2026–2027

HARVARD MEDICAL SCHOOL

# *Guide to* PROSTATE DISEASES

Essential information for understanding and navigating prostate cancer, benign prostatic hyperplasia, erectile dysfunction, prostatitis, and related conditions

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*2026–2027 Guide to*

# PROSTATE DISEASES

## Contents

**Founder and Editor in Chief Marc B. Garnick, M.D.**

# A message from the editor in chief

Nearly all men develop benign prostatic hyperplasia (BPH) as they get older, and prostate cancer remains the second most common cancer in men (after skin cancer). Despite the prevalence of these conditions, men often feel distressed by symptoms as well as overwhelmed by treatment choices. This *Guide to Prostate Diseases*, updated for 2026-2027, is designed to make coping with prostate disease a little easier by equipping you with the information you need to effectively partner with your doctor.

For nearly two decades, it has been my great privilege to serve as the founding editor in chief of the *Harvard Medical School's Guide to Prostate Diseases*. This latest edition covers advances in the detection, management, and treatment of BPH and prostate cancer, as well as prostatitis and erectile dysfunction. One change from prior editions is the incorporation of important new medical research findings into the body of individual chapters, rather than having such advances described in a separate section.

The landscape of prostate cancer research has transformed dramatically in recent years, with breakthroughs spanning diagnosis and treatment. We highlight new innovations in diagnostic imaging that reveal cancer in its earliest and most treatable stages. Such innovations include PSMA PET scans as well as biparametric magnetic resonance imaging, which can deliver highly accurate diagnostic results in just 10 minutes without the need for intravenous contrast injections.

Treatment advancements covered in this report include the expanding use of radiopharmaceuticals—specialized drugs that kill cancer cells throughout the body with precisely targeted doses of radiation. We also cover new uses for hormonal therapies that block testosterone and its cancer-promoting effects. By using these drugs in sophisticated combinations, doctors are keeping prostate cancer under control for longer and improving quality of life for men with advanced forms of the disease.

Men with BPH will want to take note of our roundtable discussion, which features insights from a panel of experts from Harvard Medical School and its affiliated hospitals into an expanding array of therapies for treating BPH (see page 14).

Wherever you are in your prostate health journey, we hope you find this guide to be an invaluable resource for you and your family members that provides the knowledge necessary to make informed decisions about your health.

Marc B. Garnick, M.D.
Founding Editor in Chief

Editor's note: *For simplicity, we use the term "men" throughout this guide to refer to individuals assigned male at birth; this language does not imply any assumptions about gender identity.*

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# An introduction to the prostate gland

***The what, where, and why of a male-only gland***

How can a gland the size of a walnut cause so much trouble?

One source of problems relates to the prostate's position in a very crowded place in the body. The prostate is located in front of the rectum (the last part of the colon) and just below the bladder, the hollow organ that holds urine before it is excreted out of the body (see Figure 1). Trouble stems from the fact that the prostate wraps around the upper part of the urethra, the slender tube that carries urine from the bladder out of the body through the penis. At birth, a baby boy's prostate gland weighs less than half an ounce, and the gland goes through growth spurts during adolescence and young adulthood. It's normal for the prostate to start growing again when men are in their late 40s and 50s. But when it does, the gland may become so enlarged that it presses on the urethra, preventing urine from flowing freely. That leads to a variety of urinary problems. Other sources of prostate trouble include inflammation and cancer. All of these issues are addressed in detail in the pages of this report.

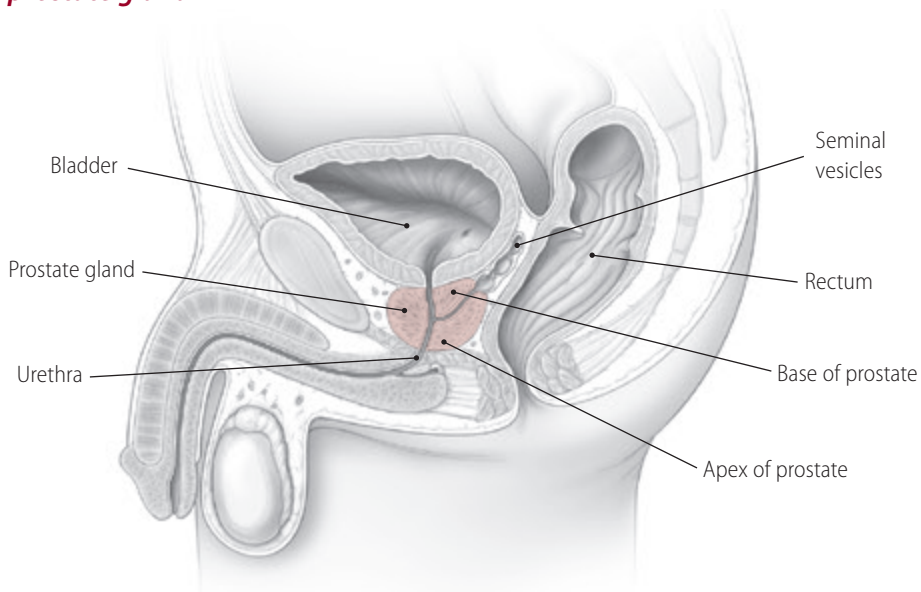
But the prostate performs useful functions as well. While the job of the testicles is to produce sperm, the prostate gland helps supply the semen, the thick, milky fluid that nourishes and protects sperm cells during their travels.

The inside of the gland is made up of an intricate series of ducts lined with cells that produce the prostatic fluid. During ejaculation, the prostate pushes that fluid through the ducts and then into the urethra, where it combines with sperm. Prostatic fluid is alkaline, so it helps sperm survive in the acidic environment of the vagina.

Seminal vesicles—slender glands that sit on either side of the prostate—also contribute

***Figure 1. Locating the prostate gland***

The prostate is located just below the bladder, in front of the rectum, and wraps around the upper part of the urethra. Counterintuitively, the base is located at the top of the gland and the apex at the bottom.



secretions to semen. By volume, their contribution is actually greater than that of the prostate gland.

The prostate is also tied in to the body's infinitely complex system of hormones. To function properly, it requires adequate amounts of certain hormones. These include testosterone (which is produced by the testicles) as well as other hormones that come from the pituitary gland (which hangs off the base of the brain) and from the adrenal glands (which sit on top of the kidneys).

Although the prostate is sometimes depicted as having a simple, round shape, it is actually divided into several lobes—right, left, and a central portion that, when enlarged, is responsible for many symptoms of benign prostatic hyperplasia. It's also tapered at one end. The wider part, called the **base**, is paradoxically located at the top of the gland, next to the bladder. Most prostate cancers develop toward the back of the base.

The tip, or **apex**, is farthest away from the bladder, at the lower portion of the gland. If the prostate were an arrow, it would be pointing down. If the orientation is front and back, then the front is referred to as the anterior of the gland, and the back, the posterior. The area between the base and the apex is referred to as the mid-gland.

These divisions of the gland and the medical terms for them matter when it comes to prostate cancer. Cancers that are located near the base have a propensity to spread to the surrounding tissue, including the seminal vesicles. Cancers in the apex can be difficult to remove surgically, since this location is very close to the muscle that controls urinary continence. Cancer surgery can also threaten two tiny packages of blood vessels and nerves that run along the prostate's surface on each side. Called the neurovascular bundles, they help control a man's ability to have an erection.

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# Inflammation of the prostate (prostatitis)

***Help for an all-too-common condition***

Prostatitis gets little press, but it's a common condition that accounts for nearly two million visits to doctors' offices in the United States each year. Depending on how you define the term, prostatitis (pronounced pros-ta-TIE-tis) affects 9% to 16% of men at some point in their lives. When it comes to age, it's an equal-opportunity disorder: prostatitis affects men of all ages, unlike benign prostatic hyperplasia (BPH) and prostate cancer, which tilt toward an older demographic.

This chapter provides an overview of what leading researchers know about prostatitis, so you can work more effectively with your physician to find a lasting solution.

## What is prostatitis?

The *-itis* suffix means inflammation, so prostatitis means inflammation of the prostate. But doctors use the term to refer to a loose assemblage of inflammatory syndromes characterized by urinary problems such as burning or painful urination, a need to go (urgency), and trouble voiding; difficult or painful ejaculation; and pain in the perineum (the area between the scrotum and the anus) or lower back. Although it causes some of the same symptoms as BPH (see "Lots of LUTS: Symptoms of BPH," page 14) and can occur at the same time, prostatitis is a separate condition that can significantly affect a man's well-being and quality of life.

Some cases of prostatitis are straightforward. They're caused by bacteria that can be easily detected with standard cultures and treated with antibiotics. The associated symptoms include the classic indications of infection—fever, chills, and muscle pain—as well as urinary problems. But bacterial prostatitis occurs infrequently, accounting for just 5% to 10% of prostatitis cases overall.

The remaining 90% to 95% of prostatitis cases are harder to get a handle on. The causes are complicated and may involve several factors. It can be frustratingly difficult, if not impossible, to identify the underlying triggers that cause a man to develop symptoms. Some evidence points to immunological problems. Your immune system might target the prostate and produce inflammatory compounds that irritate the gland, leading to chronic pain.

Cigarette smoking has inflammatory effects that can target the prostate, and symptoms may also be triggered by inflammatory compounds in spicy foods, coffee, and alcoholic beverages that irritate the urinary tract. In this case, simply avoiding these products might help relieve symptoms.

A complicating piece of the puzzle is that chronic prostatitis can go hand-in-hand with psychological problems, such as depression, stress, and anxiety. Indeed, a 2023 study published in *Prostate* found that major depression elevates the risk for prostatitis, even after accounting for other risk factors men might have, such as consuming excess alcohol and smoking. But some evidence also suggests that depression may instead result *from* prostatitis, rather than the other way around. Which of these conditions comes first is still a matter of debate.

