National Comprehensive Cancer Network®

2026

NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

Advanced-Stage Prostate Cancer



Presented with support from NCCN FOUNDATION Guiding Treatment. Changing Lives.

Available online at NCCN.org/patientguidelines



NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Prostate Cancer, Version 5.2026 — January 23, 2026.

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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.

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About advanced-stage prostate cancer

5 What is prostate cancer?

7 How is prostate cancer treated?

7 How can I get the best care?

The prostate is a gland located deep inside of the pelvis. Everyone with a prostate has a chance of getting prostate cancer. This chapter gives an overview of this common cancer and the many treatments for it.

What is prostate cancer?

Prostate cancer is a disease where cells in the prostate gland grow out of control.

The prostate is a gland located just below the bladder in the pelvis, deep inside of the area of your body between your hip bones. The prostate is an important part of the male reproductive system. This system also includes the penis, seminal vesicles, and testicles.

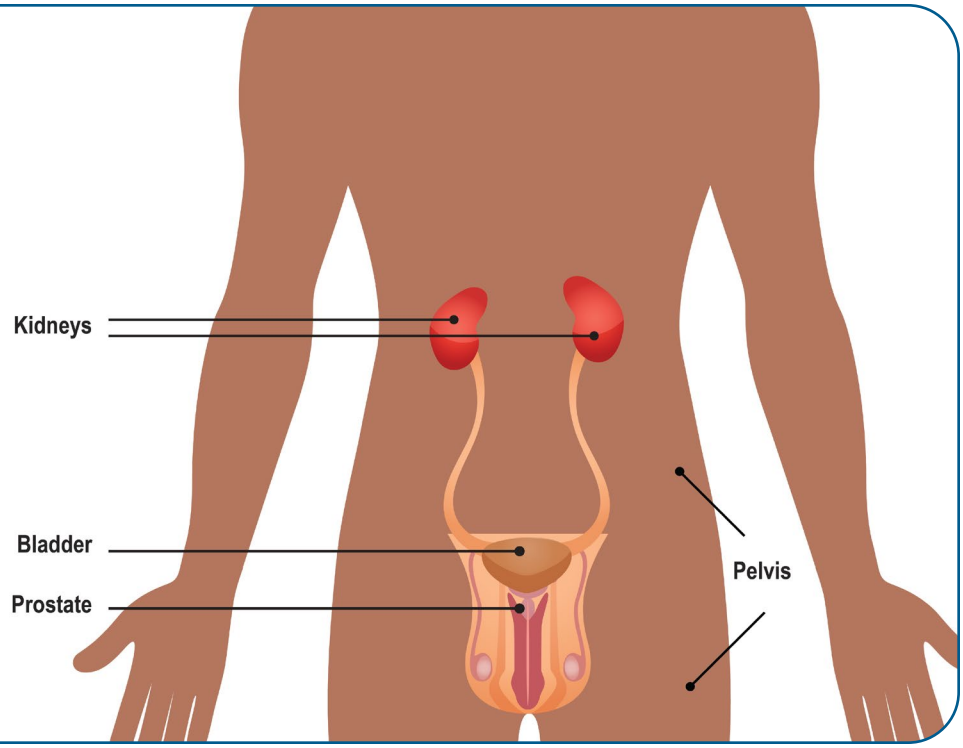
Prostate cancer is one of the most common types of cancer. Cancer happens when something goes wrong with the natural cell process, causing some cells to multiply and spread.

Cancer cells don't behave like normal cells. Cancer cells develop genetic changes (mutations) that allow them to make many more cancer cells. The cancer cells crowd out and overwhelm normal cells. This can end up harming the body.

Cancer cells survive much longer than normal cells do. They can replace many normal cells and cause organs to stop working well. Cancer cells can also spread outside of the prostate to other areas of the body.

The prostate gland is an important part of the male reproductive system. It's located in the pelvis just below the bladder.

The prostate is about the size of a ping-pong ball at age 20. It grows larger with age.



Prostate cancer is described as either early stage or advanced stage.

Early-stage prostate cancer

Early-stage prostate cancer, also called localized prostate cancer, has not spread beyond the prostate. The cancer usually grows slowly and stays inside of the prostate gland.

Advanced-stage prostate cancer

Advanced stage means the cancer has spread beyond the prostate to other areas of the body. This spreading is called metastasis or metastatic cancer. Metastatic prostate cancer may spread to lymph nodes, bones, liver, lungs, and other organs.

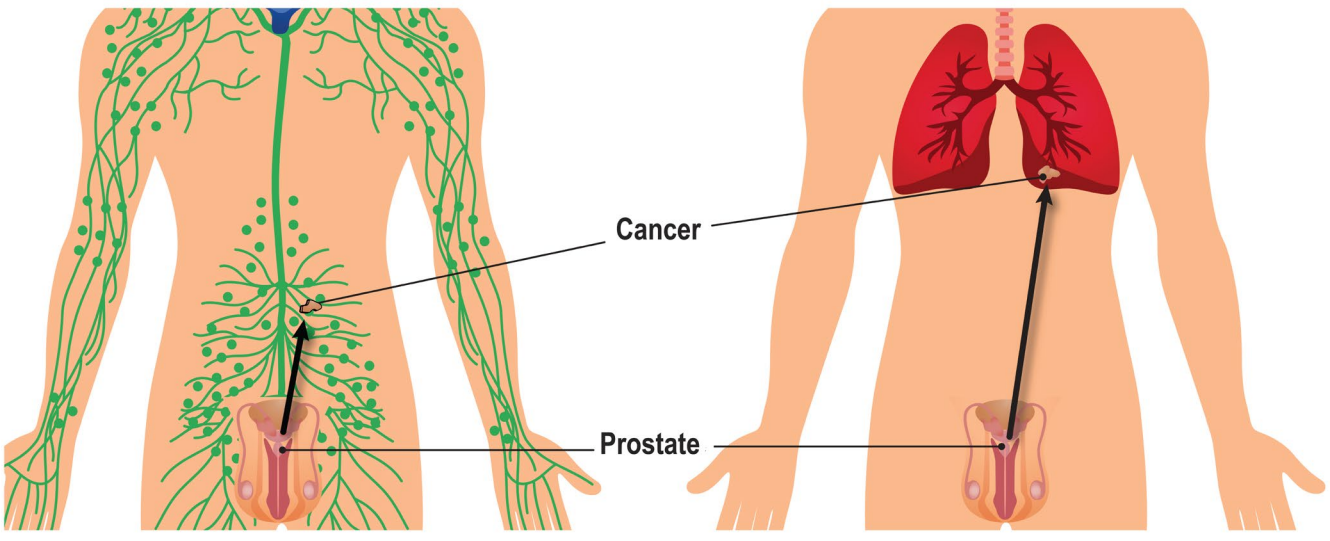
- Cancer that grows from the prostate gland to nearby lymph nodes in the pelvis is called **regional prostate cancer**. (It's also called locally advanced prostate cancer. This guide will call it regional prostate cancer to avoid confusion between localized and locally advanced.)
- Cancer that spreads beyond the prostate and regional lymph nodes to other parts of the body is called **metastatic prostate cancer**.

Cancer cells use the bloodstream like a highway to travel to distant areas of 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.

An important part of the lymphatic system are the lymph nodes. Lymph nodes are small

What is advanced-stage prostate cancer?

Advanced-stage prostate cancer is cancer that grows outside of the prostate and spreads to other areas in the body, such as distant lymph nodes (bottom left), bones, or organs like the liver or lungs (bottom right). This is also called metastatic prostate cancer.



disease-fighting clusters that filter lymph fluid to remove germs. Lymph vessels and nodes are found everywhere in the body.

How is prostate cancer treated?

Recommended treatments for advanced-stage prostate cancer include hormone therapy, chemotherapy, targeted therapy, radiopharmaceuticals, and others.

Advanced-stage prostate cancer is usually a lifelong disease. But treatment can destroy much of the cancer, slow down its growth, reduce symptoms, and help you live longer.

Improved detection methods and better treatments continue to reduce the number of deaths from prostate cancer. Many people with advanced-stage prostate cancer continue to live with the cancer and, in the end, may die of something else.

How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

Don't know what to ask? You're not alone. That's why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

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Symptoms and risk factors for prostate cancer

9 What are the symptoms of prostate cancer?

9 How did I get prostate cancer?

12 Key points

12 Questions to ask

Cancer researchers don't know exactly what causes prostate cells to become cancerous, but certain factors can increase your risk. People with prostate cancer usually have one or more of these risk factors.

What are the symptoms of prostate cancer?

Prostate cancer often grows slowly and shows no symptoms for a long time. You don't have to have symptoms to have prostate cancer.

Symptoms, if they occur, may include:

- Difficulty urinating or emptying the bladder
- Urinating too frequently
- Blood in the urine or semen
- Burning or pain while urinating
- Unexplained weight loss
- Bone, hip, or back pain

It's important to know that advanced prostate cancer has many of the same symptoms as a non-cancerous condition called **enlarged prostate** (also called benign prostatic hyperplasia, or BPH). It's difficult to tell the difference between enlarged prostate and prostate cancer based on symptoms alone.

If you do have any symptoms, be sure to tell your health care providers.

In BPH, the enlarged prostate can push against the bladder and compress the urethra. This slows the flow of urine and can cause a feeling you haven't fully emptied your bladder.

BPH is much more common than prostate cancer. Enlarged prostate occurs in about half of males by 60 years of age. It becomes even more common as you grow older.

BPH doesn't cause prostate cancer, and it won't turn into prostate cancer. But it's important to know that you can have BPH and **also** have prostate cancer.

How did I get prostate cancer?

Cancer researchers don't know what causes prostate cells to grow out of control (become cancerous).

The fact is, everyone with a prostate has a risk for prostate cancer. This includes males as well as transgender females.

Several factors are linked to a higher risk for 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 people aged 65 years and above. Your chances of getting prostate cancer increase as you become older.

Where does the prostate fit in?

The prostate is a gland located in the pelvis—the area between your hips. The prostate is important for sexual reproduction.

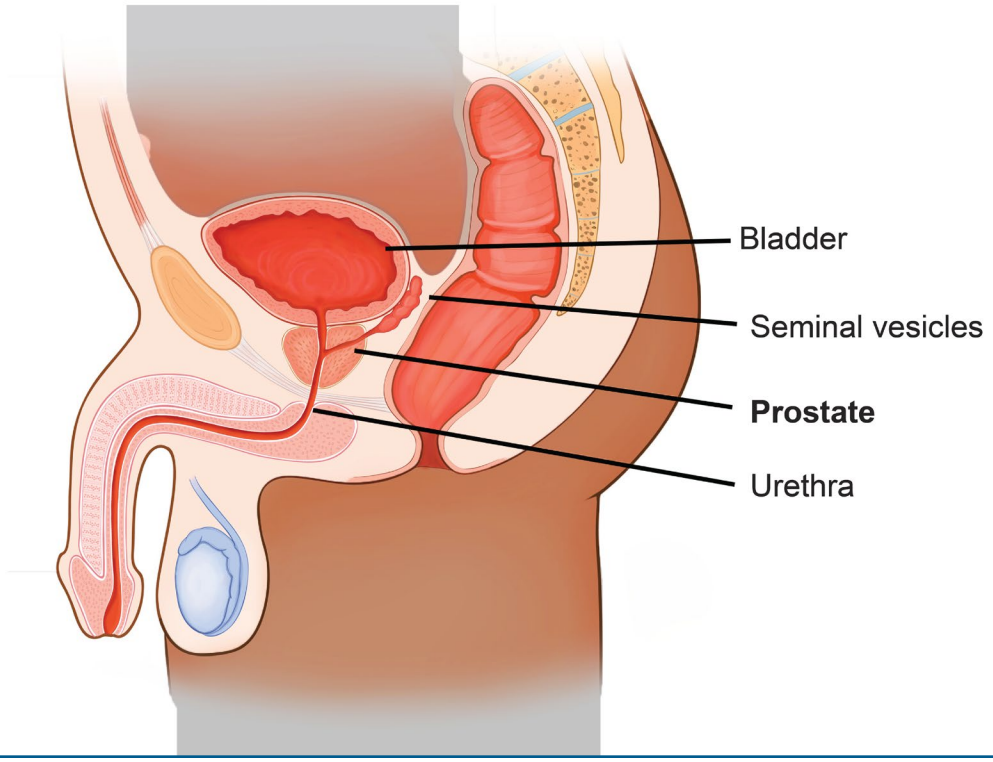
Prostate: A gland in the male reproductive system. A gland is an organ that makes fluids or chemicals the body needs. The prostate gland makes a fluid that nourishes and helps transmit sperm. The prostate also contains muscles that help propel semen through the urethra during ejaculation.

