnosed. Or your cancer may become metastatic after you've already had treatment.

Areas where prostate cancer tends to spread are:

- Lymph nodes farther away from the prostate
- **Bones** in your spine, pelvis, or ribs
- Organs such as the liver, lungs, brain, or others

If your test results or symptoms suggest your cancer has metastasized, a variety of treatments are available to target the cancer, stop or slow its progress, and reduce your symptoms.

# Treatment

Which treatment you'll have for metastatic prostate cancer depends on a number of considerations. These include:

- > Your previous treatment (if any)
- > Location of the metastasis in your body
- > Amount of metastatic disease
- > Symptoms
- > Potential side effects
- > Your preferences

Treatment for metastatic prostate cancer typically involves systemic therapy. Systemic therapy affects your whole body, not just a part of it. The main systemic treatment for metastatic advanced-stage prostate cancer is hormone therapy, specifically androgen deprivation therapy (ADT).

ADT is sometimes given by itself, but adding one or two other therapies to ADT may help you live longer and with fewer symptoms. You may hear this called doublet therapy (ADT + another therapy) or triplet therapy (ADT + two other therapies). Participating in a clinical trial is also an option. Talk to your treatment team about which therapy might be best for you.

Last but not least, all patients with advanced cancer should be offered supportive care.

#### Supportive care

Supportive care treats cancer symptoms, the side effects of cancer treatment, and other related health issues.

## 8 Metastatic prostate cancer

#### Treatment

Supportive care may be especially useful for patients with bone metastases. Prostate cancer that metastasizes to bones can cause severe pain and fractures (breaks) in bones. Fractures, pain, and bone loss (osteoporosis) can also result from hormone therapy.

Supportive care for bone problems include:

- Bone-targeted therapy denosumab or zoledronic acid to help prevent fractures
- Palliative chemotherapy for pain symptoms
- Other treatments calcium or vitamin D supplements to help prevent fractures

## ADT

Patients with newly diagnosed metastatic prostate cancer will begin androgen deprivation therapy at castration level (testosterone less than 50 ng/dL). Patients with metastatic prostate cancer who are already being treated will continue on ADT at this level.

#### Combined therapy

Although ADT is the main therapy for advanced prostate cancer, it's not usually given on its own any more. Adding one or two additional therapies to ADT (doublet or triplet therapy) may help you live longer and with fewer cancer symptoms.

Additional therapies include secondary hormone therapy, chemotherapy, immunotherapy, radiopharmaceuticals, and targeted therapy.

#### Secondary hormone therapy

Secondary hormone therapy is commonly added to ADT for treating advanced prostate cancer. It can delay your cancer from progressing further. You'll probably also take a steroid (such as prednisone or dexamethasone) to increase the secondary hormone's effect.

Secondary hormone therapies include:

- Abiraterone
- Enzalutamide
- Darolutamide
- Apalutamide
- > Other secondary hormone therapy

#### Chemotherapy

ADT plus chemotherapy can be the first treatment tried for metastatic prostate cancer or it can be tried later if other treatments didn't work well. Chemotherapy can be given as a single drug (such as docetaxel) or as a pair (cabazitaxel and carboplatin) if the cancer is more aggressive. You'll also take a daily steroid while on chemotherapy.

Common chemotherapy options include:

- Docetaxel
- Cabazitaxel
- Cisplatin
- Carboplatin
- Mitoxantrone

#### Testing for progression

#### Immunotherapy

Immunotherapy drugs boost the body's own immune system to fight cancer. However, immunotherapy for prostate cancer is used only in certain patients. Immunotherapy includes:

- > Sipuleucel-T
- Pembrolizumab

## Radiopharmaceuticals

If ADT and chemotherapy haven't worked well, your doctor may suggest trying a radiopharmaceutical drug. Lutetium-177 is a relatively new radiopharmaceutical that directly attacks prostate cancer cells. Another radiopharmaceutical, radium-223, is also used to lessen the pain of bone metastases.