Prostatitis can also accompany other chronic pain conditions without an obvious source, such as fibromyalgia, chronic fatigue syndrome, and headaches. These findings suggest that, for some men, holistic treatment strategies focusing on their ability to cope with pain, such as cognitive behavioral therapy, may be especially promising.

Is there a link between prostatitis and prostate cancer? Some evidence suggests repeat biopsies for

prostate cancer can increase the risk for prostatitis. But whether the longstanding inflammation associated with prostatitis increases the risk of prostate cancer over time remains uncertain. Studies have also suggested chronic inflammation could give rise to cancer, but there is no proof of a direct connection. One thing to keep in mind is that prostatitis itself can increase prostate-specific antigen (PSA) levels, so you should not be alarmed if your PSA spikes during a bout of prostatitis. This doesn't necessarily signify cancer. Your PSA level can take months to return to its normal level (see "Prostatitis and PSA," page 10).

Also note that prostatitis is not contagious and can't be sexually transmitted.

## Diagnosing prostatitis

No single test or diagnostic procedure can confirm a case of prostatitis. If you experience urinary discomfort, such as painful or burning urination or pain in the pelvic area, your doctor will start to look for signs of inflammation and infection by performing a digital rectal exam. An inflamed prostate often feels swollen and mushy to the doctor, like an overripe piece of fruit. Pelvic imaging—performed with a computed tomography (CT) scan, ultrasound, or magnetic resonance imaging (MRI)—can in some cases provide additional information to help diagnose your condition.

Your doctor will also have your urine tested to check for bacteria and white blood cells. A common method, called the **two-glass test**, measures the number of white blood cells in urine samples you provide before and again after your doctor performs a prostate massage. (This test must be performed at least 72 hours after the most recent ejaculation, because ejaculation can temporarily increase the white blood cell count in prostatic fluids.) If both bacteria and white blood cells are present in urine, a bacterial infection is probably the cause, and your doctor will likely prescribe antibiotics. More often, though, only white blood cells are discovered—a sign of inflammation but not necessarily a bacterial infection. In that case, the prostatitis is classified as one of the nonbacterial types, which are more difficult to treat.

## Treating prostatitis

Prostatitis is generally divided into four categories, each discussed in the sections below:

- acute bacterial prostatitis
- chronic bacterial prostatitis
- chronic nonbacterial prostatitis/chronic pelvic pain syndrome, which is divided into inflammatory (IIIA) and noninflammatory (IIIB) subtypes
- asymptomatic inflammatory prostatitis.

### Category I: Acute bacterial prostatitis

Acute bacterial prostatitis, which is marked by sudden inflammation of the prostate, is most often caused by bacteria that normally live in the colon. The organisms get on the skin near the anus, multiply there, and then find a way to travel up the urethra and infect the prostate. *Escherichia coli* is the most common culprit, but many different kinds of bacteria can cause acute bacterial prostatitis, particularly among men with compromised immune systems. Recent advances with ultrasensitive DNA technologies make it possible to identify harmful bacteria in a man's urine and prostate secretions much more accurately. These new methods help in the selection of antibiotics that can effectively treat an infection.

The symptoms of acute bacterial prostatitis come on swiftly and include high fever, chills, joint and muscle aches, and profound fatigue. In addition, you may have pain around the base of the penis, behind the scrotum, and in the lower back. Some men experience an uncomfortable feeling of fullness in the rectum. As the prostate becomes more swollen, you may find it difficult to urinate, and the urine stream may dwindle to a trickle. If you can't urinate at all, it's a medical emergency. The prostate may be so swollen and inflamed that it completely blocks urine flow. Depending on the severity of symptoms, hospitalization may be necessary.

The good news is that antibiotics are a highly effective treatment for acute bacterial prostatitis. Typically, doctors start with broad-spectrum antibiotics that target a broad range of different bacteria. One antibiotic, called piperacillin-tazobactam (Zosyn), is reserved for severe cases that require hospitalization. This drug is given intravenously. More often, doctors

**Table 1. Medications to treat prostatitis**

| Medications | Side effects | Comments |
|---|---|---|
| ***Antibiotics*** | | |
| cefixime (Suprax)<br>ceftriaxone* (Rocephin)<br>ciprofloxacin (Cipro)<br>fosfomycin (Monurol)<br>levofloxacin (Levaquin)<br>ofloxacin<br>trimethoprim/sulfamethoxazole (Bactrim, Septra)<br>piperacillin-tazobactam (Zosyn)<br>trimethoprim-sulfamethoxazole (Bactrim)<br>doxycycline | Nausea, vomiting, stomach pain, indigestion, diarrhea, upset stomach, and loss of appetite are most common.<br>In rare cases, fluoroquinolone antibiotics, including ciprofloxacin, levofloxacin, and ofloxacin, can cause permanent and severe side effects affecting the muscles and central nervous system. The drugs carry a small risk of tendinitis and tears in the Achilles tendon and other tendons. Another rare side effect is aortic dissection, or tears in the inner layer of the large blood vessel branching off the heart. The FDA warns against these drugs for people with pre-existing risk factors. Zosyn side effects can include diarrhea and headache. | Used to treat bacterial infection (such as in Category I and Category II prostatitis); may also be tried in newly diagnosed patients with Category IIIA (inflammatory) prostatitis based on the assumption that infection is present (even if it can't be detected in urinary cultures). |
| ***Anticholinergic drugs*** | | |
| oxybutynin chloride<br>tolterodine (Detrol) | Dry mouth, blurred vision, dry eyes or nose, dry skin, upset stomach, stomach pain, and headache are most common. | Reduce urinary urgency or leakage by decreasing bladder contractions. |
| ***Alpha blockers (nonselective)*** | | |
| doxazosin (Cardura)<br>terazosin | Dizziness, headache, and fatigue are most common. Nasal congestion, dry mouth, and swelling in the ankles can also occur. Low blood pressure (hypotension), although rare, may pose a danger for some people. | Relax the muscles at the neck of the bladder, easing the flow of urine; should be used carefully by people with hypertension or heart disease. |
| ***Alpha blockers (selective)*** | | |
| alfuzosin (Uroxatral)<br>silodosin (Rapaflo)<br>tamsulosin (Flomax) | Dizziness, headache, and fatigue are most common. Nasal congestion, dry mouth, and swelling in the ankles can also occur. | Like nonselective alpha blockers, these drugs relax the muscles at the neck of the bladder, easing the flow of urine; however, these do not lower blood pressure. |
| ***PDE5 inhibitor*** | | |
| tadalafil (Cialis) | Flushing, headache, dizziness, nasal congestion, and muscle pain are common but generally dissipate with time. Rarely, allergic reactions occur. | Relaxes smooth muscle at the bladder neck, easing the flow of urine; used to treat severe chronic prostatitis/chronic pelvic pain syndrome in patients with benign prostatic hyperplasia. |

* Generic only.

give oral antibiotics in the fluoroquinolone class, which include ciprofloxacin (Cipro), levofloxacin, and ofloxacin (see Table 1).

### Category II: Chronic bacterial prostatitis

Chronic means lasting a long time, and chronic bacterial prostatitis is exactly what the name suggests: prostatitis caused by a bacterial infection that lingers, usually for several months. It appears to be more common in older men who have BPH. Between 5% and 10% of acute bacterial prostatitis cases become chronic. However, chronic bacterial prostatitis often begins as a subtle, low-grade infection that causes moderate symptoms.

Men with chronic bacterial prostatitis are usually troubled by on-again, off-again urinary symptoms,

such as a sudden urge to go or frequent urination. Some men have low back pain, rectal pain, or a feeling of heaviness behind the scrotum. Others have pain after ejaculation, and the semen may be tinged with blood. As with the urinary symptoms, these symptoms wax and wane, and they are sometimes so mild that men don't notice them.

For the most part, the same types of bacteria that cause acute bacterial prostatitis cause the chronic version of the disease, and the same antibiotics—oral fluoroquinolones—are prescribed (see Table 1, page 9). A four- to six-week course usually does the trick.

However, bacterial resistance against fluoroquinolones is a growing threat, and that's driving a need for alternatives. One possibility is the antibiotic fosfomycin (Monurol), which works by blocking proteins that help build up the bacterial wall and was long used to treat urinary tract infections. Sometimes described as an old and forgotten antibiotic, in recent years it has been revived as a potentially useful alternative for treating infections that are resistant to multiple drugs. A 2025 review published in the *European Journal of Clinical Microbiology and Infectious Diseases* affirmed that fosfomycin can be effective for prostatitis when other drugs stop working, although the authors cautioned that more research is needed to clarify the drug's safety and optimal dosing regimens.

Other alternatives for treating fluoroquinolone-resistant cases include trimethoprim-sulfamethoxazole (Bactrim), which combines two drugs that keep bacteria from making folic acid, a key nutrient they need to grow and survive; and another drug called doxycycline, which is used for a broad range of bacterial infections in different parts of the body.

### Category III: Chronic nonbacterial prostatitis/chronic pelvic pain syndrome

The most common form of prostatitis is called chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS). The symptoms are similar to those of chronic bacterial prostatitis, but there is no evidence of a bacterial infection. The trigger may be stress, an undetectable infectious agent, or physical trauma that causes inflammation or nerve damage in the genitourinary area. Over time, the nervous system may become more sensitive to symptoms.

Some physicians and researchers are beginning to think this condition may affect not just the prostate gland but the entire pelvic floor—all of the muscles, nerves, and tissues that support the bladder, rectum, prostate, and other pelvic organs involved with bowel, bladder, and sexual function. In these cases, the pelvic floor muscles can tighten up and spasm. Targeted physical therapy can provide some relief. However, men with CP/CPPS should avoid performing Kegel exercises, which further tighten muscles near the prostate and can make symptoms worse.