Semen: 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 surrounds the urethra just beneath the bladder.

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

Bladder: The organ that holds urine.



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. Having a close family member with prostate cancer (a sibling or parent) increases the chance of getting it yourself.

People with a family history of certain cancers (breast, ovarian, colon, pancreatic, and others) may also be at higher risk for prostate cancer.

Genetic factors

If cancer occurs often in your family, genetic testing can be done to find specific genetic changes known to be linked to prostate cancer and other cancers. For instance, having an inherited genetic change in the *BRCA1* or *BRCA2* gene increases your risk for prostate cancer.

Race

In the United States, 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. Black males are also twice as likely to die of prostate cancer than white males.

Several things contribute to these differences, such as barriers to accessing health care (including early detection screening), biological and genetic factors, and other causes. Researchers are trying to understand the reasons for these differences and what can be done to improve outcomes.

What does aggressive mean?

When health care professionals describe cancer as aggressive, they mean the cancer is likely to grow or spread more rapidly than average.

Aggressive can also be used to describe therapy that may be stronger or more intense than other treatment options.

In light of these issues, Black males are encouraged to talk with their health care providers about getting screening tests earlier and perhaps more often than what's recommended for those at average risk.

Diet and lifestyle

No diet has been found to cause prostate cancer or to prevent it. However, eating food high in fat, such as meat and dairy products, has been linked to an increased risk for prostate cancer. Smoking and obesity also increase the risks for developing and dying of prostate cancer.

On the other hand, those who eat more fruits and vegetables have a lower risk for advanced prostate cancer. Maintaining a healthy body weight through diet and exercise may slow the growth of prostate cancer and lower your risk for dying of it.

Key points

- Everyone with a prostate is at risk for prostate cancer.
- Advanced-stage prostate cancer has spread outside of the prostate and the pelvis to other areas of the body. This spreading is called metastasis.
- Advanced-stage prostate cancer is usually a lifelong disease. Treatment can slow it down, reduce its symptoms, and help people live longer.
- Age is the leading risk factor for prostate cancer. As you age, your chances of developing prostate cancer increase.
- Having a close family member with prostate cancer means you have a higher chance of getting it yourself.
- People with a family history of certain other cancers may also be at a higher risk for prostate cancer.

Questions to ask

- If I don't have any symptoms, do I need any treatment?
- Am I more likely to get prostate cancer if I have more risk factors?
- Is my prostate cancer hereditary?
- How does having a relative with breast cancer increase my risk for prostate cancer?
- What are the chances the cancer has spread from my prostate to another part of my body?

"It's OK to have bad days, but don't let yourself stay there. A positive attitude goes a long way."

3

Testing for advanced-stage prostate cancer

14 Common prostate tests

16 General health tests

17 Diagnostic tests

24 Tumor staging

25 Key points

25 Questions to ask

Several tests are needed to diagnose prostate cancer and learn how advanced it is. The results of these tests will help your doctors and care team plan the best treatment for you.

Health care providers use a variety of tests to find prostate cancer and to determine how advanced the cancer is.

Tests are used to plan treatment, check how well treatment is working, and monitor your health after treatment ends.

This chapter will help you know what tests you might have and what to expect during testing. Not every person with prostate cancer will receive every test listed here. See **Guide 1**.

Common prostate tests

Common prostate cancer tests are used to detect the possibility of prostate cancer in someone who has no symptoms. So these are often called early detection tests or screening tests.

These tests are also used in people who have been diagnosed with prostate cancer to monitor the cancer and to check whether their treatment is working.

These 2 tests are the prostate-specific antigen (PSA) test and the digital rectal exam.

PSA test

This is a blood test that measures the amount of PSA in your bloodstream.

PSA is a protein made inside of the prostate gland. Its job is to help semen transport sperm. While most PSA goes into semen, a little bit ends up in the bloodstream, too.

All prostate cells, both normal cells and cancer cells, make PSA.

Guide 1
Possible tests for advanced-stage prostate cancer

Common prostate tests

- PSA test
- Digital rectal exam

General health tests

- Health history
- Family history
- Symptoms and quality of life assessment
- Blood and urine tests

Imaging tests

- MRI scan
- CT scan
- PET scan (PET/CT, PET/MRI)
- Bone scan

Biopsy

- Biopsy of the prostate
- Biopsy of a metastasis

Biomarker and genetic tests

- Biomarker test
- Genetic test for inherited risk

If there's something wrong with the prostate—like prostate cancer—the prostate can release more PSA into the bloodstream.

An unusually high amount of PSA in the blood may be a sign of prostate cancer. Likewise, an increase in PSA after treatment for prostate cancer may indicate the treatment is losing effectiveness.

However, age and other factors—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 this test is often paired with imaging or a digital rectal exam, or both, to decide whether you need further testing.

PSA level (also called total PSA) is measured in nanograms of PSA per milliliter (ng/mL) of blood.

Digital rectal exam

A digital rectal exam (also called a prostate exam) may be an awkward and unpleasant form of testing. But it's the simplest and most direct way to check the size and texture of your prostate.

For this test, the doctor will insert a gloved finger into your rectum to feel your prostate for any signs of cancer. An irregular or hardened part of the prostate could be a sign of a tumor.

Not all parts of the prostate can be felt during a digital rectal exam, though. So it should be paired with a PSA test and other factors—your age, race, family history, and more—to determine whether you need further testing.

Some doctors don't recommend a digital rectal exam because it's not very good at finding cancer on its own. So your doctor might leave the choice whether to have it up to you. NCCN

PSA testing

Prostate-specific antigen (PSA) is a protein made inside of the prostate gland. If there's something wrong with the prostate, it can release more PSA. An unusually high amount of PSA in the blood may be a sign of prostate cancer.

But a high PSA level doesn't automatically mean you have prostate cancer. Rather, it's a warning sign you may need further testing.



experts say a digital rectal exam is most useful for individuals who have a higher PSA level.

General health tests

Health history

Your care team needs 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. Also tell your care team about any symptoms you have.

Bring a list of your regular medications and any over-the-counter medicines, herbals, or supplements you take. Some of these (such as saw palmetto, St. John's wort, or finasteride [Propecia] for hair loss) can cause changes in your PSA level, so your health care team needs to know if you're taking them.

Family history

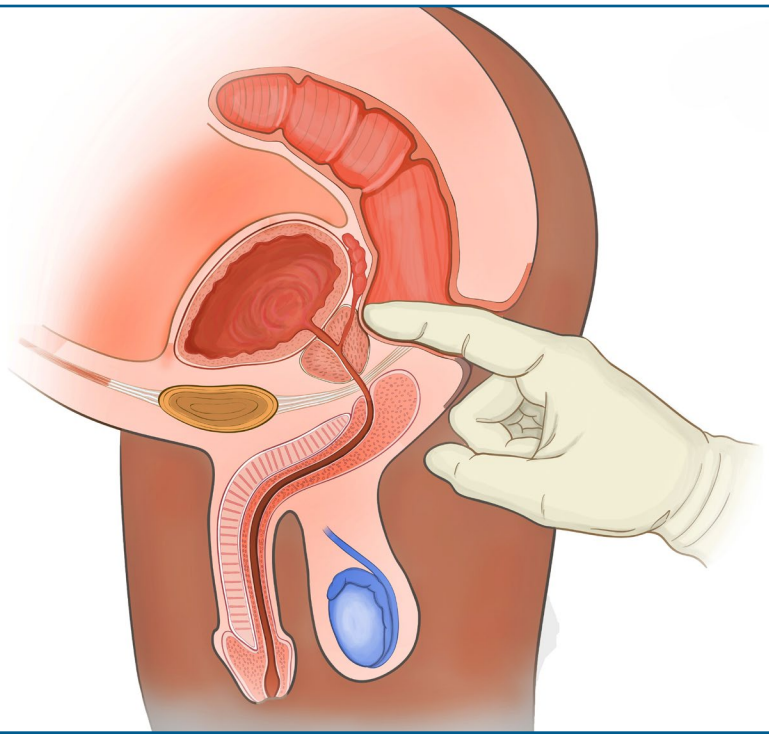
Some cancers and other diseases can run in families. Your care team will ask about the health history of family members who are blood relatives. This information is called a family history.

It's important to ask members from both sides of your family about all cancers, not just prostate cancer. Ask your family members if any relatives had cancer, at what age they were diagnosed, and if they died from it.

Also ask family members about other health issues like heart disease, stroke, and diabetes. Share this information and any changes to your family history with your care team.

Digital rectal exam

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



Symptoms and quality of life assessment

Your doctor or another member of your care team will ask you a series of questions about what symptoms you may have (such as peeing frequently, difficulty peeing or pooping, or sexual problems). You'll also be asked how these symptoms affect your quality of life.

Quality of life refers to your overall satisfaction with your well-being and your ability to participate in regular activities. It's important to answer all of these questions honestly and completely so your care team has a full and up-to-date assessment of how you're doing.

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 of the blood are tested for signs of disease or other conditions.

If your PSA level is high, you may need additional blood or urine testing.

Diagnostic tests

Diagnostic tests are used to confirm you have cancer. They're also used to find out if the cancer is localized or advanced. Diagnostic tests can help plan treatment after you've been diagnosed and can detect whether the cancer is still growing or spreading after treatment.

Diagnostic tests include imaging scans, biopsies, and genetic tests.

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, such as the size of the prostate itself. The images may show where the cancer started (primary tumor) and whether the cancer has spread (metastasized).

When you go for health care visits, bring someone with you to listen, ask questions, and write down the answers.



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

Imaging can come before, during, or after a biopsy. Imaging may also be used after cancer treatment to see how well it worked and to check if the cancer comes back.

Imaging methods for prostate cancer include MRI, CT, PET, bone scan, ultrasound, or a combination of these.

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to provide a 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.

An MRI scan of the prostate can help decide whether a biopsy is needed. MRI is frequently used before a biopsy to locate any suspicious areas in the prostate for the biopsy to target.

More commonly, MRI is used after diagnosis to learn whether the cancer has advanced outside of the prostate or into the lymph nodes. MRI can help to plan treatment and is also used after treatment to check if the cancer has come back (recurrence).

Because an MRI uses magnets, you can't bring any metal objects (such as a phone, jewelry, wristwatch, or belt with a metal buckle) into the imaging room.



Who's on your care team?

Treating prostate cancer takes a team approach. Some members of your care team will be with you throughout your treatment, while others will be there for parts of it.

Your team should communicate and work together to bring the best knowledge from each specialty.

Lead members of your team should include prostate cancer specialists such as a urologist, radiation oncologist, and medical oncologist.

Other common team members include your primary care doctor, nurse, physical therapist, physician assistant, mental health care provider, nutritionist or dietitian, genetic counselor, pharmacist, patient navigator, social worker, sex therapist, and others.

CT scan

A computed tomography (CT or CAT) scan takes many x-rays of your body from different angles. A computer combines the x-rays into a series of cross-sectional images of your pelvis.

A CT scan is most often used after diagnosis to determine the extent of cancer in your body (your cancer stage).

PET scan

A positron emission tomography (PET) scan highlights cells in your body that may be cancerous. A PET scan is 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. The tracer targets your cancer cells, which show up as bright spots on the scan.

Because PET uses a different imaging method, it's often combined with CT or MRI to provide an even more detailed image. These combined methods are called PET/CT and PET/MRI scans.

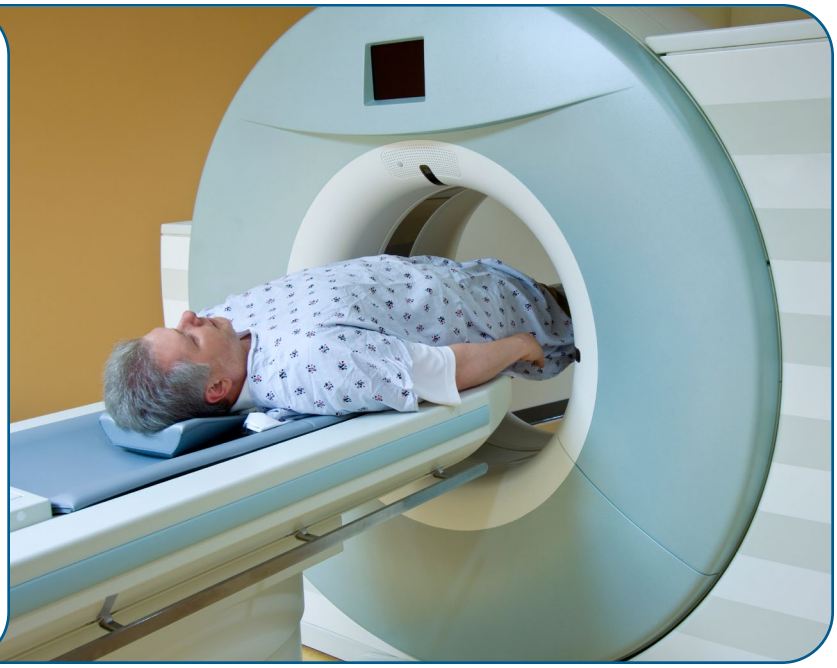
PSMA-PET scan

PET scans use different types of tracers. The most common tracer in prostate cancer locates a protein called prostate-specific membrane antigen (PSMA) on the surface of prostate cancer cells. Prostate cancer cells can make a lot of PSMA, so tracers that target this specific protein were developed.