- Lutetium-177
- Radium-223

## **Targeted therapy**

Targeted therapies are only useful in patients who have mutations in specific genes. Targeted therapy options include:

- Olaparib
- Rucaparib

# Consider quality of life

Quality of life is a term used often in cancer care. It refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in regular activities. In certain cases, aggressive cancer treatment may extend a person's life but reduce their quality of life. That's one example of why quality of life should be an important consideration when making decisions about cancer treatment.

# Testing for progression

During or after your treatment, your doctors will watch you closely for signs that your cancer may be progressing. Testing also looks for any side effects of treatment. Tests include:

- Physical exam with PSA test every 3 to 6 months or more often
- Imaging if cancer symptoms occur
- Imaging to monitor ADT treatment

#### No progression

If there's no progression, you'll stay on your current treatment unless changes begin to occur. Your doctor will also continue giving you tests. If your cancer doesn't get worse, your current treatment may be keeping your cancer stable.

#### Progression

If your cancer progresses or your treatment stops working, your doctor may suggest you try the therapy again or try a different therapy. You'll continue to be offered supportive care.

It's possible to try all the treatment options. Talk with your doctor about what you want from treatment. You can always decide not to continue with systemic therapy.

# Survivorship

Survivorship focuses on the health and wellbeing of a person with cancer from diagnosis until the end of life. This includes the physical, mental, emotional, social, and financial effects of cancer that begin at diagnosis, continue through treatment, and arise afterward. Survivorship also includes concerns about follow-up care, late effects of treatment, cancer recurrence, and quality of life. Support from family members, friends, and caregivers is also an important part of survivorship.

Read more about survivorship in NCCN Guidelines for Patients: Survivorship Care for Healthy Living and Survivorship Care for Cancer-Related Late and Long-Term Effects, available at NCCN.org/ patientguidelines.



# Key points

- The areas where prostate cancer tends to spread are the lymph nodes, bones, and organs.
- Everyone with advanced-stage prostate cancer should be offered supportive care.
- The first treatment for advanced metastatic prostate cancer is usually androgen deprivation therapy (ADT).
   Adding another therapy or two to ADT may improve your outcome.
- Secondary hormone therapy is commonly added to ADT for treating advanced prostate cancer.
- Immunotherapy drugs boost the body's own immune system to fight cancer.
- During or after your treatment, your doctors will watch you closely for signs that your cancer is progressing.
- Survivorship focuses on the health and well-being of a person with cancer from diagnosis until the end of life.
- Quality of life refers to a person's overall enjoyment of life, including their sense of well-being and ability to participate in regular activities.

# 9 Making treatment decisions

- 72 It's your choice
- 72 Questions to ask your doctors
- 79 Online resources



NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2022 It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

# It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What's important to you may not be important to someone else. Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- > Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- > Quality of life and length of life
- How active you are and the activities that are important to you

Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

#### **Second opinion**

It's normal to want to start treatment as soon as possible. While cancer shouldn't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you'll see for your second opinion.

#### Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

## Questions to ask your doctors

Possible questions to ask your doctors are listed on the following pages. Feel free to use these or come up with your own. Think about what you want from treatment. Be clear about your goals for treatment and find out what to expect from treatment. Keep a notebook handy to record answers to your questions.

## Questions to ask about testing and staging

- 1. Can my cancer be cured? If not, how well can treatment stop it from growing?
- 2. What tests will I have? Will my insurance pay for these tests?
- 3. When will I have a biopsy? Will I have more than one? What are the risks?
- 4. Where do I go to get tested? How long will the tests take? Will any test hurt?
- 5. Will I have any genetic tests?
- 6. How often are these tests wrong?
- 7. Should I bring someone with me?
- 8. Should I bring a list of my medications?
- 9. How soon will I know the results and who will explain them to me?
- 10. Can you give me a copy of the pathology report and other test results?
- 11. What is the cancer stage? What does this stage mean in terms of survival?
- 12. Who will talk with me about the next steps? When?
- 13. Who can I call if I need help immediately?
- 14. Can I get a second opinion? Who would you recommend I see for a second opinion?