Men with the inflammatory subcategory of this condition have white blood cells in their semen or urine, while men with the noninflammatory subcategory do not. But that distinction makes little difference for how the condition is treated.

Treatments for chronic prostatitis include the following:

- antibiotics for men whose prostatitis is preceded by a urinary tract infection
- nonsteroidal anti-inflammatory pain relievers, such as aspirin and ibuprofen
- anticholinergics to reduce urinary urgency
- alpha blockers to relax smooth muscles in the

#### Prostatitis and PSA

When a man has either the acute or chronic bacterial form of prostatitis, prostate-specific antigen (PSA) may leak from prostate cells into the bloodstream, and a PSA test will show a large increase. A jump in PSA levels can be alarming (see "Prostate-specific antigen test," page 38). But if a man has prostatitis, that condition—not prostate cancer—may very well be the reason for the rise in PSA.

If an increase in PSA is caused by an infection, PSA levels will fall after the infection has cleared, although that may take three to six months. Because PSA levels will be high, you might hold off on prostate cancer screening or having a repeat test until after you're done taking antibiotics.

If you are at high risk for prostate cancer and your PSA seems particularly high even after accounting for the possible effect of prostatitis, your doctor might recommend repeat PSA testing or a biopsy.

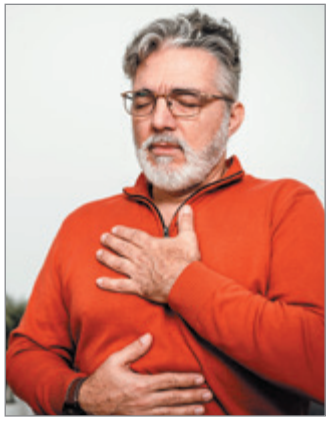
bladder neck and prostate, thus reducing muscle tightness and spasms that can prevent normal urine flow
- PDE5 inhibitors to improve blood flow to the prostate and relax the organ
- acupuncture to control pain pathways and promote the release of the body's own pain-relieving compounds
- low-intensity shock-wave therapy to reduce pain and help restore normal urine flow
- psychological therapy as a stand-alone treatment or as part of a broader treatment plan.

Promising evidence suggests men can benefit from combined treatment with fluoroquinolones and another drug called tadalafil (Cialis), which is ordinarily used for treating erectile dysfunction and BPH. Tadalafil can also be helpful on its own, but because it improves blood flow to pelvic organs, it helps antibiotics penetrate affected tissues and improve the clearance of inflammatory compounds.

Acupuncture has also shown long-lasting benefits. The treatment involves inserting single-use needles into "acupoints" at various locations in the body, then manipulating them manually or with heat or electrical stimulation. Men will ordinarily attend 10 to 20 sessions over the course of several weeks. Clinical trial evidence shows acupuncture can provide symptom improvements lasting up to six months after these treatments are completed.

Just how acupuncture relieves prostatitis symptoms is unclear. It may be that treatments cause the body to release naturally occurring substances, such as enkephalins, endorphins, and dynorphins, which have pain-killing properties. Acupuncture may also have anti-inflammatory effects, and the experience of being treated might have psychological benefits that result in symptom improvement.

Indeed, early evidence suggests that changing negative thought patterns about prostatitis-associated pain can help men feel better. This approach, called cognitive behavioral therapy, involves talking with a therapist who can help you develop practical strategies for coping with the condition. Another promising strategy, called paradoxical relaxation training, works by slowing your breathing rate to about six breaths per minute. This technique, which can be taught by a pelvic pain specialist or urologist who treats the condition, can potentially ease prostatitis pain by relaxing pelvic floor muscles.



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Relaxation techniques, such as breathing exercises, may help ease prostatitis pain.

The UPOINT system is another example that involves taking a holistic approach. Used more commonly outside the United States, it is a treatment framework that stresses the importance of fully understanding which symptoms are troubling a given patient and addressing those symptoms individually. UPOINT stands for the following six areas of common CP/CPPS symptoms: urinary; psychosocial (for example, depression or anxiety); organ-specific; infectious; neurologic/systemic (arising from conditions such as chronic fatigue syndrome); and skeletal muscle tenderness.

If all else fails, your doctor might suggest trying low-intensity shock-wave therapy (LiST), which is commonly used for treating CP/CPPS in Canada and other countries outside of the United States. Also referred to as extracorporeal shock-wave therapy, it relies on handheld devices that deliver acoustic waves (shock waves) noninvasively to damaged tissues to reduce pain and promote healing. A 2023 study published in *Prostate Cancer and Prostatic Diseases* found symptom improvements lasting up to 12 months among men who were not responding to other therapies after they were treated with LiST either once or twice a week over six weeks.

### Category IV: Asymptomatic inflammatory prostatitis

This form of the disease has no symptoms. It is diagnosed when white blood cells are found in prostate secretions or in prostate tissue during an evaluation for other prostate disorders. Given that it creates no problems and has no known cause, doctors do not treat it.

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# Prostate enlargement (benign prostatic hyperplasia)

***Getting this "going"—and "growing"—problem under control***

The normal prostate in men ages 20 to 30 weighs approximately 20 grams—less than an ounce. But from around the time of a man's 50th birthday (sometimes earlier), his prostate begins to grow, often reaching 50 to 100 grams by the time he turns 80. In some men, it grows even more. Weights of over 500 grams have been recorded.

This natural enlargement, called benign prostatic hyperplasia (BPH), obstructs the flow of urine out of the body. It is called benign because it is not cancerous, and hyperplasia is the medical term for an increase in the number of cells in a tissue or an organ. Although BPH does not lead to prostate cancer, the two problems can coexist.

If you live long enough, you will almost certainly experience some degree of BPH, though it doesn't always cause problems. Between 50% and 60% of men with BPH do not develop symptoms and are never bothered by the condition. Others find that BPH can make life miserable, causing lower urinary tract symptoms, or LUTS (see "Lots of LUTS: Symptoms of BPH," page 14), that lead them to seek treatment.

Apart from age, risk factors for BPH include

- abdominal obesity
- diabetes
- high blood pressure (hypertension)
- smoking
- inflammation of the prostate (prostatitis)
- a family history of BPH
- lack of physical activity
- Western dietary patterns (high intake of red meat, refined grains, and sugar).

Some men also have unusually high levels of an enzyme called 5-alpha-reductase 2 that converts testosterone—the male sex hormone—into a byproduct known as dihydrotestosterone (DHT). DHT has strong growth-stimulating effects on the prostate.

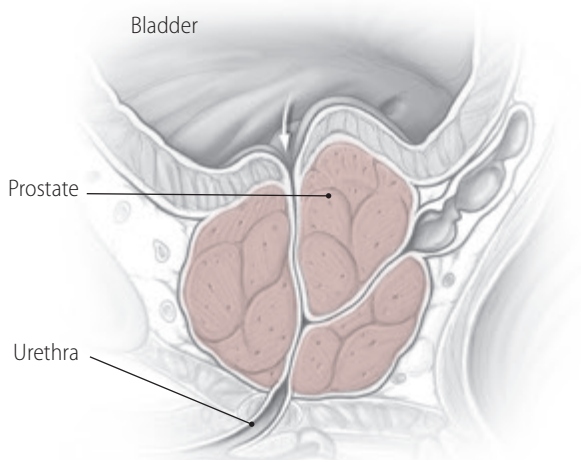
## How BPH progresses

As the prostate enlarges, it starts to press against the urethra and the bladder, like a foot stepping on a garden hose or fingers pinching a straw (see Figure 2, page 13). This pressure eventually obstructs the flow of urine, forcing the bladder to squeeze harder to push urine through the urethra. But straining to urinate only makes matters worse. Like any muscle, the bladder wall becomes thicker with work. That thickness reduces the amount of urine the bladder can hold, causing it to contract even when it contains only small amounts of urine and resulting in more frequent urination.

The narrowing of the urethra and resulting difficulty in emptying the bladder cause many of the problems associated with BPH. You may feel as though you have to urinate immediately, yet strain to do so. You may have a weak urinary stream or one that stops and starts. You may dribble after urinating or feel as if you're not emptying your bladder completely. And you may feel the need to urinate frequently, even every few minutes. At night, the continual need to go to the bathroom can make it impossible to sleep well, causing all sorts of adverse health consequences. Some men also experience urinary incontinence (the involuntary discharge of urine).

Most physicians advise against medical or surgical treatment for men with mild symptoms because the side effects of the treatment outweigh the potential benefits. But if symptoms worsen, ordinary activities may become a challenge. You may find it hard to sit through a lengthy meeting. Aisle seats become a necessity on a flight so there's a quick escape to the bathroom. Many men wear absorbent pads or limit themselves to dark clothing to conceal their incontinence.

***Figure 2. An inside look at BPH***




As the prostate gland enlarges, it constricts the urethra, the tube that carries urine out of the body. This impedes urine flow, so the bladder has to work harder to force stored urine out (see arrow). Over time, the bladder walls thicken, leaving less room for urine.

BPH can also result in some serious complications. If an enlarged prostate keeps your bladder from emptying completely, you may be vulnerable to frequent urinary tract infections. The risk of developing bladder stones increases. A growing prostate can rupture blood vessels in the urethra, causing blood to appear in the urine. (A thorough medical evaluation is necessary any time there's blood in the urine.)