Not everyone with prostate cancer will need a PSMA-PET scan. It's mostly used to monitor prostate cancer for recurrence. It's also used to determine whether radiopharmaceutical therapy that targets PSMA can treat certain cases of metastatic prostate cancer.

PET imaging

A positron emission tomography (PET) scan highlights cells in your body that may be cancerous. A PET scan is 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.



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 metastasis, or have changes in certain test results. Bone scans may also be used to monitor how well treatment is working.

A bone scan uses a radioactive tracer to make pictures of the inside of bones. Before the pictures are taken, the tracer is injected into your bloodstream.

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 damaged areas show up as bright spots on the scans.

Ultrasound

Ultrasound imaging is commonly used to help guide a biopsy of the prostate. This is called transrectal ultrasound (TRUS) imaging.

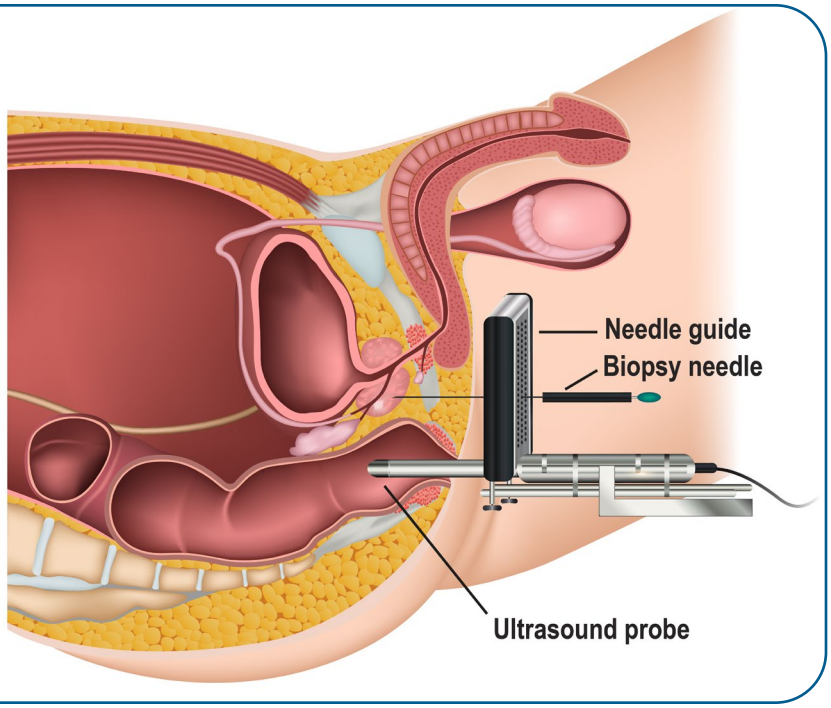
During a biopsy, an ultrasound probe is inserted into the rectum. The probe is about the size of a finger. The device uses high-energy sound waves to create a view of the prostate from inside of the body.

These images allow the surgeon to remove a small sample of the prostate without having to open up your abdomen.

At some centers, your saved MRI images can be combined with real-time ultrasound to provide a more detailed view for a more precise biopsy. This is called MRI-TRUS fusion.

Biopsy of the prostate

A biopsy removes a sample of tissue that is tested for cancer. Shown here is 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. MRI scans of your prostate may be combined with the ultrasound image to provide a highly accurate picture of the cancer.



Biopsy

A biopsy is a procedure in which a sample of cells, fluid, or tissue is removed from your body and tested for cancer. It's the main way to confirm whether you have cancer. You and your doctors will decide when, or if, you need a biopsy.

A biopsy sample may be taken from the prostate, from the metastasis (an area of cancer that has spread outside of the prostate), or sometimes from both.

Biopsy of the prostate

Your biopsy procedure may be done in a surgical center under sedation or in your doctor's office with local anesthesia to numb the pain.

If done in the office, you'll lie on your side with your knees curled up or you'll lie on your back with your legs raised. Your doctor will insert a lubricated probe into your rectum. The probe provides ultrasound images that allow your care team to see your prostate inside of your body.

Using the ultrasound (with or without MRI) for guidance, your doctor will insert a hollow needle either through the perineum (the skin between the anus and scrotum) or through the rectum and into the prostate gland.

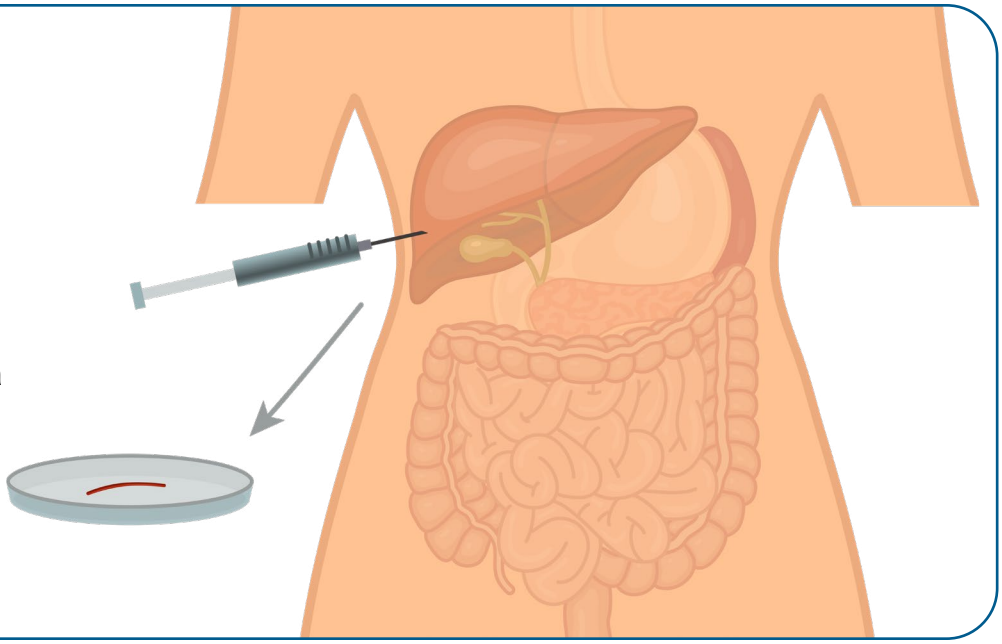
When the needle is removed, it will pull out a small sample of prostate tissue called a core. A core sample is about the size of a grain of rice.

Your doctor will usually take at least 12 core samples from different parts of the prostate as well as several targeted samples from suspicious areas of the prostate identified on the MRI. Checking different areas provides a more complete evaluation of cancer throughout the gland.

After the biopsy samples are removed, a specialist called a pathologist will examine the samples under a microscope and test them for cancer cells. The pathologist will find out how

Biopsy of a metastasis

Prostate cancer may metastasize (spread) from your prostate to lymph nodes, bones, or internal organs. A biopsy of a metastasis (as seen here, taken from the liver) uses a hollow needle to remove a small core of tissue. The tissue is tested in a lab to look for cancer cells.



many of the core samples contain cancer and will also measure the percentage of cancer in each core.

With this information, the pathologist can estimate how much cancer is in the prostate and how aggressive it may be. Also, by learning where each core sample was taken, your team will know if the cancer is concentrated in a certain section of the prostate.

The pathologist will put these results into a report. Ask your doctor or another member of your care team to review the pathology report with you.

Biopsy of a metastasis

A biopsy can be taken from a metastatic tumor in a lymph node, an internal organ, or a bone. This biopsy is performed in a similar way to a prostate biopsy—using a hollow needle to remove cores of tumor tissue and image scanning to guide the needle.

Biopsy complications

Most biopsies are safe, but sometimes a biopsy may cause complications. A complication is an unwanted and unplanned result from a procedure. Complications may include infection, bleeding from the rectum, or blood in the urine, stool, or semen. These usually go away after a few days. Blood in the semen may take longer to go away.

It's important to know that a biopsy won't cause prostate cancer to spread or worsen.

Feeling distressed?

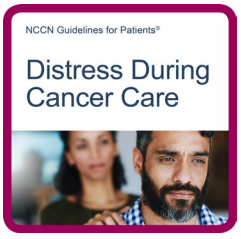
Distress is mental, physical, social, or spiritual anxiety or suffering. It comes from being overwhelmed by pressures, difficulties, or losses. It often affects how you think, feel, or act.

Distress is very common among people with cancer. It can disrupt how you cope with cancer, its symptoms, or its treatment.

If you're feeling distressed, tell your care team so they can help you. They might show you a distress scale represented as a thermometer, where **0** on the thermometer means **no distress** and **10** represents **extreme distress**. You'll then be asked to point to your current level of distress on this scale.

If you're feeling any level of distress, ask your care team what supportive care they can provide. See *Chapter 7: Supportive care and other assistance*.

More information about cancer and distress is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Biomarker test

A biomarker is something found in your body that can be measured to provide information about your health. In cancer care, a biomarker can be used to identify certain cancer cells. This information can then be used to find and destroy those cells.

For example, certain mutations (changes) in the cancer's DNA are biomarkers, which can be targeted with specific treatments. In advanced-stage prostate cancer, the most common type of biomarker testing looks for such changes.

Biomarker testing—also called tumor mutation testing or tumor profiling—is typically performed on a piece of tumor tissue removed during a biopsy or surgery, or on a sample of your blood.

Importantly, biomarker testing can help guide treatment. It can find out whether someone's cancer has a mutation that can be treated with therapy that targets that specific mutation.

Biomarker testing can also provide clues about whether the cancer is at a lower or higher risk for growing and spreading. If the cancer is low risk, you may be able to put off treatment, which also avoids treatment-related complications and side effects. If the cancer is high risk, your provider may recommend starting certain treatments sooner.

Biomarker-targeted therapy is discussed in *Chapter 4: Types of Treatment*.

Biomarker testing is different than hereditary genetic testing. Biomarker testing looks for somatic mutations in genes. Somatic (or acquired) mutations happened in your lifetime and can't be passed down in families. Genetic testing looks for germline (inherited) mutations, which are passed from parents to children.

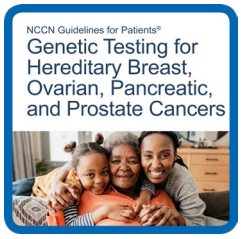
Ask your care team if biomarker testing is right for you.

Genetic test for inherited risk

Most prostate cancers are not hereditary. But if you have a family history of certain cancers or if you have higher-risk or advanced prostate cancer, your doctor might suggest genetic testing to find out if you have a germline (inherited) cancer risk.

Your doctor can talk to you about testing or refer you to a genetic counselor. A genetic counselor is an expert who has special training in genetic diseases. A genetic counselor can help you decide whether you're a good candidate for genetic testing, including whether your risk is high enough to make genetic testing worthwhile. A genetic counselor can also interpret the results of these tests for you.

For more information, see *NCCN Guidelines for Patients: Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancers*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Tumor staging

Tumors come in different shapes and sizes. So it's not easy to compare one tumor to another. To solve this problem, cancer experts created the tumor, node, metastasis (TNM) system to describe any tumor. It's based on the results of your imaging scans, biopsies, and blood tests.

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 of the prostate
- **N (node)** – Identifies whether cancer has spread to nearby (regional) lymph nodes
- **M (metastasis)** – Indicates if cancer has spread (metastasized) to parts of the body beyond the regional lymph nodes

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

Staging is a way to describe how much cancer is in your body and how far it has spread. It's done when you're first diagnosed. Knowing your stage is important for predicting the course of your disease and for making a treatment plan.

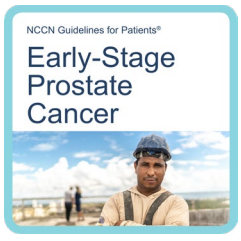


How to read a TNM score

Let's say your prostate cancer is given a TNM score of T4, N1, M1. This score means the tumor has grown outside of the prostate gland (T4) and has spread to nearby lymph nodes (N1) and to one or more distant parts of the body (M1).

Why know your TNM score? For one, it lets you know the extent of your cancer. It also helps predict your risk for the cancer to spread. Your level of risk helps indicate the most appropriate treatment for you.