## Questions to ask about treatment

- 1. What are my treatment options? Are you suggesting options from the NCCN Guidelines, or have you modified the standard approach in my situation?
- 2. Which treatment do you recommend and why?
- 3. How long do I have to decide about treatment?
- 4. What will happen if I do nothing?
- 5. How do my age, health, and other factors affect my options?
- 6. Does any option offer a cure or long-term cancer control? Are my chances any better for one option than another? Less time-consuming? Less expensive?
- 7. When will I start treatment? How long will treatment take?
- 8. Will the treatment hurt?
- 9. Do I have to go to the hospital or elsewhere? How often? How long is each visit?
- 10. How much will the treatment cost? Will my insurance pay for it?
- 11. What are my options if treatment stops working?
- 12. What are the possible complications?
- 13. What are the chances my cancer will return? How will it be treated if it returns?
- 14. Which treatment will give me the best quality of life?
- 15. Can I stop treatment at any time? What will happen if I stop treatment?
- 16. Who can I call on weekends or non-office hours if I have an urgent problem with my cancer or my cancer treatment?

## Questions to ask about surgery

- 1. What type of surgery will I have? How many of these have you done?
- 2. What will be removed during surgery?
- 3. How long will it take me to recover from surgery?
- 4. How much pain will I be in? What will be done to manage my pain?
- 5. How will surgery affect my bladder? How long will I need a catheter?
- 6. What will you do to help with the discomfort of the catheter?
- 7. How will surgery affect my ability to get and maintain an erection?
- 8. What are my risks for long-term urinary issues?
- 9. What other side effects can I expect from surgery?
- 10. What treatment will I have before, during, or after surgery?

# Questions to ask about radiation therapy

- 1. What type of radiation therapy will I have?
- 2. Will you be targeting the prostate alone or will you also treat the lymph nodes?
- 3. Will you use hormone therapy with radiation? If so, for how long?
- 4. How many treatment sessions will I require? Can you do a shorter course of radiation?
- 5. Do you offer brachytherapy here? If not, can you refer me to someone who does?
- 6. How does radiation therapy compare with surgery in terms of cure?
- 7. How will radiation affect my bladder?
- 8. How will radiation affect my bowels?
- 9. How will radiation affect my sexual function?

## Questions to ask about side effects

- 1. What are the side effects of treatment?
- 2. What are my chances of experiencing urinary incontinence, bowel problems, or erectile dysfunction from prostate cancer or its treatment?
- 3. How long will these side effects last?
- 4. What can be done to prevent or relieve the side effects of treatment?
- 5. Will you stop treatment or change treatment if I have side effects? What do you look for?
- 6. What side effects should I watch for? When should I call? Can I text?
- 7. What side effects are life-long or irreversible after completing treatment?
- 8. What medicines may worsen the side effects of treatment?

## Questions to ask about clinical trials

- 1. What clinical trials are available for my type and stage of prostate cancer?
- 2. What are the treatments used in the clinical trial?
- 3. What does the treatment do?
- 4. Has the treatment been used before? Has it been used for other types of cancer?
- 5. What are the risks and benefits of joining the clinical trial?
- 6. Will the treatment need a biopsy sample?
- 7. What side effects should I expect? How will the side effects be controlled?
- 8. How long will I be on the clinical trial?
- 9. Will I be able to get other treatment if this doesn't work?
- 10. How will you know the treatment is working?
- 11. Will the clinical trial cost me anything? If so, how much?