If obstructive BPH goes untreated for too long, muscles in the bladder wall may weaken. Your bladder may become so stretched out that urine cannot adequately empty from the kidneys. BPH can in some cases progress to renal failure, which is a condition that occurs if the kidneys become unable to filter wastes and excess fluids from blood. Your bladder may also not have enough power to push urine past the obstructing prostate gland, a condition known as acute urinary retention. Not being able to urinate at all is painful and a true medical emergency, requiring the temporary passage of a catheter (a thin tube) through the urethra to allow the bladder to drain. Fortunately, such complications are uncommon: most men seek medical attention well before serious problems develop.

## Diagnosing BPH

If you experience symptoms of BPH, see your doctor. Be aware that BPH symptoms can overlap with those of other conditions, such as an overactive bladder. Urinary symptoms that develop and worsen suddenly can also be a warning sign for prostate cancer.

During the exam, expect questions about your urinary flow problems, how long the symptoms have been present, and any prior genitourinary surgery or procedures. You will probably be asked about your health habits and the medications you are taking. For instance, antihistamines can cause urinary symptoms because they affect the muscle in the wall of the bladder.

Your doctor may also ask you to complete a questionnaire, such as the American Urological Association Prostate Symptom Score—also known as the International Prostate Symptom Score in international settings—to help evaluate the severity of your BPH (see "Your urinary symptom score," page 17).

A physical exam and diagnostic workup include a post-void residual urine test, which uses ultrasound to measure the amount of urine left in the bladder after you use the bathroom, a digital rectal examination (DRE) and, if you and your doctor agree, a blood test for prostate-specific antigen (PSA; see "Prostate-specific antigen test," page 38). It also comprises several other laboratory tests, including urinalysis, which allows your doctor to rule out bacterial infections and look for untreated diabetes (another possible cause of frequent urination, particularly at night).

BPH symptoms can often be controlled with medication. You might have to try a few before you find the best fit.

## Treating BPH

Often a man's lifestyle will determine how burdensome he finds BPH. The symptoms that disrupt the daily activities of a man who is conducting business or traveling may not bother another man who spends much of his day at home within easy reach of a bathroom.

When symptoms are not particularly bothersome, you and your doctor may elect to hold off on treatment and instead monitor your BPH with an approach called watchful waiting. To determine if this is the right choice for you, your doctor may ask if your symptoms prevent you from engaging in enjoyable activities. If they do not, then it is safe to just keep an eye on the condition until it becomes bothersome enough to justify treatment. You will probably visit the doctor every year or six months, depending on your symptoms. Follow-up tests will likely include a PSA measurement, as well as a urinalysis to look for blood and any sign of infection. Between visits to the doctor, you'll be encouraged to make simple changes in behavior that can help to ease urinary symptoms (see "Tips for relieving BPH symptoms," page 18).

### Medications approved specifically to treat BPH

Before suggesting surgery, your doctor is likely to recommend medication for BPH (see Table 2, page 15). The FDA has approved three types of drugs for BPH:

- alpha blockers, including alfuzosin (Uroxatral), doxazosin (Cardura), prazosin (Minipress), silodosin (Rapaflo), tamsulosin (Flomax), and terazosin
- 5-alpha-reductase inhibitors, including dutasteride (Avodart) and finasteride (Proscar)
- the PDE5 inhibitor tadalafil (Cialis).

The FDA has also approved Jalyn, a combination of the 5-alpha-reductase inhibitor dutasteride and tamsulosin, an alpha blocker. These drugs work in different ways to alleviate urinary symptoms, and they often work well together.

A good way to think about the difference between alpha blockers and 5-alpha-reductase inhibitors is that alpha blockers target the "going" problem, while 5-alpha-reductase inhibitors target the "growing" problem. Alpha blockers help with the act of urination by relaxing certain muscles in the prostate and bladder. The 5-alpha-reductase inhibitors reduce the encroachment of the prostate on the urethra and the lower part of the bladder by decreasing the size of the prostate.

PDE5 inhibitors are a class of drugs normally used to treat erectile dysfunction, but they also help to relax muscles in the bladder neck (which connects the bladder to the urethra), and some men who take these medications find that their urinary symptoms improve. The PDE5 inhibitor tadalafil is approved for both erectile dysfunction and BPH. When used to treat BPH—with or without erectile dysfunction—the medication is taken at a 2.5- or 5-milligram (mg) dose once daily. (Doses used solely for treating erectile dysfunction can range up to 20 mg.)

*continued on page 16*

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Whether your start BPH treatment right away or postpone it, blood and urine tests can help your doctor monitor your health.

### Lots of LUTS: Symptoms of BPH

The most common symptoms of BPH involve changes or problems with urination. They are often grouped together and referred to as LUTS, which stands for lower urinary tract symptoms. They include

- a hesitant, interrupted, or weak urine stream
- urgency, leaking, or dribbling
- a sense of incomplete emptying
- more frequent urination, especially at night.

Note that while many men with BPH have LUTS, there are other causes of LUTS—meaning not all men with LUTS have BPH.

**Table 2. Medications for BPH**

| Medications | Side effects | Comments |
|---|---|---|
| ***Alpha blockers (nonselective)*** | | |
| doxazosin (Cardura)<br>terazosin (Hytrin, Tezruly) | Dizziness, headache, and fatigue are most common. Nasal congestion, dry mouth, and swelling in the ankles can also occur. Low blood pressure (hypotension), although rare, may pose a danger for some people. Retrograde ejaculation. | Should be used carefully by those with high blood pressure (hypertension) or heart disease. May increase risk of aggressive prostate cancer; important to monitor PSA (see "5-alpha-reductase inhibitors, alpha blockers, and cancer," page 18). |
| ***Alpha blockers (selective)*** | | |
| alfuzosin (Uroxatral)<br>prazosin (Minipress)<br>silodosin (Rapaflo)<br>tamsulosin (Flomax) | Dizziness, headache, and fatigue are most common. Nasal congestion, dry mouth, and swelling in the ankles can also occur. Can cause rash. Retrograde ejaculation. | Have less blood pressure–lowering effects than non-selective alpha blockers. May cause blood pressure to drop suddenly upon standing, causing temporary dizziness. |
| ***5-alpha-reductase inhibitors*** | | |
| dutasteride (Avodart)<br>finasteride (Proscar) | Although uncommon, decreased libido, decreased ejaculate volume, and impotence may occur. (Problems with libido may continue after you stop taking finasteride.) Cardiovascular effects and depression may occur in some men. Breast enlargement or tenderness may occur. Minor reports of rash. New data suggest a heightened risk of osteoporosis. | Help shrink larger prostate glands. Reduce need for surgery. Not beneficial for small prostates. Slow to act; can take up to two years to see full benefits. Can lower PSA levels by 50%. May increase risk of aggressive prostate cancer; important to monitor PSA (see "5-alpha-reductase inhibitors, alpha blockers, and cancer," page 19). In some men, finasteride can lead to problems in sexual function, depression, and other changes in mood. |
| ***Combination therapy*** | | |
| dutasteride and tamsulosin (Jalyn) | Dizziness, headache, and fatigue are most common. Low blood pressure, although rare, may pose a danger for some. | Can lower PSA levels considerably. May increase risk of aggressive prostate cancer; important to monitor PSA. |
| finasteride and tadalafil (Entadfi) | Side effects of both drugs are possible, including impotence, decreased sex drive, decreased ejaculate volume, breast enlargement and tenderness, headache, and indigestion. | Do not take if you are also taking nitrates (commonly used to treat angina), because the combination can cause blood pressure to drop suddenly. Not recommended for longer than 26 weeks because effects after that duration are unknown. |
| ***PDE5 inhibitor*** | | |
| tadalafil (Cialis) | Headache, flushing, upset stomach, and nasal congestion can occur. Temporary disturbances in color vision are possible. In rare cases, may cause priapism (an erection that lasts too long). | Can also treat erectile dysfunction. Do not take more than one pill in 24 hours. To avoid risk of low blood pressure that can cause fainting, do not take if you are also taking alpha blockers or nitrate medications. |
| ***Beta-3 adrenergic agonists*** | | |
| mirabegron (Myrbetriq)<br>vibegron (Gemtesa) | Headache (both drugs); increase in blood pressure and difficulty urinating are uncommon but possible (mirabegron). | Currently the most common types of drugs prescribed for incontinence. |
| ***Antimuscarinics*** | | |
| fesoterodine (Toviaz)<br>oxybutynin (Ditropan)<br>tolderodine (Detrol) | Dry mouth, dilation of pupils and sensitivity to light, increased fluid pressure in the eye, and dry skin may occur. Can increase the risk of urinary tract infections. | Used primarily for treating overactive bladder and urinary urgency. May accelerate existing cognitive decline in the elderly. The risk of side effects likely outweighs the potential for symptom improvements when used for BPH treatment, according to recent evidence.<br>*continued on page 16* |

**Table 2. Medications for benign prostatic hyperplasia** *continued from page 15*

| Medications | Side effects | Comments |
|---|---|---|
| ***Antidiuretic hormone*** | | |
| desmopressin acetate* | Dizziness is the most problematic, potentially leading to falls. Others include nasal discomfort, cold symptoms, increased blood pressure, and back pain. | Can be effective for treating nocturia (nighttime urinary urgency) that may not be resolved by other BPH medications. Available in nasal spray form to limit nighttime urination. Can depress sodium levels in blood. Should not be taken by men with low sodium levels, as excessively low values can lead to dizziness, fainting, and coma in rare instances. Should not be taken by men with heart failure or uncontrolled hypertension. |

*Generic only.

*continued from page 14*

Evidence shows that alpha blockers, 5-alpha-reductase inhibitors, and PDE5 inhibitors are all generally safe and well tolerated for BPH treatment. The following sections explore each type of BPH drug in more detail.