Measurements and assessments not covered in this guide include PSA density, Gleason score, Grade Group, and risk groups. To learn more about these terms, see *NCCN Guidelines for Patients: Early-Stage Prostate Cancer*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Key points

- Tests are used to plan treatment and check how well treatment is working.
- A high or rising amount of prostate-specific antigen (PSA) in the bloodstream may be a sign of prostate cancer.
- Imaging tests are used to see where the cancer has spread beyond the prostate. Imaging also shows the size and location of the cancer.
- A biopsy is a procedure that removes samples of cells or tissue, which are tested for cancer.
- In cancer care, a biomarker is a characteristic that can be used to identify certain cancer cells. Therapy that targets such characteristics can find and destroy those cells.
- A genetic test can be used to find out if you have an inherited risk for cancer.

Questions to ask

- What tests will I have? How do I prepare for testing?
- Do the tests have any risks?
- Will any of the tests hurt?
- What are the advantages and disadvantages of having genetic testing?
- How soon will I know my test results and who will explain them to me?

What's next?

After you've been tested and diagnosed with prostate cancer, your care team will work with you to develop a plan for treatment.

The next chapter describes the different treatment options for advanced-stage prostate cancer. After that chapter, you'll read about which of those treatments may be right for you and your particular type of cancer.

4
Types of treatment

27 Hormone therapy

30 Non-hormone therapy

35 Clinical trials

36 Supportive care

37 Your treatment goals

38 Key points

38 Questions to ask

There's more than one treatment for advanced prostate cancer. This chapter describes the many treatment options. Talk with your care team about which treatment might be best for you.

Advanced-stage prostate cancer is a complex disease with many treatment options. Recommended treatments include hormone therapy as well as non-hormone therapies like chemotherapy, immunotherapy, biomarker-targeted therapy, radiopharmaceuticals, and radiation therapy.

Often, hormone therapy is combined with one or more other therapies. Combining therapies can be more effective than using either therapy alone.

Hormone therapy

Hormone therapy is a treatment that adds, blocks, or removes hormones. A hormone is a natural chemical made by a gland in the body. Its 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 helps produce sperm, among other functions.

But testosterone also helps prostate cancer 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. This can shrink the tumor or slow tumor growth for a while.

Hormone therapies for prostate cancer include luteinizing hormone-releasing hormone (LHRH) agonists and LHRH antagonists, both of which cause the testicles to stop making testosterone. Most LHRH agonists and LHRH antagonists are injections. They may be given monthly, or 2, 3, or 4 times a year. Relugolix (Orgovyx) is an LHRH antagonist that comes as a tablet taken once a day.

Anti-androgens and androgen synthesis inhibitors are also available as pills and taken 1 to 3 times a day, depending on the medication.

Anti-androgens block prostate cancer cells from using androgens to grow. Androgen synthesis inhibitors prevent the glands—and the cancer itself—from making androgen. See **Guide 2**.

You might hear the term **castration** used when describing prostate cancer or its treatment. This term describes a drastic reduction of testosterone. Castration can be done with hormone-lowering medication or by surgical removal of one or both testicles (orchiectomy).

Although orchiectomy is a surgical procedure, it's still considered hormone therapy because it removes the primary source of testosterone: the testicles. While drug hormone therapy can be reversed when the medication is stopped, orchiectomy is permanent and can't be reversed.

Surgical removal of the testicles is much less common today because androgen deprivation therapy is often just as effective at blocking testosterone. Still, some individuals prefer this one-time procedure over daily medications or periodic injections.

Newer hormone therapies

Hormone therapy is the main treatment for advanced-stage prostate cancer. Therapies that have been used for decades (such as bicalutamide, flutamide, and nilutamide) are occasionally still used for treating prostate cancer. These are often called first-generation anti-androgens.

However, newer hormone therapies are better at delaying the spread of cancer and extending life. These newer drugs include abiraterone, apalutamide, darolutamide, and enzalutamide. You may hear your treatment team refer to these as novel, advanced, or second-generation anti-androgens. One of these newer therapies is often added to another hormone-lowering treatment, and together they're called doublet therapy or intensified therapy.

Side effects of hormone therapy

Hormone therapy can have 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 things.

Guide 2
Hormone therapy drugs for advanced-stage prostate cancer

Anti-androgens block receptors on prostate cancer cells from receiving testosterone.	**Newer anti-androgens:** • Apalutamide (Erleada) • Darolutamide (Nubeqa) • Enzalutamide (Xtandi) **Traditional anti-androgens:** • Bicalutamide (Casodex) • Flutamide (Eulexin) • Nilutamide (Nilandron)
LHRH agonists prevent the release of luteinizing hormone-releasing hormone (LHRH), which causes the testicles to stop making testosterone.	• Goserelin (Zoladex) • Leuprolide (Lupron Depot, Eligard) • Triptorelin (Trelstar)
LHRH antagonists block or stop the pituitary gland (located in the brain) from making LHRH. This causes the testicles to stop making testosterone.	• Degarelix (Firmagon) • Relugolix (Orgovyx)
Androgen synthesis inhibitors block androgen production.	• Abiraterone (Zytiga, Yonsa) • Ketoconazole (Nizoral)

In general, the longer you're on hormone therapy, the greater your risk for side effects.

These can include tiredness (fatigue), hot flashes, mood changes, weight gain, changes in penis length and testicle size, tenderness and growth of your breasts, and loss of muscle mass.

Sexual side effects – The sexual side effects of hormone therapy can be a significant cause of stress. Hormone therapy may lower your desire for sex, cause erectile dysfunction, and reduce the size of the penis and testicles.

Erectile dysfunction means having difficulty or being unable to have an erection of the penis. Erectile dysfunction medicines (such as Viagra and Cialis) aren't as effective for individuals on hormone therapy. These drugs don't restore the loss of sexual desire caused by lower androgen levels.

However, some treatments that may improve erectile function include injections of medication into the penis, vacuum constriction devices (penis pump), or surgical implants that produce an erection.

Your sex drive and your ability to have an erection may gradually return after stopping hormone therapy, though the process may take up to a year or more. Some individuals never regain full ability to have an erection.

Erectile dysfunction is a leading cause of depression in people with prostate cancer. Ask your care team about therapy or counseling if you're having problems due to erectile dysfunction or symptoms of depression. Help is available.

TIP

Regular exercise can lessen the symptoms and side effects of hormone therapy, including:

- Weight gain
- Fatigue
- Loss of bone and muscle mass

Physical activity can also improve your general health and make you feel better. Ask your care team to recommend an exercise program for you.

Loss of sex drive, erectile dysfunction, and other sexual side effects usually go away after you stop hormone therapy. In the meantime, consider talking to your partner and/or a therapist to help you deal with any problems you're having. You're not alone—emotional support is an important part of cancer care.

Bone thinning and fractures – Thinning and weakening of your bones (osteoporosis) and bone fractures can also happen. When you start ADT, you'll have a test to measure your bone density. If your bone density is low, your care team can recommend medications to strengthen your bones. Taking daily calcium and vitamin D can also help keep your bones strong while you're on ADT.

Diabetes and heart disease – Hormone therapy also increases the risk for diabetes and cardiovascular disease. If you already have either of these conditions, hormone therapy can cause them to get worse. Hormone therapy may also increase the risk for death from heart issues. Be sure to talk to your care team about your personal risk.

Testosterone flare – LHRH agonists can cause a surge in testosterone for a few weeks before dropping to an undetectable 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 an anti-androgen medicine to prevent testosterone flare.

Talk to your care team about how to manage the side effects of hormone therapy. They have ways to lessen or soothe most of these problems. Bones can be strengthened with medicine as well as with physical activity. Exercise and eating a healthy diet can also help with fatigue, mood, and maintaining a healthy weight.

Hormone therapy resistance

Hormone therapy can be very effective at shrinking or slowing the growth of your prostate cancer. But for patients with metastatic prostate cancer, hormone therapy can lose this effect over time, even when their testosterone is at a very low level.

Why? Because the cancer eventually learns how to survive without using much testosterone, which makes hormone therapy less effective. In other words, the cancer can resist the hormone therapy. So this is called hormone-resistant prostate cancer (also called castration-resistant prostate cancer).

> **“Now more than ever, those living with cancer are living better, longer lives thanks to the power of research and advancements in treatment.”**

It’s important to know that prostate cancer that’s resistant to hormone therapy is still treatable. So if you develop hormone-resistant prostate cancer, you’ll stay on ADT to keep your testosterone at a low level.

Other hormone-reducing drugs are also still used to treat hormone-resistant prostate cancer. These hormone therapies are often combined with non-hormone treatments like chemotherapy, targeted therapy, or immunotherapy to help get better results.

Non-hormone therapy

Hormone therapy may be the first treatment recommended for advanced prostate cancer, but it’s not the only one. Other treatments that don’t use hormones can also slow cancer growth, prevent cancer symptoms, and prolong life.

If you’re given non-hormone therapy, you’ll also stay on ADT to make sure your testosterone remains at the lowest possible level. See **Guide 3**.

Chemotherapy

Chemotherapy damages rapidly dividing cells throughout the body. Cancer cells divide and multiply rapidly, which makes them a good target for chemotherapy.

But chemotherapy can harm healthy cells, too. Harm to healthy cells is what causes side effects. Because chemotherapy can be a tough treatment to go through, it's recommended only for those who can physically tolerate it.

Guide 3
Non-hormone therapies for advanced-stage prostate cancer

Type of therapy	Generic name	Brand name	Drug form
Chemotherapies	Docetaxel	Taxotere	Infusion into a vein
	Cabazitaxel	Jevtana	
	Carboplatin	Paraplatin	
	Cisplatin	Platinol	
	Mitoxantrone	Novantrone	
Immunotherapies	Sipuleucel-T	Provenge	Infusion into a vein
	Pembrolizumab	Keytruda	
Biomarker-targeted therapies	Rucaparib	Rubraca	Tablet
	Olaparib (taken with abiraterone)	Lynparza	
	Niraparib and abiraterone	Akeega	
	Talazoparib (taken with enzalutamide)	Talzenna	Capsule
Radiopharmaceuticals	Lutetium Lu 177 vipivotide tetraxetan	Pluvicto	Infusion into a vein
	Radium-223	Xofigo	
Bone-targeted therapies	Denosumab	Prolia, Xgeva	Injection
	Zoledronic acid	Zometa	Infusion into a vein
	Alendronate	Fosamax	Tablet

Despite the side effects, chemotherapy can help people with metastatic prostate cancer live significantly longer.

Chemotherapy for prostate cancer is a liquid medicine given by intravenous infusion. This means that it's slowly injected into a vein for up to an hour. It's given every 3 weeks for a total of 6 to 10 times (cycles), along with a daily steroid.

Common chemotherapy medicines for prostate cancer include docetaxel and others.

Docetaxel

Docetaxel (Taxotere) is the chemotherapy medicine used most often to treat people with advanced prostate cancer. Although docetaxel can't cure prostate cancer, it can help people live longer while reducing pain and other symptoms. Docetaxel is an option for some people taking ADT for the first time. Docetaxel is also used to treat metastases if ADT fails to stop cancer growth.

Cabazitaxel

Cabazitaxel (Jevtana) 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.

Carboplatin and cisplatin

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

Mitoxantrone

Mitoxantrone (Novantrone) is used to relieve pain and decrease the need for pain medications. It's an option if you aren't able to tolerate other therapies.

Immunotherapy

The immune system is the body's natural defense against infection and disease. Immunotherapy boosts the ability of your immune system to find and destroy cancer cells. Immunotherapy is usually given by itself for treating prostate cancer.

Immunotherapy drugs include sipuleucel-T and pembrolizumab.

Sipuleucel-T

Sipuleucel-T (Provenge) is intended for those with hormone-resistant metastatic prostate cancer who have few or no symptoms.

Sipuleucel-T 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 (Keytruda) is a type of immunotherapy called an immune checkpoint inhibitor.

For a small percentage of people whose prostate cancer is due to specific genetic mutations, pembrolizumab can restore the immune system's ability to detect and destroy cancer cells.

Biomarker-targeted therapy

This treatment targets specific genetic changes—germline (inherited) or somatic (acquired) mutations—that are found through biomarker testing.

Biomarker-targeted therapies are useful only in people whose prostate cancer is due to such genetic changes. This includes mutations in *BRCA1*, *BRCA2*, and other genes that repair damaged DNA. About 1 in 4 people with metastatic hormone-resistant prostate cancer have this kind of genetic mutation.

Biomarker-targeted therapies (also known as PARP inhibitors) for advanced prostate cancer include rucaparib (Rubraca), olaparib (Lynparza), niraparib and abiraterone (Akeega), and talazoparib (Talzenna).

Because genetic mutations differ between people, a treatment that helps one person may not help another.