Online resources

### Online resources

American Cancer Society (ACS) cancer.org/cancer/prostate-cancer.html

California Prostate Cancer Coalition (CPCC) prostatecalif.org

CancerCare cancercare.org/diagnosis/prostate\_cancer

Cancer.Net cancer.net/cancer-types/prostate-cancer

Cancer Support Community cancersupportcommunity.org

Malecare Cancer Support malecare.org

National Cancer Institute cancer.gov/types/prostate

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

National Coalition for Cancer Survivorship canceradvocacy.org

PAN Foundation panfoundation.org National Prostate Cancer Awareness Foundation (PCaAware) pcaaware.org

Prostate Cancer Foundation pcf.org

Prostate Cancer Nomograms mskcc.org/nomograms/prostate

Prostate Conditions Education Council (PCEC) prostateconditions.org

Prostate Health Education Network (PHEN) prostatehealthed.org

U.S. National Library of Medicine Clinical Trials Database <u>clinicaltrials.gov</u>

Urology Care Foundation urologyhealth.org

Veterans Prostate Cancer Awareness (VPCa) veteransprostatecancer.org

ZERO - The End of Prostate Cancer zerocancer.org



# Words to know

#### androgen deprivation therapy (ADT)

A treatment that removes the testicles or stops them from making testosterone. ADT can be achieved through surgery or drugs.

#### anti-androgen

A drug that stops the action of the hormone testosterone.

#### benign prostatic hyperplasia (BPH)

An enlargement of the prostate gland that's not caused by cancer.

#### biomarker

Something found in your body that can be measured to assess your health.

#### biopsy

A procedure that removes fluid or tissue samples to be tested for disease.

#### brachytherapy

A treatment with radiation from an object placed in or near the tumor. Also called internal radiation therapy.

#### castration

Surgery that removes the testicles, or drugs that suppress the function of the testicles, in order to keep testosterone levels very low.

#### chemotherapy

Cancer drugs that stop the cell life cycle so cells don't increase in number.

#### computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the inside of the body.

#### digital rectal exam

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

#### erectile dysfunction

A lack of blood flow to the penis that limits getting or staying erect.

#### external beam radiation therapy (EBRT)

A cancer treatment with radiation received from a machine outside the body.

#### genetic abnormality (mutation)

An abnormal change in the genetic code (DNA) of a gene within cells.

#### germline testing

Genetic testing for a mutation that's passed down in families (hereditary) and is found in every cell in the body.

#### **Gleason score**

A rating of how much prostate cancer cells look like normal cells under the microscope.

#### Grade Group

Like a Gleason score, a Grade Group is a rating of how much prostate cancer cells look like normal cells under the microscope. Grade Groups are meant to be easier to use than Gleason scores.

#### high dose-rate (HDR) brachytherapy

Treatment with radioactive instruments that are removed at the end of the treatment session.

#### hormone therapy

A cancer treatment that stops the making or action of hormones. Also called androgen deprivation therapy.

#### immunotherapy

A drug treatment that helps a patient's own immune system find and destroy cancer cells.

#### intermittent treatment

Alternating periods of time on and off treatment.

#### life expectancy

The number of years a person is likely to live.

#### low dose-rate (LDR) brachytherapy

Treatment with radioactive objects that are placed in 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.

# Iuteinizing hormone-releasing hormone (LHRH) antagonist

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

#### lymphatic system

A network of organs and vessels that fights infection and transports a fluid called lymph.

#### magnetic resonance imaging (MRI)

A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

#### metastasis

The spread of cancer from the first tumor to a new site.

#### molecular biomarker test

A lab test of any molecule in your body that can be measured to assess your health.

#### nomogram

A mathematical tool that uses health information to predict an outcome.

#### observation

A period of watching for cancer growth or occurrence while not receiving treatment.

#### orchiectomy

An operation to reduce testosterone in the body by removing one or both testicles.

#### osteoporosis

A health condition that causes bones to thin and weaken.

#### palliative care

Health care for the symptoms of cancer or the side effects of cancer treatment.

#### pelvic lymph node dissection (PLND)

An operation that removes lymph nodes within the pelvis.

#### perineum

The body region in men between the scrotum and anus.