**Alpha blockers.** For men with moderate enlargement of the prostate and moderate urinary problems that are too bothersome not to treat, doctors often first prescribe an alpha blocker. The term "alpha blocker" is shorthand for alpha adrenergic–receptor antagonist, a type of medication that was originally approved to treat high blood pressure. Alpha blockers relax smooth muscle tissue by blocking the receptors that receive chemical signals instructing the tissue to contract. In the prostate, this relaxation of smooth muscle means that the prostate's "grip" on the urethra loosens, allowing urine to flow more freely.

Alpha blockers come in two forms: selective and nonselective. The nonselective ones (doxazosin or terazosin) have stronger blood pressure–lowering effects. Your doctor might recommend one if you have currently untreated (or undertreated) high blood pressure in addition to BPH. In other people, a nonselective alpha blocker could cause an excessive drop in blood pressure and make you faint or feel dizzy, especially when getting up from a chair or out of bed (called orthostatic hypotension). Sudden episodes of low blood pressure can be dangerous for men with vascular disease, placing them at high risk for a heart attack or stroke.

If your blood pressure is normal or low—or if you're already taking another blood pressure medication—your doctor is more apt to prescribe a selective alpha blocker such as alfuzosin, prazosin, silodosin, or tamsulosin. The "selective" nature of these drugs means they concentrate in the prostate, so they don't lower blood pressure significantly. A 2021 study in the *Journal of Urology* found that men taking selective alpha blockers are at slightly less risk of heart failure compared with men taking nonselective alpha blockers.

Other side effects of both selective and nonselective alpha blockers include ankle swelling, nasal stuffiness, and retrograde ejaculation, which is when semen flows back into the bladder rather than out through the urethra. (Although it is considered a sexual side effect of BPH treatment, retrograde ejaculation does not affect the pleasurable sensations of orgasm.) One study found that tamsulosin decreased ejaculate volume in almost 90% of men. Among all the alpha blockers, alfuzosin has the least effects on ejaculatory functioning. While alpha blockers are all reasonably effective at improving urinary symptoms, their side effects vary more from man to man than they do from drug to drug, so there can be a fair amount of trial and error before an individual patient finds the right one. Also, health plans may limit choices or make some medications more expensive than others. All of this means that working with your doctor can be a key component of successful treatment.

# Your urinary symptom score

To evaluate the severity of your benign prostatic hyperplasia, your doctor may ask you to complete a questionnaire like the International Prostate Symptom Score. Choose one number to respond to questions 1 through 7, then calculate your total urinary symptom score. Question 8 indicates how bothered you are by the condition.

Urinary symptom scores of 1–7 indicate mild symptoms. Scores of 8–18 are considered moderate, and scores of 19 or greater are severe. If you have moderate to severe symptoms, and if your answer to question 8 is a 3, 4, or 5, you may want to discuss treatment (either medication or surgery) with your physician.

**1.** Over the past month, how often have you had a sensation of not having emptied your bladder completely after you finished urinating?

0 ◯ Not at all
1 ◯ Less than 1 in 5 times
2 ◯ Less than half the time
3 ◯ About half the time
4 ◯ More than half the time
5 ◯ Almost always

**2.** Over the past month, how often have you had to urinate again less than two hours after you last finished urinating?

0 ◯ Not at all
1 ◯ Less than 1 in 5 times
2 ◯ Less than half the time
3 ◯ About half the time
4 ◯ More than half the time
5 ◯ Almost always

**3.** Over the past month, how often have you stopped and started again several times while urinating?

0 ◯ Not at all
1 ◯ Less than 1 in 5 times
2 ◯ Less than half the time
3 ◯ About half the time
4 ◯ More than half the time
5 ◯ Almost always

**4.** Over the past month, how often have you found it difficult to postpone urination?

0 ◯ Not at all
1 ◯ Less than 1 in 5 times
2 ◯ Less than half the time
3 ◯ About half the time
4 ◯ More than half the time
5 ◯ Almost always

**5.** Over the past month, how often have you had a weak urinary stream?

0 ◯ Not at all
1 ◯ Less than 1 in 5 times
2 ◯ Less than half the time
3 ◯ About half the time
4 ◯ More than half the time
5 ◯ Almost always

**6.** Over the past month, how often have you had to push or strain to begin urination?

0 ◯ Not at all
1 ◯ Less than 1 in 5 times
2 ◯ Less than half the time
3 ◯ About half the time
4 ◯ More than half the time
5 ◯ Almost always

**7.** Over the past month, how many times, typically, did you get up to urinate between the time you went to bed and the time you got up in the morning?

0 ◯ None
1 ◯ Once
2 ◯ Twice
3 ◯ Three times
4 ◯ Four times
5 ◯ Five times or more

**Urinary symptom score: _____**

**8.** How would you feel if you had to live with your urinary condition the way it is now, no better, no worse, for the rest of your life?

0 ◯ Delighted
1 ◯ Pleased
2 ◯ Mostly satisfied
3 ◯ Mixed
4 ◯ Mostly not satisfied
5 ◯ Unhappy

**Quality of life score: _____**

## Tips for relieving BPH symptoms

These simple steps can help alleviate some of the symptoms of BPH:

- Reduce stress by exercising regularly and practicing relaxation techniques such as meditation. Some men who are nervous and tense urinate more frequently.
- Avoid drinking fluids in the evening, particularly caffeinated and alcoholic beverages. Both can affect the muscle tone of the bladder and stimulate the kidneys to produce urine, leading to nighttime urination.
- When you go to the bathroom, take the time to empty as much of your bladder as you can. This will reduce the need for subsequent trips to the toilet and minimize the chances that urine will collect and become stagnant in the bladder, leading to possible infections and bladder stones.
- Sip beverages slowly and avoid drinking lots of fluids before going out in public or starting a trip.
- Talk with your doctor about all your prescription and over-the-counter medications; some, such as antihistamines and decongestants, may affect urination. Your doctor may be able to adjust dosages, change your schedule for taking these drugs, or prescribe different medications that cause fewer urinary problems.
- On long airplane flights, avoid drinking alcohol and try to urinate every 60 to 90 minutes.

**5-alpha-reductase inhibitors.** If alpha blockers don't work, or if side effects such as orthostatic hypotension (dizziness upon standing), headaches, or retrograde ejaculation become overly troublesome, then your doctor will likely switch you to a 5-alpha-reductase inhibitor (5-ARI). The two FDA-approved 5-ARIs, dutasteride and finasteride, work by shrinking the prostate, but they take a while to work.

5-ARI drugs work by altering hormone ratios within the prostate. Specifically, they interfere with the action of 5-alpha reductase, which is the enzyme that converts the well-known male hormone testosterone to its lesser-known relative, DHT.

As noted previously, DHT acts on the prostate in ways that cause it to grow. By reducing DHT levels in the prostate, these drugs help to shrink the gland, leading to improvements in urinary symptoms that typically occur within three to six months. Symptoms may continue to improve for up to a year after commencing treatment as the prostate shrinks further. (The same hormonal effects also make 5-ARIs useful for treating hair loss.) Research with up to 15 years of follow-up has also found that men who took 5-ARIs for BPH were less likely than men who took alpha blockers alone to suffer from urinary retention and eventually need surgery.

Men who take finasteride and dutasteride have reported various unwanted sexual side effects, such as low libido, reduced ejaculate volume, and problems with getting and keeping an erection. These drugs can lower sperm counts, which is a potential concern for men who may still want to father children. In studies, however, fewer than 10% of men reported these problems.

In men who don't have prostate cancer, both dutasteride and finasteride tend to lower PSA levels by about 50%. For that reason, it's important to obtain a baseline PSA value before you begin treatment with a 5-ARI, then measure levels again after six months to a year. If your PSA level hasn't decreased by about the expected 50%, or if it rises, you may need a biopsy to determine if this is a sign of cancer. Conversely, if you're screened for prostate cancer while taking a 5-ARI—and you haven't obtained a baseline value—then the measured PSA level should be doubled to correct for the drug's PSA-lowering effects. Otherwise, the reading will be deceptively low.

Treatment with finasteride and dutasteride, especially in elderly patients, can also have troubling side effects, including depressed mood. Finasteride, in particular, has been associated with higher risks of suicidal thinking and various other psychological problems in men who use the drug either for treating hair loss or BPH, especially if they suffered previously from mood disorders.

Other symptoms associated with 5-ARIs include erectile dysfunction, fatigue, and sleep disturbances. Sexual side effects can persist, sometimes for months,

## 5-alpha-reductase inhibitors, alpha blockers, and cancer

In addition to treating BPH, 5-ARIs have also been tested as a means of preventing prostate cancer. In two separate trials, finasteride and dutasteride were shown to lower the overall risk of prostate cancer by about 25% to 30%. Here's the catch—and it is an important one: both medications were also associated with a small but statistically significant increase in risk for high-grade prostate cancer. In other words, 5-ARIs might help to lower your risk of developing prostate cancer, but if you had cancer that wasn't detected before you started 5-ARI treatment—or if cancer develops after you start taking the drugs—then it could grow more aggressively. In fact, the FDA requires 5-ARI medications to carry a warning about an increased risk of high-grade cancer.

On a more reassuring note, a 2024 study published in *JAMA Network Open* found no increased risk of death from prostate cancer among men who took a 5-ARI before a prostate cancer diagnosis.

If you are taking a 5-ARI, an alpha blocker, or the combination pill Jalyn (which contains dutasteride along with the alpha blocker tamsulosin) for BPH, talk with your doctor about the cancer risk and discuss what you should do.

after men stop taking the drugs. In studies, these affect only a small minority of men—less than 10%. But doctors say that in actual practice, sexual side effects are much more common, affecting up to a third of their patients.