Radiopharmaceuticals

A radiopharmaceutical is a medicine that contains a radioactive substance. This 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.

Radiopharmaceutical drugs include lutetium Lu 177 vipivotide tetraxetan and radium-223.

Lutetium Lu 177 vipivotide tetraxetan

Lutetium Lu 177 vipivotide tetraxetan (Pluvicto) is a targeted radiopharmaceutical that looks for a particular protein (prostate-specific membrane antigen, PSMA) on the surface of prostate cancer cells anywhere in the body. When the drug finds PSMA, it attaches itself to the cancer cells and implants a small amount of its radioactive substance in them. The cancer cells absorb the radiation from the drug and die.

Lutetium Lu 177 vipivotide tetraxetan is an intravenous infusion given once every 6 weeks for up to 6 doses. You'll need a PSMA-PET scan to find out if this treatment may work for you.

Radium-223

Radium-223 (Xofigo) is used to treat prostate cancer that has metastasized in bone but hasn't spread to other organs.

Radium-223 is an injection given once a month for 6 months. It collects in bones and gives off radiation that can kill prostate cancer cells there. You'll need to have blood tests before each dose. A bone-targeting therapy, either denosumab or zoledronic acid, is often given with radium-223.

Radium-223 is also used to reduce pain from bone metastases.

Radiation therapy

Radiation therapy uses high-energy rays to kill cancer cells and shrink tumors. Radiation therapy is given in regular doses over a certain period of time.

External beam radiation therapy (EBRT) is the type of radiation used for prostate cancer.

EBRT uses a machine that aims radiation precisely at cancer inside of the body while trying to avoid healthy tissue. This technique delivers higher doses of radiation more safely.

For metastatic prostate cancer, radiation therapy is often used for cancer that returns after initial treatment (recurrence). Radiation therapy is also used as palliative treatment to relieve the pain of bone metastases.

Some of the possible side effects of radiation therapy for prostate cancer are urinary and bowel problems, erectile dysfunction, and fatigue.

Radiation for metastases

Another way to use radiation is emerging. It's called metastasis-directed therapy. This is radiation therapy that targets metastases to improve overall cancer control.

Metastasis-directed radiation therapy is used for advanced prostate cancer when just a few (up to 5 or so) metastatic tumors are detected in only a few locations in the body. These metastases are typically located in the lymph nodes or bones, or sometimes in organs like the liver and lungs.

Cancer in the prostate itself can also be a target if it hasn't been treated yet.

Metastasis-directed radiation therapy only treats a few specific areas of the body where imaging scans have found metastases. It isn't meant to treat metastatic cancer that's widespread. Compare this to drug treatments like immunotherapy or chemotherapy, which affect metastases throughout the whole body.

The goals of metastasis-directed therapy are:

- To reduce or delay the development of new metastases
- To put off the need for more aggressive treatment
- To give you more time to live

In many cases, ADT hormone therapy and one of the newer (next-generation) hormone therapies are given along with metastasis-directed radiation therapy to improve results.

Everyone with cancer can ask for and should be given information about clinical trials.

Knowing all of your options means not missing out on clinical trial opportunities for promising new treatments.



Clinical trials

Another way to receive treatment for metastatic prostate cancer may be through a clinical trial.

A clinical trial is a type of medical research study. After being developed and tested in a lab, 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. FDA.

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

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

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the safety and benefit of an FDA-approved treatment.



Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Without clinical trials, our treatment wouldn't change. It would always remain the same. Some people refer to clinical trials as receiving tomorrow's best treatment today."

Informed consent

Clinical trials are managed by a research team. This group of experts 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 people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by insurance.

Supportive care

Supportive care (also called palliative care) treats cancer symptoms, the side effects of cancer treatment, and other related health issues.

Supportive care is available at any stage of cancer, not just at the end of life. In fact, people who start supportive care when they begin treatment tend to have better quality of life and potentially improved outcomes.

Bone-targeted therapy

Supportive care may be especially useful for people with bone metastases. Prostate cancer that metastasizes to bones can cause severe pain, fractures (breaks) in bones, bone loss (osteoporosis), and squeezing (compression) of the spinal cord.

Some treatments for prostate cancer, like hormone therapy, can also cause osteoporosis and increase your risk for fractures.

Medicines that target bones can help to relieve bone pain and reduce the risk for bone problems. Some medicines work by slowing or stopping one breakdown, while others help increase bone thickness. Drugs include Prolia (denosumab), Xgeva (denosumab), Zometa (zoledronic acid), and Fosamax (alendronate).

For more information, see *Chapter 7: Supportive care and other assistance*.

Your treatment goals

Everyone's cancer and life situation are different. Here's a step-by-step self-assessment to help you think about what matters most to you, so you can talk with your doctors and care team about your goals for treatment.

Step 1: Understanding shared decision-making

Your doctor is the expert on prostate cancer and its treatments. You are the expert on **you**—your body, values, and life priorities. Working together with your doctors and care team helps create a plan that fits both your medical needs and your personal goals. This is called shared decision-making.

Step 2: What matters most to you?

Below are examples of common treatment goals. Check (✓) any that are important to you or add your own in the blank spaces.

Step 3: Questions to ask your care team

Use the questions at the end of each chapter of this guide to begin conversations with your doctors and care team.

Step 4: Review and revisit your goals

Your goals may change over time as your treatment and life circumstances evolve. Revisit this self-assessment regularly and share updates with your care team.

Your health and treatment goals

- ☐ Live as long and as well as possible
- ☐ Prevent or control symptoms such as pain, fatigue, and urinary difficulties
- ☐ Prevent or delay further growth or spread of the cancer
- ☐ Keep treatment side effects manageable

Your quality of life goals

- ☐ Maintain my daily activities
- ☐ Spend quality time with my family and friends
- ☐ Manage the financial cost of treatment
- ☐ Keep my independence and mobility
- ☐ Retain the ability to have an erection
- ☐ Take care of my emotional and mental well-being
- ☐ Feel informed and involved in every treatment decision

Add your other personal goals or concerns

- ☐ _____
- ☐ _____
- ☐ _____

Key points

- Testosterone helps prostate cancer grow.
- Hormone therapy treats prostate cancer by stopping testosterone from being made or by blocking cancer cells from using testosterone.
- Hormone therapy can eventually lose its effectiveness against prostate cancer. This is called hormone-resistant prostate cancer.
- Hormone therapy is often combined with one or more other therapies, which can be more effective together at slowing or shrinking advanced prostate cancer.
- Other treatments used with hormone therapy for advanced prostate cancer include chemotherapy, immunotherapy, target therapy, radiopharmaceuticals, and radiation therapy.
- Hormone therapy can cause a number of possible side effects. But treatment and therapy are available.
- Supportive care relieves the symptoms caused by cancer and the side effects caused by its treatment. Everyone with advanced-stage prostate cancer should be offered supportive care.

Questions to ask

- Does any option offer a cure or long-term cancer control?
- How do my age, race, overall health, and other factors affect my treatment options?
- What symptoms and side effects should I report right away, and who should I contact?
- Will treatment affect my ability to urinate? Or have an erection?
- Will you stop or change my treatment if there are serious side effects?

What's next?

This chapter described the available treatment options for advanced-stage prostate cancer, which includes both regional and metastatic prostate cancer.

If you've been diagnosed with regional prostate cancer, turn to the next chapter to read about the typical therapies included in your treatment plan.

If you've been diagnosed with metastatic prostate cancer, go to *Chapter 6: Metastatic prostate cancer treatment* to read about the common (and uncommon) treatment options for this advanced-stage cancer.

5

Regional prostate cancer treatment

40 About regional prostate cancer

40 Treatment

44 Testing after treatment

45 Treatment for persistence or recurrence

46 Testing after persistence or recurrence

47 Key points

47 Questions to ask

Regional prostate cancer has grown outside of the prostate gland to nearby areas like lymph nodes, but not any farther. It usually requires radiation therapy or prostate surgery and hormone therapy.

About regional prostate cancer

Regional prostate cancer is cancer that has spread from the prostate gland to neighboring tissue, such as nearby lymph nodes, the bladder, or the rectum. But it hasn't spread any farther. (To read about prostate cancer that **has spread** to distant lymph nodes, bones, or organs, turn to *Chapter 6: Metastatic prostate cancer treatment*.) Regional prostate cancer is also sometimes called locally advanced prostate cancer.

Treatment

The key concern about prostate cancer that spreads just outside of the prostate is that it could continue to spread farther (metastasize) to other areas of the body. As a result, treatment for regional prostate cancer is more aggressive than treatment for early-stage prostate cancer.

Treatment takes aim at cancer in the prostate itself as well as cancer outside of the prostate. So it often includes both treatment directed at the prostate (radiation therapy or prostate surgery) and drug therapy (hormone therapy) that has effects throughout the body.

Treatment options are also based on life expectancy and symptoms. The longer a person's life expectancy and the more symptoms they have, the more aggressive their treatment will be. See **Guide 4**.

Life expectancy

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

It's important to know that life expectancy—when used for cancer care—is an estimate based on large numbers of people. That means life expectancy can be applied to a certain population or age range, but it's not as easy to make a precise estimate of the lifespan of an individual person.



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Life expectancy: More than 5 years or you have symptoms

If your life expectancy estimate is more than 5 years or you have symptoms, treatment options include:

Radiation and hormone therapy

External beam radiation therapy (EBRT) along with long-term (2 years) hormone therapy plus abiraterone (Zytiga, an androgen synthesis inhibitor) is the preferred initial treatment for people who have regional prostate cancer and a longer life expectancy or symptoms. Preferred treatments have the most evidence that they may work better and be safer than other therapies.

EBRT treats cancer in the prostate as well as in regional lymph nodes, while long-term hormone therapy lowers testosterone to a minimal level to prevent the cancer from getting worse.

Another option for initial treatment is radiation therapy plus long-term (2 to 3 years) hormone therapy without the addition of abiraterone. This may be an option for someone who can't take abiraterone due to other health conditions.

Hormone therapy with or without abiraterone

Androgen deprivation therapy (ADT) on its own is an option for people with regional prostate cancer who have other significant or life-threatening health problems.

Guide 4
Regional prostate cancer: Initial therapy options

Life expectancy estimate	Initial treatment
More than 5 years or you have symptoms	Radiation and androgen deprivation therapy (ADT) with Abiraterone (preferred)
	Radiation and ADT
	ADT with Abiraterone
	ADT
	Radical prostatectomy and removal of pelvic lymph nodes
5 years or less and you have no symptoms	Observation
	Radiation therapy
	Radiation and ADT

Abiraterone can be added to ADT, which may help people live longer although it may come with more side effects. You'll take a steroid to reduce these effects.

Prostate surgery

Prostatectomy means removing the prostate gland by surgery. A radical prostatectomy removes not only the entire prostate but also the surrounding tissue and seminal vesicles.

A pelvic lymph node dissection (PLND) is an operation to remove the nearby lymph nodes. A radical prostatectomy with PLND is a treatment option only in certain cases of regional prostate cancer. It's used when:

- The tumor has not grown outside of the prostate.
- The tumor can be removed completely with surgery.
- You have an estimated life expectancy of 10 or more years.
- You have no other serious health conditions.

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

The nerves near your prostate (called cavernous nerves) control the ability to have erections. Surgeons do their best to avoid these nerves when performing a prostatectomy, but damage to the nerves during surgery is sometimes unavoidable.

Possible side effects of radical prostatectomy can include urinary incontinence and erectile dysfunction.

Urinary incontinence (being unable to hold your urine) is usually temporary. Most people gradually recover control of their bladder after a few months or so. Doing exercises to strengthen the pelvic floor can help. If incontinence continues to be a problem, another surgical procedure can be done to improve it.

Erectile dysfunction may slowly improve over several months to 2 years after the surgery. However, you may never regain the same erectile function you once had. Treatment options include pills (like Viagra and Cialis), injections of medication into the penis, vacuum constriction devices (penis pump), and surgical implants that produce an erection.

Erectile dysfunction is a leading cause of depression in people with prostate cancer. Ask your care team about therapy or counseling if you're having any problems due to erectile dysfunction or any symptoms of depression. Help is available.

Additional therapy after prostate surgery

After the surgery, the removed prostate tissue will be tested. If you had pelvic lymph node dissection, the lymph nodes will also be tested. If testing shows adverse (high-risk) features in the tissue (see **Guide 5**) or if cancer has spread to the lymph nodes, you might need additional treatment.