#### positron emission tomography (PET)

A test that uses radioactive material to see the shape and function of body parts.

#### prostate-specific antigen (PSA)

A protein mostly made by the prostate. It's measured in nanograms per milliliter of PSA (ng/mL).

#### **PSA** density

The level of PSA in relation to the size of the prostate. PSA density may indicate risk for prostate cancer.

#### PSA doubling time (PSADT)

The time during which the level of PSA doubles. A faster PSADT is linked to a higher risk for prostate cancer.

#### radiation therapy

Treatment that uses high-energy rays (radiation) to kill cancer cells.

#### radical perineal prostatectomy

An operation that removes the prostate through one cut made between the scrotum and anus.

#### radical retropubic prostatectomy

An operation that removes the prostate through one large cut made below the belly button.

#### radiopharmaceutical

A drug that contains a radioactive substance.

#### recurrence

The return of cancer after a disease-free period.

#### risk factor

Something that increases the chance of getting a disease.

#### seminal vesicles

Two male glands that make fluid that sperm use for energy.

#### staging

The process of rating the extent of cancer in the body.

#### supportive care

Health care for the symptoms of cancer or the side effects of cancer treatment. Also called palliative care.

#### surgical margin

The normal-looking tissue around a tumor that is removed during an operation.

#### testosterone

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

#### transrectal ultrasound (TRUS)

A test that sends sound waves through the rectum to make pictures of the prostate.

#### ultrasound

A test that uses sound waves to take pictures of the inside of the body.

#### urethra

A tube that carries urine from the bladder to outside the body. In men, the urethra carries urine and semen through the penis.

#### urinary incontinence

A health condition in which the release of urine can't be controlled.

# NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Prostate Cancer, Version 4.2022. It was adapted, reviewed, and published with help from the following people:

Dorothy A. Shead, MS Senior Director Patient Information Operations Susan Kidney Senior Graphic Design Specialist John Murphy Medical Writer

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines<sup>®</sup>) for Prostate Cancer, Version 4.2022 were developed by the following NCCN Panel Members:

Edward M. Schaeffer, MD, PhD/Chair Robert H. Lurie Comprehensive Cancer Center of Northwestern University

\*Sandy Srinivas, MD/Vice-Chair Stanford Cancer Institute

Yi An, MD Yale Cancer Center/Smilow Cancer Hospital

Andrew J. Armstrong, MD, ScM Duke Cancer Institute

Daniel Barocas, MD, MPH Vanderbilt-Ingram Cancer Center

Brian Chapin, MD The University of Texas MD Anderson Cancer Center

Heather H. Cheng, MD, PhD Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance

Anthony Victor D'Amico, MD, PhD Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center

Brian J. Davis, MD, PhD Mayo Clinic Cancer Center

Neil Desai, MD, MHS UT Southwestern Simmons Comprehensive Cancer Center

Tanya Dorff, MD City of Hope National Cancer Center

\*James A. Eastham, MD Memorial Sloan Kettering Cancer Center

\*Thomas A. Farrington Prostate Health Education Network (PHEN)

Xin Gao, MD Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center Shilpa Gupta, MD Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Thomas Guzzo, MD Abramson Cancer Center at The University of Pennsylvania

Eric Mark Horwitz, MD Fox Chase Cancer Center

Joseph E. Ippolito, MD, PhD Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Michael R. Kuettel, MD, MBA, PhD Roswell Park Comprehensive Cancer Center

Joshua M. Lang, MD, MS University of Wisconsin Carbone Cancer Center

Tamara Lotan, MD The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

\*Rana R. McKay, MD UC San Diego Moores Cancer Center

Todd Morgan, MD University of Michigan Rogel Cancer Center

George Netto, MD O'Neal Comprehensive Cancer Center at UAB

Julio M. Pow-Sang, MD Moffitt Cancer Center

Robert Reiter, MD, MBA UCLA Jonsson Comprehensive Cancer Center

Mack Roach, III, MD UCSF Helen Diller Family Comprehensive Cancer Center Tyler Robin, MD, PhD University of Colorado Cancer Center