Men who develop sexual side effects often benefit from adding the PDE5 inhibitor tadalafil. Studies show that finasteride and tadalafil are suitable in combination, especially for men with moderate to severe BPH.

**Combination therapy.** Because alpha blockers and 5-ARIs work differently, they often control urinary symptoms more effectively when taken together rather than by themselves. That's especially true for men with very large prostates. When a doxazosin-finasteride combination was tested in a large trial, it was more effective than either medication alone at preventing LUTS from getting worse. However, multiple studies have found this combination is also more likely to cause sexual side effects, and the story is similar for the dutasteride-tamsulosin combination sold as Jalyn.

**PDE5 inhibitors.** Tadalafil (Cialis) is in a class of drugs for erectile dysfunction called phosphodiesterase-5 (PDE5) inhibitors, but it also relieves symptoms of BPH when taken daily at a low dose. It is the only PDE5 inhibitor specifically approved by the FDA for BPH. It has been approved as a stand-alone treatment for BPH and as a dual treatment for BPH and erectile dysfunction.

Other PDE5 inhibitors, including sildenafil (Viagra) and vardenafil, are mainly used for erectile problems but may also help with urinary symptoms. Besides improving blood flow to the penis, these drugs relax muscles in the bladder neck, urethra, and prostate. Neither drug is approved for treating BPH, however.

Combining tadalafil with the alpha blocker tamsulosin is also an option. Some research shows the combination relieves urinary symptoms more effectively than tadalafil by itself and without compromising sexual functioning. Tadalafil can reduce blood flow to the heart, so experts advise against prescribing the drug to men with heart problems. Men who take nitroglycerin or another nitrate medication to treat heart problems should not use tadalafil, because the combination can drastically lower blood pressure.

Another combination option is Entadfi, a single pill that that contains tadalafil as well as finasteride (see page 18). Researchers found that giving the two drugs together improved BPH symptoms more effectively than finasteride used by itself. However, Entadfi is not recommended for use beyond 26 weeks, since researchers have not yet evaluated the benefits and safety of taking tadalafil and finasteride together for longer durations.

PDE5 inhibitors, like other BPH medications, come with potential side effects. Short-term side effects include headache, flushing, upset stomach, and nasal congestion.

### Beta-3 adrenergic agonists

Some men with BPH also have overactive bladders. Symptoms include frequent urination (over eight times a day) and strong urges to urinate right away. A beta-3 adrenergic agonist such as mirabegron (Myrbetriq) or vibegron (Gemtesa) might help.

Drugs in this class activate a nerve pathway that relaxes bladder muscles so you can hold more urine and thereby prevent urinary urgency, frequency, and incontinence. They tend to have fewer side effects compared to the older class of incontinence medications called anticholinergics (see below). Uncommon side effects of mirabegron can include an increase in blood pressure, difficulty urinating, and headache. Vibegron can cause headaches.

### Anticholinergics

Drugs in this class are also prescribed for incontinence. They block receptors in the smooth muscle tissue in the wall of the bladder so that this muscle is less likely to contract. Anticholinergics include oxybutynin, tolterodine (Detrol), and fesoterodine (Toviaz).

A 2017 study showed that men are more likely to stick with alpha blocker treatment if they're also combining it with an anticholinergic. But the combination is controversial. Results from an analysis of 12 clinical trials published in 2023 showed that adding one of these drugs *did not* reduce urgency symptoms in men taking alpha blockers for BPH. Anticholinergics may also increase the risk of urinary retention among men who take this combination, the authors warned.

In addition, experts advise caution when prescribing anticholinergics in the elderly, since the drugs can accelerate existing cognitive decline and raise the risk for falls. Anticholinergics are not approved by the FDA for use in BPH treatment.

### Antidiuretic hormone

A nasal spray called desmopressin acetate is approved by the FDA as a treatment for adults who wake up at least twice per night to urinate. This distressing problem, called nocturia, can be caused by a variety of medical conditions, including diabetes and overactive bladder as well as BPH.

Desmopressin is a synthetic version of a hormone called vasopressin, which retains fluid in the body and decreases your need to urinate. The drug must be used with caution because it can lower blood sodium levels, which, in turn, can lead to confusion and increase the tendency to fall. If you use desmopressin, your doctor should regularly monitor your sodium levels.

### Herbal remedies

According to Dr. Marc Garnick, editor in chief of this publication, there is little reason to believe that any herbal remedies (including saw palmetto and beta sitosterol) are effective, since none of the randomized trials to date have shown any benefit. They're probably not worth the money, and therefore are not covered here.

### Surgery for BPH

If medication hasn't helped enough and symptoms of BPH are so bothersome they affect your quality of life, surgery might be the next step. About nine out of 10 American men who opt for surgery do so after first trying medication to control their urinary problems caused by an enlarged prostate.

### Transurethral resection of the prostate

In the past, if BPH symptoms were severe—or if they were modest but still disrupted a patient's life—doctors almost universally recommended a surgical procedure called transurethral resection of the prostate (TURP). Other, less-invasive procedures have since become more common, but TURP is still considered the historical gold standard alternatives should be judged against (see "Surgical alternatives to TURP," page 22).

Often inelegantly referred to as the "roto-rooter" technique, TURP is an incision-free surgical procedure that cuts away excess prostate tissue with an electrical loop (see Figure 3, page 21). The removed tissues can then be examined by a pathologist to see if any cancer is present.

TURP is usually more successful than medication. It relieves urinary obstruction in at least 85% to 90% of men, and the improvement usually lasts. However, urinary problems can recur if the prostate tissue grows back. Not surprisingly, the younger you are, the more likely it is that you'll eventually need another treatment.

The hourlong procedure takes place in an operating room under general or spinal anesthesia. Only about a third of men who undergo TURP are dis-

charged the same day of the procedure, so you will likely spend one or two days recovering in the hospital. While recovering, you will urinate through a catheter inserted into the bladder through the penis. Once home, you may have to restrict heavy physical activity for two weeks or more to prevent bleeding.

About two-thirds of the men who have TURP experience retrograde ejaculation, in which semen travels backward into the bladder when they ejaculate. The semen released is soon flushed out of the body in urine. Retrograde ejaculation has no effect on orgasm sensation, though it can make it more difficult to father children.

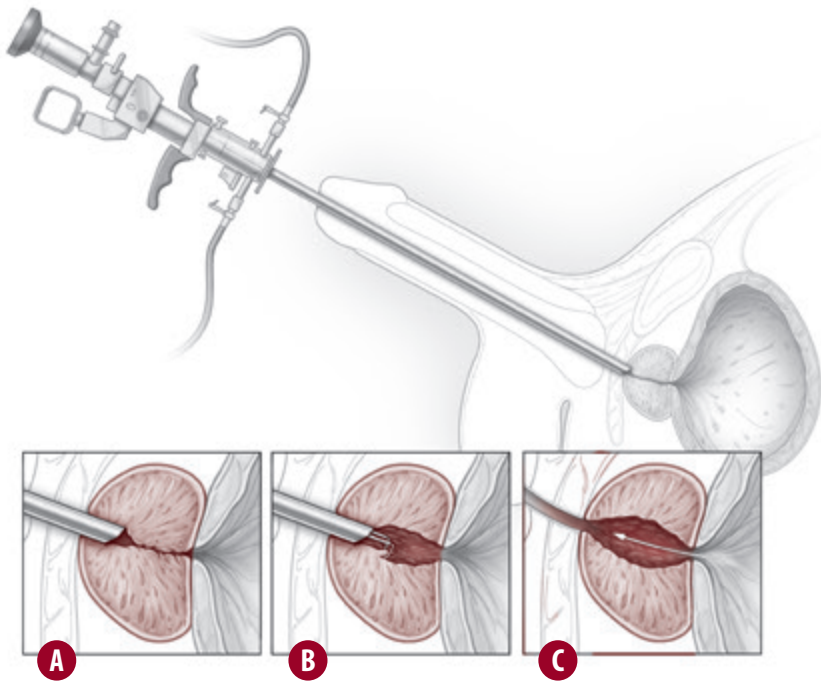
Between 5% and 10% of TURP patients experience serious complications, such as blood loss, impotence, urinary incontinence, infections, and anesthesia-related problems. The risk of these complications needs to be considered when choosing a treatment.

TURP might also increase the risk of a worse outcome after prostate cancer surgery, should it be needed later in life, according to a large review published in 2023 in *Prostate Cancer and Prostatic Diseases.* The authors analyzed data from 25 retrospective studies with a total of 11,101 men who had TURP or another surgery for BPH, then years later had a radical prostatectomy, which is an operation to remove the prostate gland in a man with prostate cancer. TURP (as opposed to the other BPH procedures) was associated with a small increase in the risk of positive margins, meaning that cancer cells may remain in the body after the prostate is removed and further surgery may be necessary.

About 2% of men who have TURP will go on to develop a condition known as post-TURP syndrome, or simply TURP syndrome, shortly after having the procedure. This short-lived state results from over-absorption of an electrolyte-free irrigation fluid (sometimes called a monopolar fluid) that doctors use to keep the surgical area clean during TURP. The fluid dilutes sodium in the blood, leading to symptoms that include confusion, nausea, vomiting, high blood pressure, and problems with eyesight.

### *Figure 3. Transurethral resection of the prostate*

During transurethral resection of the prostate (TURP), the surgeon inserts a thin tube called a resectoscope into the urethra and threads it up into the enlarged prostate (**A**). The resectoscope contains a tiny camera—which enables the surgeon to view the gland throughout the operation—as well as an electrical loop. The surgeon uses the loop to chip away at overgrown prostate tissue that's pressing on the urethra and narrowing it (**B**). After the procedure, the enlarged passageway allows urine to flow more easily (**C**).