- **No adverse features and no cancer in lymph nodes** – These results mean no additional treatment is needed. Your cancer will be monitored. Monitoring involves periodic PSA tests and sometimes digital rectal exams. If your PSA level begins to rise during monitoring, you may need treatment for PSA recurrence.
- **Adverse features** – If test results find adverse features in prostate tissue but no cancer in the lymph nodes after surgery, the preferred option is being monitored for cancer recurrence. Additional treatment may be another option.
- **Cancer found in lymph nodes** – If your prostate surgery shows that cancer has spread to your lymph nodes but there are no other adverse features, then additional treatment may be your next option. Monitoring is also a reasonable option if your PSA level is undetectable. However, if your PSA level begins to rise during monitoring, you may need treatment for PSA recurrence.

Additional treatment for PSA recurrence is discussed later in this chapter on page 45.

Life expectancy: 5 years or less and you have no symptoms

Treatment is less aggressive for people with regional prostate cancer whose life expectancy estimate is 5 years or less and who have no symptoms.

Observation

Observation is an option for people with a life expectancy of 5 years or less. It's for those with other serious health problems whose prostate cancer isn't causing any symptoms. Observation involves occasional PSA tests and watching for symptoms, which can be treated with pain-relieving (palliative) therapy.

Guide 5
Adverse features that may be found after prostate surgery

If tests show any of these high-risk features after prostate surgery, you may need additional therapy:	Cancer in the normal-looking tissue removed with the tumor (surgical margin)
	Cancer outside of the layer surrounding the prostate
	Cancer in the seminal vesicle(s)

Radiation therapy with or without hormone therapy

If you have no symptoms at this time but you or your doctor feel symptoms are likely to develop, you have the option of radiation therapy or long-term hormone therapy, or both, to prevent symptoms from developing.

Hormone therapy

ADT on its own is an option for people with regional disease, no symptoms, and a life expectancy of 5 years or less. It's used to slow cancer and delay or reduce symptoms. ADT may include an LHRH agonist, an LHRH antagonist, or surgical removal of the testicles.

"My doctor reminded me that stress cannot help me, but it can hurt me! It helped me remember to control those things I could control and relax in front of those that I could not control."

Testing after treatment

After initial treatment, you'll have follow-up tests to find out how well your therapy is working. Periodic prostate-specific antigen (PSA) tests and occasional imaging scans can indicate whether the cancer is under control.

If you've had a radical prostatectomy, all of the cells that make PSA should have been removed by this surgery. So your PSA level should be undetectable by the time you have your first PSA check after surgery. If you had radiation therapy, your PSA should fall steadily and then remain at a low level.

PSA is very low or undetectable

If your PSA is very low after radiation therapy or undetectable after prostate surgery, you'll be monitored for cancer recurrence.

Monitoring involves PSA testing every 6 to 12 months for several years. People with a high risk for recurrence may have PSA testing more often, such as every 3 months. You'll continue to be monitored on an ongoing basis or until new signs or symptoms occur.

PSA is elevated or rising

If your PSA doesn't fall to an undetectable level after prostate surgery, you may still have cancer (persistence). Or if your PSA drops after initial treatment but rises again months or years later, it probably means the cancer has come back (recurrence). In either case, further treatment is available.

Treatment for persistence or recurrence

If you have PSA persistence or recurrence after your initial therapy, your life expectancy estimate will guide what treatment you may have next.

Life expectancy: 5 years or less

If your life expectancy estimate is 5 years or less and you have persistent or recurrent prostate cancer, observation may be a better option than undergoing treatment. Observation involves checking up on your prostate cancer and noting symptoms.

Treatment for symptoms is mainly focused on supportive care. This means easing or stopping the symptoms instead of trying to treat the cancer. This approach helps maintain your quality of life without the burden of unnecessary treatment.

Life expectancy: More than 5 years

Before deciding on any treatment for PSA persistence or recurrence, you'll need some more tests to find out how aggressive the cancer may be.

Tests include PSA doubling time; imaging with whole-body PSMA-PET, CT, or MRI scan with or without a bone scan; and possibly a biopsy. Results of these tests will indicate the best way to manage or treat the prostate cancer.

Treatment for cancer persistence or recurrence is also based on whether your initial treatment for regional prostate cancer was radiation therapy or prostate surgery. See **Guide 6**.

Focal therapies

Focal therapies are treatments that precisely focus energy on cancer cells or small tumors while avoiding nearby healthy organs or tissue.

Focal therapies are designed to be less aggressive than treatments like surgery or radiation therapy. And they might be less likely to cause side effects like erectile dysfunction or urinary incontinence.

But because the energy from focal therapies doesn't travel far or wide, they're only used for regional prostate cancer, particularly in people whose estimated life expectancy is more than 5 years. They're also generally less effective than surgery or radiation therapy, so they're often given together with hormone therapy for a more complete result.

Focal therapies for prostate cancer include:

Cryotherapy – Also known as cryosurgery or cryoablation, cryotherapy destroys cancer cells by freezing them.

High-intensity focused ultrasound – Called HIFU for short, this treatment destroys prostate tumor tissue with heat generated by high-energy ultrasound waves.

Re-irradiation – More radiation—using external beam radiation therapy or internal radiation therapy (called brachytherapy)—aims to reach all of the cancer in the prostate.

Electroporation – This treatment transmits quick zaps of high-voltage electricity to destroy tumor cells.

Testing after persistence or recurrence

After you've been treated for persistent or recurrent regional prostate cancer, you'll continue to have tests and visits to watch for the cancer to return or to treat your existing cancer.

Surveillance is a key part of your follow-up plan. Be sure to continue to go to follow-up visits, have your PSA tested regularly, and stay in touch with your treatment team.

Guide 6
Treatments for regional prostate cancer persistence or recurrence

Initial therapy	Test results	Management options
Radical prostatectomy	Raised PSA, but no other signs of cancer found	• Radiation therapy (preferred) with or without androgen deprivation therapy (ADT) • Monitoring
	Cancer found in pelvic lymph nodes	• Radiation therapy and ADT • Radiation therapy and ADT with Abiraterone
	Cancer has spread to another area of the body (metastasized)	• Advanced treatment required
Radiation therapy	Raised PSA or abnormal digital rectal exam, but no other signs of cancer found or Cancer found only in the prostate or Cancer found in pelvic lymph nodes	• Monitoring • ADT • Radical prostatectomy and removal of pelvic lymph nodes with or without ADT • Cryotherapy with or without ADT • High-intensity focused ultrasound with or without ADT • Re-irradiation with or without ADT • Electroporation with or without ADT
	Cancer has spread to another area of the body (metastasized)	• Advanced treatment required

Key points

- Regional prostate cancer is cancer that has spread from the prostate gland to neighboring tissue, but no farther.
- The main concern about regional prostate cancer is that it could continue to spread to other areas of the body.
- Treatment for regional prostate cancer often includes radiation therapy and hormone therapy or prostate surgery.
- The preferred initial treatment for regional prostate cancer in people with a longer life expectancy or symptoms is external beam radiation therapy (EBRT), long-term androgen deprivation therapy (ADT), and abiraterone.
- Treatment is less aggressive for people with regional prostate cancer whose life expectancy is 5 years or less and who have no symptoms.
- Prostate-specific antigen (PSA) persistence is when your PSA doesn't fall to an undetectable level. This indicates the cancer hasn't gone away.
- PSA recurrence is when your PSA level drops after initial treatment but rises again. This indicates the cancer has come back.

Questions to ask

- How long do I have to decide about treatment? Is there a social worker or someone who can help me decide?
- Will the treatment hurt? How soon will I be able to go back to work?
- When will you know if the treatment is or isn't working?
- What are the chances my cancer will progress or metastasize after treatment?
- Will my choice of treatment now affect my options if the cancer returns in the future?

What's next?

If regional cancer comes back but doesn't spread beyond the pelvis, you can continue to have treatment for persistence/recurrence.

If the cancer comes back but spreads to another area of the body, you'll need advanced treatment. See the next chapter for treatment of metastatic prostate cancer.

6

Metastatic prostate cancer treatment

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

About metastatic prostate cancer

Metastatic prostate cancer is cancer that has spread (metastasized) outside of the prostate gland and beyond the pelvis to other areas of the body.

Areas where prostate cancer tends to spread are:

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

You may already have metastatic cancer when you're first diagnosed. Or your cancer may become metastatic after you've had treatment for early-stage or regional prostate cancer.

Metastatic prostate cancer can be difficult to treat. However, a variety of therapies are available to target the cancer, stop or slow its progress, reduce symptoms, and prolong life.

Main treatment

The main treatment for metastatic prostate cancer is hormone therapy, specifically androgen deprivation therapy (ADT).

The aim of ADT is to reduce androgens (mostly testosterone) to a point where they don't provide fuel for the cancer. This low point is called castration level, which is when there's nearly zero testosterone in the bloodstream.

People whose metastatic prostate cancer is newly diagnosed will begin ADT to get their testosterone down to castration level. People with metastatic prostate cancer who are already being treated with ADT will continue the treatment to keep testosterone at a minimal level.

ADT comes in a few forms. These include:

- LHRH (luteinizing hormone-releasing hormone) **a**gonist with or without an anti-androgen
- LHRH **ant**agonist
- Surgery to remove the testicles

Although ADT is the main therapy for advanced prostate cancer, it's not usually given on its own anymore. Adding 1 or 2 additional therapies to ADT may help you live longer and with fewer symptoms. You may hear this called doublet therapy (ADT with-another therapy) or triplet therapy (ADT with 2 additional therapies).

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

Which additional therapy you'll have depends on several considerations. The first consideration is whether ADT is still effective for you. To put it into medical terms, is your cancer **hormone resistant** or is it **hormone sensitive**?

Hormone-resistant prostate cancer (also called castration-resistant prostate cancer) is cancer that learns how to grow without using testosterone as its fuel. As a result, hormone therapy is no longer as effective against it—most of the cancer becomes **resistant** to ADT.

If you've had ADT but it's no longer working well, read about treatment options for hormone-resistant metastatic prostate cancer starting on page 53.

Hormone-sensitive prostate cancer (also called castration-sensitive prostate cancer) is cancer that's not currently being treated with ADT or has never been treated with ADT. (This doesn't include ADT given as short-term additional therapy, such as hormone therapy given during radiation therapy.)

As a result, this cancer is **sensitive** to hormone therapy. That is, hormone therapy can still treat it.

If this describes your cancer, read the next section about treatment options for hormone-sensitive prostate cancer.

"When you are deciding on your treatment options, remember that even though some decisions need to be made fast, don't rush. Think through your options and get second, or even third, opinions. Have people you can trust to talk through your options, so you feel comfortable in your decisions."



Hormone-sensitive treatment

As its name implies, hormone-sensitive metastatic prostate cancer is treated mainly with hormone therapy.

ADT is considered the first hormone therapy. But a second hormone-reducing therapy is commonly added to ADT for treating advanced prostate cancer. It can prevent your cancer from growing and spreading farther. See **Guide 7**.

Preferred treatments

Preferred treatments have the most evidence they may work better and be safer than other therapies. Preferred treatment options for hormone-sensitive prostate cancer include ADT plus a second hormone-reducing medicine (doublet therapy).

Medical research has shown that people on ADT plus another hormone-reducing medicine tend to live longer than those on ADT alone.

The preferred options for second hormone-reducing medicines are abiraterone, apalutamide, or enzalutamide. Your care team will talk to you about which medicine might work best for you.

If you're prescribed abiraterone, you'll also be given a steroid to help reduce its side effects.

Preferred treatments for hormone-sensitive metastatic prostate cancer also include the following triplet therapy option:

- ADT, and
- chemotherapy (docetaxel), and
- a second hormone-reducing medicine (abiraterone or darolutamide)

Adding a steroid on top of triplet therapy amounts to a lot of medicine. That's why triplet therapy is most often recommended for people who can physically tolerate chemotherapy, hormone therapy, plus other treatment.

Guide 7
Preferred treatment options for metastatic hormone-sensitive prostate cancer

Doublet therapy options	ADT with Abiraterone (Zytiga)		
	ADT with Apalutamide (Erleada)		
	ADT with Enzalutamide (Xtandi)		
Triplet therapy options	ADT with chemotherapy (Docetaxel)	with	Abiraterone (Zytiga)
			Darolutamide (Nubeqa)

Other recommended treatments

Besides preferred treatments, there are other recommended treatments. Other recommended treatments can provide effective results but may have less evidence, more side effects, or may not work quite as well as preferred therapies.

While this guide doesn't include every recommended treatment for hormone-sensitive prostate cancer, your doctor can tell you about all of your options and explain which ones may be best for you, based on your cancer and your overall health.

In some cases, external beam radiation therapy (EBRT) may be combined with ADT, or both may be given together with an androgen receptor pathway inhibitor. In other cases, docetaxel chemotherapy may be combined with ADT and an androgen receptor pathway inhibitor.

Follow-up visits

After treatment, you'll have follow-up tests regularly to see how well the treatment is working and to check for any signs or symptoms that the cancer has returned.