Stan Rosenfeld University of California San Francisco Patient Services Committee Chair

Ahmad Shabsigh, MD The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Daniel Spratt, MD Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

\*Benjamin A. Teply, MD Fred & Pamela Buffett Cancer Center

Jonathan Tward, MD, PhD Huntsman Cancer Institute at the University of Utah

Richard Valicenti, MD UC Davis Comprehensive Cancer Center

#### NCCN Staff

Deborah Freedman-Cass, PhD Ryan Berardi, MSc Dorothy A. Shead, MS

\* Reviewed this patient guide. For disclosures, visit <u>NCCN.org/disclosures</u>.

NCCN Guidelines for Patients® Advanced-Stage Prostate Cancer, 2022

# **NCCN Cancer Centers**

Abramson Cancer Center at the University of Pennsylvania *Philadelphia, Pennsylvania* 800.789.7366 • <u>pennmedicine.org/cancer</u>

Case Comprehensive Cancer Center/ University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute *Cleveland, Ohio* 800.641.2422 • UH Seidman Cancer Center <u>uhhospitals.org/services/cancer-services</u> 866.223.8100 • CC Taussig Cancer Institute <u>my.clevelandclinic.org/departments/cancer</u> 216.844.8797 • Case CCC <u>case.edu/cancer</u>

City of Hope National Medical Center Los Angeles, California 800.826.4673 • <u>cityofhope.org</u>

Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center *Boston, Massachusetts* 617.732.5500 • <u>youhaveus.org</u> 617.726.5130 <u>massgeneral.org/cancer-center</u>

Duke Cancer Institute Durham, North Carolina 888.275.3853 • <u>dukecancerinstitute.org</u>

Fox Chase Cancer Center *Philadelphia, Pennsylvania* 888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center Omaha, Nebraska 402.559.5600 • <u>unmc.edu/cancercenter</u>

Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance Seattle, Washington 206.606.7222 • <u>seattlecca.org</u> 206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah Salt Lake City, Utah 800.824.2073 • <u>huntsmancancer.org</u>

Indiana University Melvin and Bren Simon Comprehensive Cancer Center Indianapolis, Indiana 888.600.4822 • <u>www.cancer.iu.edu</u> Mayo Clinic Cancer Center Phoenix/Scottsdale, Arizona Jacksonville, Florida Rochester, Minnesota 480.301.8000 • Arizona 904.953.0853 • Florida 507.538.3270 • Minnesota mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center *New York, New York* 800.525.2225 • <u>mskcc.org</u>

Moffitt Cancer Center Tampa, Florida 888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB *Birmingham, Alabama* 800.822.0933 • <u>uab.edu/onealcancercenter</u>

Robert H. Lurie Comprehensive Cancer Center of Northwestern University *Chicago, Illinois* 866.587.4322 • <u>cancer.northwestern.edu</u>

Roswell Park Comprehensive Cancer Center *Buffalo, New York* 877.275.7724 • <u>roswellpark.org</u>

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine *St. Louis, Missouri* 800.600.3606 • <u>siteman.wustl.edu</u>

St. Jude Children's Research Hospital/ The University of Tennessee Health Science Center *Memphis, Tennessee* 866.278.5833 • <u>stjude.org</u> 901.448.5500 • <u>uthsc.edu</u>

Stanford Cancer Institute Stanford, California 877.668.7535 • <u>cancer.stanford.edu</u>

The Ohio State University Comprehensive Cancer Center -James Cancer Hospital and Solove Research Institute *Columbus, Ohio* 800.293.5066 • <u>cancer.osu.edu</u> The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Baltimore, Maryland 410.955.8964 www.hopkinskimmelcancercenter.org

The University of Texas MD Anderson Cancer Center *Houston, Texas* 844.269.5922 • <u>mdanderson.org</u>