A safer alternative uses saline (saltwater) solution in combination with a special surgical instrument that contains two closely positioned electrodes right at the tip. Known as bipolar TURP, this procedure avoids the absorption of the monopolar fluids that cause TURP syndrome. Bipolar procedures are also associated with a lower risk of blood clots that block the flow of urine out of the bladder. Men treated this way need less time with a catheter and have shorter hospital stays after surgery. There are no differences between bipolar and monopolar TURP in terms of sexual side effects and other complications, but some doctors will still use the monopolar technique if they are more accustomed to it and have a history of achieving successful outcomes.

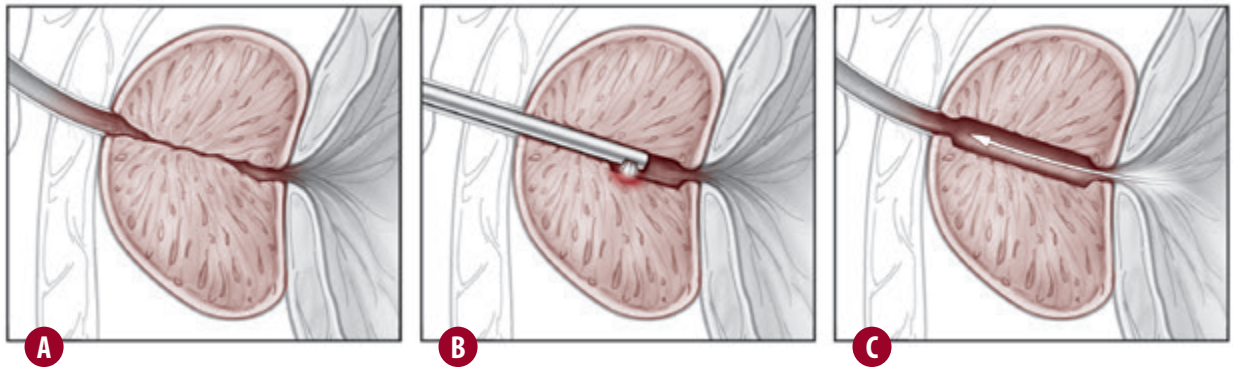
### Surgical alternatives to TURP

Newer procedures provide symptom relief with fewer short-term complications and side effects. Like TURP, most of these techniques involve removing

**Table 3. Procedures for BPH**

| Procedure | What's involved | Side effects |
|---|---|---|
| Transurethral resection of the prostate (TURP) | Performed in operating room.<br>Requires general or spinal anesthesia. May require one to two days in the hospital, with catheter inserted to enable urination for one to three days.<br>Heavy physical activity may be restricted for two weeks or more to prevent bleeding.<br>Full recovery may take four to six weeks. | May cause retrograde ejaculation.<br>Blood loss, urinary incontinence, infections, and complications from anesthesia are uncommon but do occur. |
| Photoselective vaporization of the prostate (PVP or GreenLight) | Most patients treated in outpatient setting.<br>Catheter usually in place overnight.<br>Patients can resume light activity within two to three days and vigorous activity in four to six weeks. | Ejaculatory problems similar to TURP.<br>Less bleeding than TURP.<br>Urinary frequency or urgency in first month. |
| Holmium laser enucleation of the prostate (HoLEP) | Performed in operating room.<br>Requires general anesthesia.<br>Overnight catheter may be needed.<br>Heavy physical activity restricted for three to four weeks. | Short-term bleeding, urinary incontinence, infections, ejaculatory problems similar to TURP. |
| Thulium laser enucleation of the prostate | Performed in a hospital.<br>Most patients go home the day of their surgery. | In rare cases, may cause bleeding, urinary incontinence, and infection. |
| Transurethral electrovaporization of the prostate (TUEVP, TUVP, or TVP) | Overnight hospital stay.<br>Catheter needed for one to two days. | Likelihood of urinary retention is greater than with TURP.<br>Risk of reoperation is greater than with TURP.<br>Some urinary side effects, such as blood in the urine and irritation when urinating, that can last for a few weeks.<br>Higher risk of retrograde ejaculation. |
| Transurethral needle ablation of the prostate (TUNA) | Done on an outpatient basis.<br>May need local anesthesia.<br>Catheter usually not needed. | Patients may need additional treatments.<br>Erectile dysfunction and urinary incontinence less common than with TURP. |
| Transurethral incision of the prostate (TUIP) | Requires regional or general anesthesia.<br>Hospital stay is typically one to three days.<br>Usually reserved for men with a small prostate. | Likelihood of urinary retention and risk of reoperation greater than with TURP. |
| Aquablation | Employs a heat-free, high-pressure saltwater jet to carve away excess prostate tissue. Performed under general anesthesia. Most patients go home the same day with a catheter. | Transient blood in urine and burning sensations while urinating that clear up in two to three days. Blood in urine can sometimes persist for several weeks. |

***Figure 4. Photoselective vaporization of the prostate***




When an enlarged prostate obstructs urine flow (**A**), a laser technique may be used instead of TURP. During photoselective vaporization of the prostate (PVP), also called the GreenLight procedure, the surgeon threads a thin tube called a cystoscope through the urethra into the enlarged prostate. The surgeon then passes a fiber-optic device through the cystoscope to generate high-intensity pulses of light, which simultaneously vaporize the obstructing tissue and cauterize (seal off) blood vessels to reduce bleeding (**B**). This creates an enlarged, uniform channel through which urine can flow (**C**).

prostate tissue to reduce pressure on the urethra. The difference is in the technology used to remove that tissue.

Explanations of the most common procedures follow. Each has pluses and minuses. For a comparison of surgical options, see Table 3, page 22.

**Photoselective vaporization of the prostate (PVP; also known as GreenLight).** With this common hospital-based approach, excess prostate tissue is destroyed by laser energy, and the remnants are excreted in urine (see Figure 4). Typically, patients can go home the same day as the procedure.

A large review published in 2025 in *Translational Andrology and Urology* showed little to no difference between PVP and TURP when it comes to resolving urinary symptoms in men with BPH. But there are short-term differences. PVP is associated with fewer frequent blood transfusions, shorter hospital stays, and shorter catheterization times. It's also associated with fewer postoperative complications such as pneumonia and septic shock, though these are very rare with TURP.

Men treated with PVP typically have less pain after surgery and a quicker return to normal life compared to those who have TURP. However, men who've had TURP score better on measures of symptom control and quality of life after five years, and men who've had PVP are more likely to need a repeat procedure to address recurring urinary symptoms. This may occur if the laser is too weak to remove enough prostate tissue. As more powerful lasers have come into wider use, however, success rates of TURP and PVP are becoming comparable.

To perform PVP, the surgeon begins by guiding a thin, flexible optic fiber through the urethra to the prostate. This fiber conducts the laser light to the target area of the prostate. Most laser procedures involve focusing the energy of the laser so it destroys the overgrown tissue. However, this destruction of tissue gives laser procedures a significant disadvantage: prostate tissue destroyed with a laser can't be checked for cancer, whereas TURP yields tissue samples that a pathologist can examine.

The lasers used during a PVP produce emit a high-intensity visible green light (indeed, "GreenLight" is the brand name for one method) that is selectively absorbed by hemoglobin-rich prostate tissue. The trapped energy given off by the laser pro-

duces vapor bubbles that destroy the tissue from within. This procedure also cauterizes (seals off) blood vessels to reduce bleeding. One of the chief advantages of PVP is that patients on blood-thinning medications like warfarin can have the procedure and still take their medications.

The lasers that surgeons use today are two or even three times more powerful than those used when PVP was initially developed. The more-powerful lasers mean surgeons can work faster and operating times are shorter. They also remove tissue more effectively, reducing the likelihood that a man will need a repeat procedure later.

**Holmium laser enucleation of the prostate (HoLEP).** The HoLEP method is also laser-based, but differs from PVP in a fundamental way: where PVP vaporizes excess prostate tissue, HoLEP use a laser to remove (or "enucleate") the tissues from the body. If the tissue is removed (rather than vaporized), it will be sent to pathology for analysis. HoLEP is the only BPH surgical procedure endorsed by the American Urological Association (AUA) for all prostate sizes, leading some researchers to contend that HoLEP should now be regarded as the new gold standard for BPH surgery. Still, not all surgeons are comfortable using HoLEP for very large prostates, and, based on what they find during the operation, they may switch to an open simple prostatectomy (surgery to remove the part of the prostate causing BPH symptoms) during the procedure. In a 2022 paper published in *Urology*, researchers reported that every 20-gram increase in the size of the prostate was associated with higher odds of that happening. According to Dr. Garnick, editor in chief of this guide, patients should be forewarned of such a possibility prior to surgery.

Evidence shows that HoLEP is at least as effective as TURP for reducing BPH symptoms, with benefits potentially lasting more than 10 years. Its advantages include less need for blood transfusion as well as shorter catheterization and hospital stays. HoLEP is becoming more widely available, but it also has a steep learning curve. Dr. Garnick advises that patients interested in this surgery should seek out surgeons who have experience performing it.

**Thulium laser enucleation of the prostate.** This procedure is similar to HoLEP. The main difference is that the holmium approach uses pulsed laser energy, while the thulium procedure uses continuous laser energy. Both methods are equally effective at relieving urinary symptoms, but the thulium method may result in less blood loss during surgery and, moreover, often preserves ejaculatory function. Most men are able to ejaculate normally within three months of having the procedure.

**BPH guidelines**

Scan the QR code to read the official BPH management guidelines from the American Urological Association.

BPH treatment guidelines published by the AUA state that either HoLEP or the thulium method can be considered for treating enlarged prostates, depending on the surgeon's own experience.