If you have no signs or symptoms, your current treatment may be keeping your cancer under control. Your care team will continue to give you tests. If your situation remains stable, you'll stay on your current treatment unless changes or symptoms begin to occur.

If follow-up tests find that treatment isn't working and your hormone-sensitive prostate cancer is growing or spreading, then you may have developed hormone-resistant prostate cancer. This is discussed next.

Many people with advanced prostate cancer eventually receive several different therapies in the course of their treatment.



Hormone-resistant treatment

Hormone-resistant metastatic prostate cancer keeps growing even when testosterone is at a very low level.

It can do this because some cancer cells learn to adapt and survive without the usual supply of testosterone. Also, the cancer may get some androgens from the adrenal glands, which make a small amount of testosterone. Even the tumor itself can create androgens that help cancer cells grow. As these cells multiply, ADT gradually loses its effectiveness against the cancer.

ADT

To treat hormone-resistant metastatic prostate cancer, your testosterone needs to remain at castration level. So it's still important to have ADT. Your care team may keep you on your same ADT treatment or might ask you to switch to a different medicine.

Besides ADT, your care team will recommend additional treatment. See **Guide 8**. Which treatment you'll receive depends on a few factors. These include:

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

In addition to ADT, treatment options for hormone-resistant prostate cancer include a second hormone therapy, chemotherapy, immunotherapy, biomarker-targeted therapies, or radiopharmaceuticals—or a combination of these treatments.

Guide 8
Preferred treatment options for metastatic hormone-resistant prostate cancer

	Type of therapy	Treatment	When to use
Preferred options	Second hormone therapy	ADT with abiraterone (Zytiga)	If you **have not** been treated with abiraterone, apalutamide, darolutamide, or enzalutamide before
		ADT with enzalutamide (Xtandi)	
	Chemotherapy	ADT with docetaxel (Taxotere)	If you **have not** been treated with docetaxel before
		ADT with cabazitaxel (Jevtana)	If you **have** been treated with docetaxel before

There are also specialized treatments for those with particular features of hormone-resistant prostate cancer. Therapies used in certain cases work best for people with specific cancer features or health circumstances. See **Guide 9**.

Guide 9
Treatments for certain cases of metastatic hormone-resistant prostate cancer

Specific case	Treatment
If you have few or no symptoms and prostate cancer hasn't spread to other internal organs	ADT with sipuleucel-T (Provenge)
If you have a *BRCA* mutation and haven't already been treated with second hormone therapy	ADT with niraparib and abiraterone (Akeega) with prednisone
	ADT with olaparib (Lynparza) with abiraterone (Zytiga) with prednisone
If you have a *BRCA* mutation and were already treated with hormone therapy	ADT with rucaparib (Rubraca)
If you have a DNA-repair gene mutation (*BRCA* or other) and haven't already been treated with second hormone therapy	ADT with talazoparib (Talzenna) with enzalutamide (Xtandi)
If you have a DNA-repair gene mutation (*BRCA* or other) and were already treated with hormone therapy with or without chemotherapy	ADT with olaparib (Lynparza)
If you have aggressive metastatic prostate cancer and Docetaxel isn't a good option	ADT with cabazitaxel (Jevtana) with chemotherapy (carboplatin) with prednisone
If you need pain relief but can't take other therapies	ADT with mitoxantrone (Novantrone) with prednisone
If you have bone metastases that are causing symptoms but have no other metastases	ADT with radium-223 (Xofigo)
If your prostate cancer produces PSMA and you already received hormone therapy	ADT with lutetium Lu 177 vipivotide tetraxetan (Pluvicto)
If you have certain genetic mutations (high microsatellite instability or high tumor mutational burden) and were already treated with hormone therapy with or without chemotherapy	ADT with pembrolizumab (Keytruda)

If you were originally diagnosed with early-stage prostate cancer or hormone-sensitive prostate cancer, then you may have already had ADT and chemotherapy or next-generation hormone therapy. Having had either of these therapies will affect which treatment you'll be given next.

Second hormone therapy

ADT is the first hormone therapy used for treating metastatic prostate cancer. If prostate cancer becomes hormone resistant, then a second hormone therapy is commonly added. A second hormone therapy may be able to slow down the cancer or keep it from spreading farther.

The preferred second therapy options include newer (next-generation) hormone therapies:

- Abiraterone (Zytiga)
- Enzalutamide (Xtandi)

Other second hormone therapy

If the preferred second hormone therapies don't slow down your cancer, there are other recommended hormone-reducing options:

- Adding one of the early-generation anti-androgens (nilutamide, flutamide, or bicalutamide) may be effective if newer hormone therapies aren't an option due to cost or availability.
- Stopping an anti-androgen may also be effective. Sometimes stopping the drug causes the opposite effect: It lowers PSA levels in some people.
- A corticosteroid (hydrocortisone, prednisone, or dexamethasone) can be a hormone-reducing therapy itself when used in addition to ADT.
- Ketoconazole (Nizoral) is a pill that's occasionally prescribed when second hormone therapy or chemotherapy can't be used or isn't available. It's taken with a steroid (hydrocortisone) to reduce side effects such as nausea and vomiting.

Chemotherapy

ADT plus chemotherapy can be the first treatment for metastatic prostate cancer, or it can be given later if other treatments haven't worked 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.

Docetaxel is the preferred option for chemotherapy. Other chemotherapy drugs may be used in certain cases. These include cabazitaxel, cisplatin, carboplatin, and mitoxantrone. You'll also take a steroid (prednisone or dexamethasone) to reduce the side effects of chemotherapy.

Immunotherapy

Immunotherapy drugs boost the body's immune system to fight cancer. However, immunotherapy for prostate cancer is used only for certain individuals.

Immunotherapy drugs include:

- Sipuleucel-T (Provenge) can be used for people whose hormone-resistant metastatic prostate cancer is causing few or no symptoms. These individuals usually have less cancer and a stronger immune system, which allows this immunotherapy to be more effective. Sipuleucel-T is not recommended for those whose prostate cancer has spread to internal organs.
- Pembrolizumab (Keytruda) is recommended only for people whose hormone-resistant metastatic prostate cancer has grown or spread despite having chemotherapy and second hormone therapy. These are patients whose test results show specific genetic changes (defects in DNA called mismatch repair deficiency and high microsatellite instability).

Targeted therapy

Biomarker-targeted therapies are useful only in individuals whose hormone-resistant metastatic prostate cancer is linked with specific genetic mutations. These drugs are called PARP inhibitors because they target PARP—a protein that cells use to repair damaged DNA.

Biomarker-targeted therapies include:

- Olaparib (Lynparza) plus abiraterone and a steroid can be used by people with a *BRCA* mutation before having a second hormone therapy or chemotherapy. Olaparib may also be used by those whose metastatic cancer has grown or spread after a second hormone therapy (abiraterone or enzalutamide) and who have a mutation in a *BRCA* gene or other gene that repairs DNA.
- Rucaparib (Rubraca) can be used by individuals with a *BRCA* mutation whose cancer has already been treated with a second hormone therapy.
- Niraparib and abiraterone (Akeega) plus prednisone is a targeted therapy for people with a *BRCA* mutation. These people should also be on an LHRH agonist or LHRH antagonist, or have had orchiectomy (surgical removal of the testicles).
- Talazoparib (Talzenna), taken with enzalutamide (Xtandi), is another targeted therapy for people with a mutation in a *BRCA* or other DNA-repair gene.

Radiation therapy

In certain cases of metastatic prostate cancer, carefully targeted radiation therapy can be used if there's a small number of metastases in only a few locations in the body. These metastases are typically located in the lymph nodes or bones.

ADT and other hormone treatment are given along with the radiation therapy.

Radiopharmaceuticals

If your initial or other treatments haven't worked well, your care team may suggest a radiopharmaceutical drug.

- Lutetium Lu 177 vipivotide tetraxetan (Pluvicto) isn't used until after a second hormone therapy has been given. You'll need PSMA-PET imaging beforehand to confirm the treatment could work.
- Radium-223 (Xofigo) can be used if prostate cancer has spread mainly to bones but not to internal organs. It should only be used in combination with ADT, not with a second hormone therapy or chemotherapy.

Clinical trial

Participating in a clinical trial is often an option. You can try to join a clinical trial at any time. You don't need to wait until you feel like you have no other options.

Supportive care

Supportive care for people with bone metastases includes:

- **Bone-targeted therapy** – Denosumab or zoledronic acid to help prevent fractures
- **Palliative radiation therapy** – Direct radiation to painful bone tumors or tumors that interfere with bodily functions
- **Other treatments** – Calcium or vitamin D supplements to help prevent fractures

Many people diagnosed with cancer find support groups to be helpful.

A support group provides the opportunity to talk with others who are going through, or have been through, similar experiences.



Follow-up visits

After treatment, you'll have follow-up tests regularly to see how well the treatment is working and if there are any side effects from treatment. Tests include:

- Physical exam with PSA test every 3 to 6 months or more often
- Imaging if cancer symptoms occur
- Imaging as needed to look for cancer growth or spread

No growth or spread

If the cancer doesn't grow or spread, your current treatment may be keeping your cancer under control.

Your provider will continue to give you tests. If your situation remains stable, you'll stay on your current treatment unless changes or symptoms begin to occur.

Growth or spread

If your cancer grows or spreads, your treatment team may suggest you retry a therapy you've had before or try a new and different therapy.

Many people with advanced prostate cancer eventually receive 2, 3, or more different therapies in the course of their treatment.

If possible, consider all of your treatment options. Talk with your team about what you want from treatment. You may ask for a second opinion before you start another therapy. You can explore any clinical trials that are available. And you always have the option to stop therapy.

You'll continue to be offered supportive care.

Key points

- Metastatic prostate cancer has spread outside of the prostate and beyond the pelvis to other areas of the body, such as distant lymph nodes, bones, or organs.
- The first treatment for advanced metastatic prostate cancer is usually androgen deprivation therapy (ADT). Adding another therapy or two to ADT may help you live longer and with fewer symptoms.
- Hormone-sensitive prostate cancer is treated mainly with hormone therapy.
- Hormone-resistant prostate cancer has learned how to grow without using testosterone as its fuel. It's treated with ADT and another type of therapy—often a newer hormone therapy or chemotherapy.
- A second hormone therapy is commonly added to ADT as a preferred treatment option for advanced prostate cancer.
- Prostate cancer and its treatment may cause you to feel frustration, anger, regret, despair, and uncertainty. Know that you can still find happiness after diagnosis and treatment.

Questions to ask

- Will hormone therapy still work for me if I was treated with it already?
- If one type of hormone therapy doesn't work for me, what other treatments are available?
- What treatments can control my cancer and reduce my bone pain?
- If cancer comes back after a few years, what treatment should I have then?
- Should I consider a clinical trial, and can you help me find one?

What's next?

Surveillance is a key part of your follow-up plan. Be sure to continue to go to follow-up visits and stay in touch with your treatment team.

It's common to feel frustration, anger, regret, despair, and uncertainty—even all at the same time. Know that you can have prostate cancer and still find happiness after diagnosis and treatment.

Try to enjoy life as much as possible. Talk with family or friends. Join a support group to learn how other people are dealing with their cancer. Or talk to your doctor or another member of your care team. They can point you to professionals who can help you deal with these feelings and guide you toward your next steps.

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Supportive care and other assistance

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Supportive care addresses the symptoms and side effects of prostate cancer, as well as psychological, social, financial, and spiritual issues. Many resources are available to help you feel better and answer your questions.

The main concern for most people with cancer is to find treatment that works.

Having cancer is about more than just treatment, though. People with cancer face many additional physical and emotional challenges. It's important to know that you can get support for these challenges.

Supportive care

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment. Supportive care is for everyone with cancer and their families, not just for those at the end of life. It's also known as palliative care.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advance care and end of life

"Report any unusual feelings of sadness, loss of interest in activities, anxiety, and sleep problems to your doctor. Many people experience these feelings, and they should not go untreated."



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

Some medical centers have patient navigators or other staff members who coordinate non-clinical supportive care. Ask questions and reach out if you need more information about supportive care.

Anxiety and depression

Many people with prostate cancer have symptoms of distress, such as anxiety and depression. You may feel anxious during testing, or you may experience depression during a hard part of treatment or because your life is not the same as it was before cancer. Tell your treatment team if you're experiencing these symptoms so you can get help.

Help can include support groups, talk therapy, or medication. At your cancer center, patient navigators, social workers, and other experts can help. Some people also feel better by exercising, talking with loved ones, or relaxing.

Support groups

Many people diagnosed with cancer find support groups to be helpful. A support group provides the opportunity to talk with others who are going through, or have been through, similar experiences.

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, look at the online resources listed on pages 69–70 of this guide.