UC Davis Comprehensive Cancer Center Sacramento, California 916.734.5959 • 800.770.9261 health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center La Jolla, California 858.822.6100 • <u>cancer.ucsd.edu</u>

UCLA Jonsson Comprehensive Cancer Center Los Angeles, California 310.825.5268 • <u>cancer.ucla.edu</u>

UCSF Helen Diller Family Comprehensive Cancer Center San Francisco, California 800.689.8273 • <u>cancer.ucsf.edu</u>

University of Colorado Cancer Center Aurora, Colorado 720.848.0300 • <u>coloradocancercenter.org</u>

University of Michigan Rogel Cancer Center Ann Arbor, Michigan 800.865.1125 • <u>rogelcancercenter.org</u>

University of Wisconsin Carbone Cancer Center Madison, Wisconsin 608.265.1700 • <u>uwhealth.org/cancer</u>

UT Southwestern Simmons Comprehensive Cancer Center Dallas, Texas 214.648.3111 • <u>utsouthwestern.edu/simmons</u>

Vanderbilt-Ingram Cancer Center Nashville, Tennessee 877.936.8422 • <u>vicc.org</u>

Yale Cancer Center/ Smilow Cancer Hospital New Haven, Connecticut 855.4.SMILOW • <u>yalecancercenter.org</u>

#### Index

# Index

androgen deprivation therapy (ADT) 43, 45-47, 58-59, 61-65, 67-70 biomarkers 17-20, 23, 36-37, 43, 49 **biopsy** 16–18, 20–21, 23–29, 31–32, 35–36, 39, 58–60 bone scan 22, 47, 57 bone-targeted therapy 43, 49–50, 54 brachytherapy 48–49, 59 castration 40, 42, 54, 62–63, 65, 68 chemotherapy 12, 39-40, 42-43, 45, 54. 68–69, 72 clinical trial 51-54, 67 corticosteroids 40-41,68 digital rectal exam 15–17, 20, 23, 25–26, 31-32, 56-57 erectile dysfunction 12, 42, 47, 48, 50, 54 external beam radiation therapy (EBRT) 48, 58, 63 genetic testing 18–20 **Gleason score** 24, 29–31, 34, 36 Grade Groups 24, 30–31, 34–35, 62 hormones 9, 40–42, 54, 62–63, 65 immunotherapy 12, 40, 43, 44, 54, 68–69 intermittent treatment 12, 42, 59 life expectancy 34, 37, 41, 47, 63 local therapy 40, 58–59 lymph nodes 10, 21–22, 31–32, 46, 48, 54, 59,70

molecular biomarker test 17–20, 36–37, 44 nomogram 36–37, 57 observation 40, 50, 62-65 orchiectomy 40 pelvic lymph node dissection (PLND) 46, 48, 59 prostatectomy 46–48, 54, 56, 58–59 PSA density 26 PSA doubling time (PSADT) 57, 60, 62, 64-65 radiation therapy 12, 26, 39–40, 48–50, 54, 56-60, 62 radiopharmaceuticals 12, 39, 40, 43, 45, 54, 68, 69 recurrence 26, 55-60, 70 risk groups 25, 31–32, 34–37 staging 31 supportive care 51, 67, 70 surgery 12, 26, 46–48, 54, 56–58, 60, 72 survivorship 70 systemic therapy 40–45, 67, 70 transrectal ultrasound (TRUS) 26–27, 58 tumor, node, metastasis (TNM) score 31–32, 34-35 urinary incontinence 42, 47, 49–50, 54, 59





# Prostate Cancer Advanced Stage

2022

NCCN Foundation gratefully acknowledges the following corporate supporters for helping to make available these NCCN Guidelines for Patients: Astellas, AstraZeneca, Exact Sciences, Janssen Biotech, Inc., Lantheus, and Pfizer Inc. NCCN independently adapts, updates, and hosts the NCCN Guidelines for Patients. Our corporate supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.



PAT-N-1531-0722