Read more about the types of support you may receive in *NCCN Guidelines for Patients: Palliative Care*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Financial concerns

The financial cost of prostate cancer can be overwhelming. As a result, many people with prostate cancer and their loved ones struggle with the cost of treatment, as well as the stress of paying for it.

To make things worse, you may miss work during treatment or become unemployed. Or you may have trouble paying for or getting medicines. Or you may have too little or no health insurance.

If you struggle to pay for food, housing, treatment, follow-up care, and other expenses, or you have difficulty getting to appointments, talk with your care team's social worker, patient navigator, and hospital financial services staff. They may be able to help you find financial support and transportation options.

You can also talk to your treatment team about work, health insurance, or money problems. Your team can include information in your treatment plan to help you manage your finances and medical costs.

Be heart healthy

People with prostate cancer are also at risk for heart disease and cardiovascular events like heart attack and stroke.

This increased risk is mainly due to the cardiovascular side effects from androgen deprivation therapy (ADT) and newer (next-generation) hormone therapies.

But many factors contribute to heart disease, not just cancer treatments. Learn the ABCDEs of heart health to reduce your risks:

A is for Awareness. Be aware of the risks for heart disease, such as family history, age, race diabetes, and kidney disease—as well as the other factors in this list. **A is also for Alcohol.** Drink alcohol sparingly or, better yet, not at all.

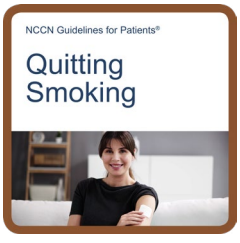
B is for Blood pressure. High blood pressure has no symptoms but it's a key risk factor for heart disease. Have your blood pressure checked often.

C is for Cholesterol. Too much cholesterol in your body builds up in the arteries and the heart. Changing your diet and taking medicine can lower your cholesterol. **C is also for Cigarettes.** Smoking causes numerous health risks, and not just to the heart. Ask for help to quit smoking.

D is for Diet. Eat a heart healthy diet that includes a lot of fruits and vegetables. Obesity is also a risk factor for cardiovascular disease (CVD). Cut back on carbohydrates, saturated fats, sugar, and salt. **D is also for Diabetes.** Adults with diabetes have a higher risk for heart disease.

E is for Exercise. Not getting enough physical activity can increase the risks for obesity, high blood pressure, high cholesterol, and diabetes—all of which contribute to heart disease. Regular exercise, even mild physical activity, can lower your risk for heart disease, increase bone density, reduce fatigue, and improve your mood.

More information can be found in the *NCCN Guidelines for Patients: Quitting Smoking*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



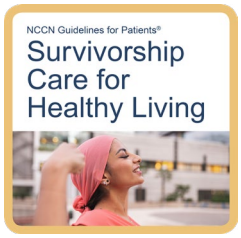
If your doctors and care providers don't talk about how to pay for treatment, it's okay for you to ask them about it first.

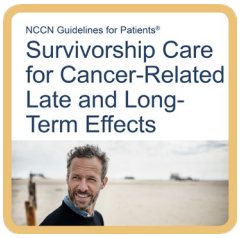
Survivorship

Survivorship focuses on the health and well-being 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 and on the NCCN Patient Guides for Cancer app.







Things to think about when making treatment decisions

Be sure to weigh all your options. There are no "correct" answers.
The right decision is the one that's best for you. Consider:

Your personal preferences	vs.	Your health care providers' recommendations
Having definitive treatment	vs.	Keeping other treatment options open
Length of life	vs.	Quality of life
Traveling for treatment	vs.	Staying close to home and family
Having more treatment	vs.	Having more side effects
Having standard treatment now, which is covered by your health plan	vs.	Waiting for specialized treatment, which requires your health plan's approval

Advance care planning

When cancer is diagnosed at an advanced stage or keeps progressing despite all treatment efforts, it may be time to consider what lies ahead. Even when cancers are curable, talking about future scenarios should begin when you start treatment.

This exploration of what's important to you is called advance care planning.

Advance care planning is for everyone, not just for people who are very sick. Advance care planning means deciding what care you would want if you become unable to make medical decisions for yourself.

The focus is on you receiving the best possible care at the end of your life and making sure that your wishes are understood and respected. People with incurable cancer can set up an advance care plan early to help them feel less stressed and better able to cope with their condition.

The advance care planning process starts with an open and honest discussion with your care team about your prognosis—what you may experience in the coming months—and the medications or therapies that may give you the best quality 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 their usual activities.

This discussion should include important people in your life such as your spouse or partner and family members or friends who are likely to be with you at the end.

Make your wishes clear. It's important that everyone clearly understands the goals of your care and your personal wishes about what should—and should not—be done. You can decide if there is a point where you might want to stop cancer treatment. You can also decide what treatments you would want for symptom relief.

Once you've made these decisions, you'll fill out a legal document that explains what you want to be done if you aren't able to tell your care team yourself. This document is called an advance directive. Your health care providers are required to follow the instructions in an advance directive when you're too ill to make decisions about your care.

Tell your care team and family about your advance directive and its contents. Give a copy of your advance directive to all of your doctors. Make sure you give a copy to anyone you've authorized to make decisions on your behalf (health care proxy).

If your family or loved ones disagree with your plan, speak to your care team. Sometimes they or other specialists can help you and your family navigate these difficult conversations.

You can change your advance care plan at any time. Frequent conversations with your care team can help.

End-of-life considerations

End-of-life care provides medical, psychological, and spiritual support for people who are close to the end of life as well as the people who love them. The goal is comfort, not cure. It may also be called comfort care or hospice.

Note that hospice is a special kind of end-of-life care. Hospice refers specifically to an insurance benefit for people whose life expectancy is 6 months or less. Hospice supports those at the end of life by bringing in additional care providers and resources, such as home care.

The goal of end-of-life care is to give people the best life possible with the time they have left. Care can be provided in your home, a hospice facility, or even in the hospital. A major goal is to keep you pain-free and make sure that you can leave this world comfortably and with dignity.

Hospice doctors, nurses, social workers, and chaplains are experts in helping people work through the spiritual and emotional challenges of coping with the end of life.

Providing support for family members is a key part of hospice care. Most programs offer counseling and support groups for family members, including support after the person has died. This is referred to as bereavement. It can be very comforting to know that your loved ones will have that kind of support after you're gone.

"Be your own advocate. Talk to someone who has gone through the same thing as you. Ask a lot of questions, even the ones you are afraid to ask. You have to protect yourself and ensure you make the best decisions for you and get the best care for your particular situation."

Key points

- Supportive care is for relieving symptoms and side effects, and for other health issues related to cancer.
- Supportive care is given at any stage of disease, not just at the end of life.
- Supportive care is treatment that involves the whole person, not just their cancer.
- Many people with prostate cancer experience anxiety and depression. Help is available.
- A support group provides the opportunity to talk with others who've been through similar experiences.
- For help with financial support and transportation options, talk with your care team's social worker, patient navigator, and hospital financial services staff.
- Advance care planning is done to ensure your end-of-life wishes are understood and respected.

Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What assistance is available for transportation, childcare, and home care?
- Who can tell me what my options for health insurance are and assist me with applying for insurance coverage?
- How much will I have to pay for my treatment? What help is available to pay for medicines and other treatment?
- How can I connect with others and build a support system?



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

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Other resources

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Want to learn more? Here's how you can get additional help.

What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- Help with choosing the right treatment
- Risks for urinary incontinence and sexual side effects
- Getting a second opinion on your test results or treatment plan
- Dealing with fears, anxiety, or hopelessness
- Talking with others who have prostate cancer

What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

Where to get help

Look through the list below and visit the provided websites to learn more about these organizations.

AnCan Foundation
ancan.org

Cancare, Inc.
cancare.org

Cancer*Care*
cancercare.org

Cancer Hope Network
cancerhopenetwork.org

Cancer Survivor Care
cancersurvivorcare.org

FORCE: Facing Our Risk of Cancer Empowered
facingourrisk.org

GRACE
cancergrace.org

Imerman Angels
imermanangels.org

Malecare
malecare.org

My Faulty Gene
myfaultygene.org

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

PAN Foundation
panfoundation.org

Prostate Conditions Education Council (PCEC)
prostateconditions.org

Prostate Health Education Network (PHEN)
prostatehealthed.org

Triage Cancer
triagecancer.org

ZERO Prostate Cancer
zerocancer.org

Questions to ask

- Are you suggesting options other than what NCCN recommends? If yes, why?
- Will I need PSA tests, digital rectal exams, and biopsies for the rest of my life?
- What will happen if I do nothing?
- If I have an inherited risk for prostate cancer, does that mean my children are going to have cancer, too?
- How do I get a second opinion?



Words to know

advanced-stage prostate cancer
Prostate cancer that has spread beyond the prostate to other areas in the body. This includes regional and metastatic prostate cancer.

androgen deprivation therapy (ADT)
Hormone therapy that stops the body from making testosterone or blocks cancer cells from using testosterone. ADT can be given through drugs or surgery.

anti-androgen
A drug that stops the action of the hormone testosterone.

biomarker
Something found in your body that can be measured to provide information about your health.

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

castration
Surgery that removes the testicles, or drugs that suppress the function of the testicles, to minimize testosterone levels.

computed tomography (CT)
An imaging test that uses x-rays from many angles to make cross-sectional images of the inside of the body.

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

early-stage prostate cancer
Prostate cancer that usually grows slowly and stays within the prostate.

enlarged prostate
An overgrowth of tissue in the prostate that isn't caused by cancer. Also called benign prostatic hyperplasia (BPH).

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

external beam radiation therapy (EBRT)
A treatment in which a machine outside of the body aims radiation precisely at cancer inside of the body.

germline mutation
A genetic change that is passed from a parent to their biological child(ren). Also called a hereditary mutation.

hormone-resistant prostate cancer
Cancer that can grow even when male hormone levels in the body are very low.

hormone-sensitive prostate cancer
Cancer that can be treated with hormone-reducing therapy because it needs male hormones to grow.

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

life expectancy
The number of years a person is estimated to live based on statistics of other people in similar circumstances.

luteinizing hormone-releasing hormone (LHRH) agonist
A drug that stops the testicles from making testosterone.

luteinizing hormone-releasing hormone (LHRH) antagonist
A drug that acts in the brain to stop the testicles from making testosterone.

lymphatic system
A network of organs and vessels that fights infections and transports a fluid called lymph.

lymph nodes
Small, bean-shaped, disease-fighting structures located throughout the body.

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 site where it started to a new site in the body.

metastatic prostate cancer
Cancer that spreads beyond the prostate to other parts of the body.

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

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

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

pathologist
A doctor who specializes in testing cells and tissue to find disease.

pelvic lymph node dissection (PLND)
An operation that removes lymph nodes in the pelvis.

perineum
The body region between the scrotum and anus.

positron emission tomography (PET)
An imaging test that uses radioactive material to see the shape and function of body parts.

prostate-specific antigen (PSA)
A protein made by the prostate that helps semen transport sperm. PSA is measured in nanograms per milliliter of blood (ng/mL).

prostate-specific membrane antigen (PSMA)
A protein found on the surface of prostate cancer cells and used as a biomarker of these cells.

PSA persistence
When PSA level is still detectable after prostate cancer treatment.

PSA recurrence
When PSA level drops after prostate cancer treatment but then rises again.

radiation therapy
Treatment that uses high-energy rays (radiation) to kill cancer cells and stop them from growing.

radical prostatectomy
An operation that removes the entire prostate as well as surrounding tissue, seminal vesicles, and sometimes nearby lymph nodes.

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

regional prostate cancer
Cancer that has grown from the prostate to neighboring areas, but no farther.

risk factor
Something that increases the chance of getting a disease.

seminal vesicles
Glands that make and store part of the fluid that becomes semen.

somatic mutation
A non-hereditary change in your DNA that occurred after conception. Also called an acquired mutation.

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

supportive care
Health care that supports the physical, emotional, social, and spiritual needs of patients, families, and caregivers. Also called palliative care.

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

testosterone
A hormone that helps male sexual organs to work.

transrectal ultrasound (TRUS)
A type of imaging that uses ultrasound to view the prostate gland, often to help guide a prostate biopsy.

ultrasound
A type of imaging that uses sound waves to take pictures of the inside of the body.

urethra
A tube that carries urine from the bladder to outside of the body through the penis. It also expels semen.

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



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

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer, Version 5.2026. It was adapted, reviewed, and published with help from the following people:

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Mass General Cancer Center
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Durham, North Carolina

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Jacksonville, Florida
Rochester, Minnesota

Memorial Sloan Kettering Cancer Center
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Madison, Wisconsin

UT Southwestern Simmons
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Dallas, Texas

Vanderbilt-Ingram Cancer Center
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Cancer care recommendations from leading experts at the
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