**Transurethral electrovaporization of the prostate (TUEVP, also called TUVP or TVP).** In this procedure, the surgeon uses a tiny, round-tipped electrode to rapidly heat and vaporize overgrown prostate tissue and seal off blood vessels in the treated area. Although vaporization limits bleeding, TUVP can cause retrograde ejaculation. Studies show that the results of TUVP and TURP are similar. However, for men on anti-clotting medications, the TUVP procedure's lower risk of bleeding during and after surgery can make it a safer option than TURP. The recovery time after a TUVP is generally two to three weeks.

**Transurethral needle ablation (TUNA).** The TUNA thermal approach uses low-level radio waves delivered through twin needles to heat and kill obstructing prostate cells. Shields are used to protect the urethra from damage. The treatment can improve symptoms, quality of life, and urine flow with little risk of sexual side effects, but TURP typically generates better results for urinary function.

**Transurethral incision of the prostate (TUIP).** This procedure also involves inserting an instrument into the prostate via the penis. But instead of cutting away or vaporizing excess tissue, the surgeon makes

one or more lengthwise incisions in the prostate at the site of the urethral constriction. This opens the urethral passage, relieving pressure on the urethra and improving urine flow while preserving the ability to ejaculate. TUIP poses a lesser risk of retrograde ejaculation than TURP and is generally reserved for prostates no larger than 30 grams. The recovery time after a TUIP is typically three to five weeks.

**Aquablation.** This newer, robotic-assisted technique destroys prostate tissue with jets of highly pressurized saline delivered under guidance from ultrasound. The robotic system ensures that only tissues mapped by ultrasound are removed. When Aquablation was first introduced, bleeding was a common complication, but doctors now use techniques such as cauterizing the bladder neck, which lowers bleeding risk.

Aquablation requires further investigation to confirm its long-term effectiveness, but the evidence so far is encouraging. Studies have shown symptom relief over follow-up durations of five years, with fewer than 10% of men needing repeat treatment with medication or an alternate procedure. Aquablation often preserves ejaculatory functioning, although outcomes vary from man to man. Aquablation can be suitable for men with medium to large prostates. However, procedures performed on prostates ranging up to 150 grams are associated with higher rates of low-grade complications, including blood loss during surgery.

**Table 4: Minimally invasive procedures for BPH**

| Minimally invasive surgical procedure treatment (MIST) type | What's involved | Common side effects |
|---|---|---|
| Prostatic artery embolization (PAE) | Performed in an outpatient setting under local anesthesia and light sedation. Most patients go home the same day of the procedure without a catheter. Heavy physical activity may be restricted for one or two weeks. | Transient blood in urine and/or semen, painful urination. Some patients experience post-embolization syndrome, which has symptoms including nausea, fever, pain, and fatigue. Side effects typically resolve within a few days or weeks. |
| Prostatic urethral lift (PUL or UroLift) | Performed in outpatient setting under local or general anesthesia.<br>Approximately 95% of treated men return home the same day without a catheter. Heavy physical activity may be restricted for two weeks or more to prevent bleeding. | Transient blood in urine and burning sensations while urinating that clear up in two to three days. |
| Water vapor thermal therapy (Rezum) | Performed in a doctor's office or outpatient facility under local anesthesia.<br>Catheter used for several days.<br>Light exercise allowed within a few days; strenuous exercise within two weeks. | Side effects, including painful urination, blood in urine or semen, frequent urination, or inability to empty the bladder completely, generally resolve within three weeks. |
| Temporarily implanted nitinol device (iTind) | Performed in doctor's office or outpatient facility under local anesthesia and light sedation. Does not require a catheter. Patients go home the same day and return 5-7 days later to have the device removed. | Blood in the urine, urgent or frequent urination, burning during urination. Pain can last during the treatment period but typically resolves shortly after the device is removed. |
| Prostatic urethral stents | Performed in outpatient settings under local anesthesia with light sedation. Patients can go home the same day. Does not require a catheter. Most people return to normal activity within a day, but heavy lifting should be avoided for a week. | Pain in the back, pelvis, or groin, frequent or urgent need to urinate, transient blood in the urine. Side effects usually resolve within a few days but can last up to two weeks. |
| Drug-coated balloon procedure (Optilume) | Performed in a doctor's office under local anesthesia. Requires the use of a catheter for 72 hours after the procedure. Full recovery can take several weeks. | Pain or discomfort during urination, blood in the urine, urinary tract infections. |

## Minimally invasive surgical options

Several minimally invasive surgical treatments, collectively known as MISTs, relieve urinary obstruction with quicker recovery and fewer side effects compared to TURP and other traditional surgical options. MISTs are generally performed with only local anesthesia in a urologist's office, though some physicians and patients may opt to use general or regional anesthesia. They work best in men with mild to moderate prostate enlargement and can often preserve ejaculatory functioning. A downside is that symptom improvements may not be as durable as those achieved with other methods. See Table 4, page 25, for a summary.

**Prostatic artery embolization (PAE).** In this procedure, a radiologist inserts a catheter into the femoral artery in the groin and guides it toward the prostate. After it's positioned in the artery supplying blood to the prostate, the catheter is used to deliver microscopic spheres (particles) that physically block blood flow. This causes the prostate to shrink. PAE is normally done under conscious sedation, so you are heavily sedated but still awake during the three-hour procedure.

PAE can be an option for men who have relatively large prostates, but are not good candidates for TURP or laser surgery. Still, the investigators behind a 2023 article published in the *World Journal of Urology* urge caution. According to their findings, PAE-treated men are more likely be hospitalized for complications than men treated with other methods, including TURP. A total of 12,902 men treated surgically for BPH in New York State were tracked for up to three months. PAE-treated patients had a 19.9% risk of hospital admission within 30 days of the procedure, most frequently for abdominal pain. Furthermore, PAE patients also had the highest retreatment rate, at 28.5% within two years. Other research has shown little difference in complication rates or symptom improvement between PAE and other BPH procedures, however. High retreatment rates may reflect PAE's use in an older, sicker group for whom TURP and other hospital-based procedures are not preferred.

PAE has been used in the United States for about a decade, but more data are needed to confirm its long-term benefits. In 2023, the AUA cautioned that PAE is technically demanding, with a challenging learning curve for physicians. If you opt for PAE, you should make sure your doctor has sufficient training in the procedure. PAE poses risks for bleeding after surgery, and it may be unsuitable for men taking anti-clotting drugs. Dr. Garnick cautions that, in rare instances, PAE can cause blood clots to accumulate in the bladder, a dangerous complication requiring surgery.

**Prostatic urethral lift (PUL or UroLift).** The PUL procedure involves using permanent implants that pull the prostate away from the urethra to improve urine flow. You will probably see this procedure referred to by its brand name, UroLift. The implants are nylon sutures held in place with thin metal tabs. Doctors will typically insert four to six implants into the prostate during a PUL procedure. The FDA has approved UroLift for prostates weighing 80 grams or less.

Research suggests PUL doesn't relieve symptoms as well as TURP. In one study, the procedure improved symptom and quality-of-life scores by 36% to 40%, respectively, over periods ranging up to five years.

Importantly, metal components in the UroLift can distort images on magnetic resonance imaging (MRI) scans of the prostate that may be needed later to diagnose and assess other conditions, including prostate cancer. However, radiologists can account for the impact of the metal by adjusting MRI parameters.

**Temporarily implanted nitinol device (iTind).** This implanted device is made of a metal alloy called nitinol. It improves urinary outflow by opening a channel into the urethra. Often referred to by its brand name, iTind, the device works similarly to PUL, but only remains in place temporarily. It was added to the AUA's practice guidelines for BHP treatment in 2023.

During an iTind procedure, a doctor passes this device, which is shaped like a tulip flower, through the urethra. The device is then pulled back and positioned at the base of the bladder neck. It expands gradually, creating an opening through which urine can readily flow. After five to seven days, the device is removed, but the open channel remains.

During an industry-sponsored study, people receiving the iTind procedure reported improvements in urinary symptoms lasting longer than six years. Use of the device is not recommended for men with an enlarged median lobe, which is a cone-shaped portion of the prostate gland that can protrude into the bladder.

**Water vapor thermal therapy (Rezum).** In this noninvasive procedure for BPH, pronounced "resume," you can be treated in a doctor's office under local anesthesia and sometimes with nerve block to minimize pain. To perform the procedure, the doctor inserts a thin, hollow tube called a scope through the penis into the prostate. The scope delivers nine-second blasts of steam that kill prostate cells, causing the enlarged tissues to shrink over time and widening the urethral channel so that you can urinate normally. Procedure-related side effects, including urine retention and painful urination, typically resolve within three weeks.

A 2025 study in the *Journal of Urology* followed 197 men treated with Rezum for five years. The results showed symptom improvement scores of between 44% and 48% for up to five years after treatment, with no reports of sexual dysfunction. The downside is that Rezum-treated men need to use a catheter for longer durations than men treated with other procedures—about seven days for prostates weighing 80 grams or less and 10 to 14 days for larger glands.

Evidence indicates that Rezum can be safe and effective for elderly men who require permanent catheterization for BPH and who cannot undergo general anesthesia because of frailty and other health problems. In 2025, the FDA expanded Rezum's approval to be used in men with prostates weighing up to 150 grams.

**Prostatic urethral stents.** A prostatic urethral stent is a small, springlike mesh cylinder. The doctor inserts the stent through the penis and, after positioning it in the narrowed area of the urethra, releases it to widen the channel, relieving pressure from the prostate tissue and permitting easier urination. This quick procedure requires only local or spinal anesthesia, involves no loss of blood, and is often done in an outpatient surgical center.

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A urologist can explain whether you're a good candidate for an outpatient procedure designed to relieve BPH symptoms.

Prostatic urethral stents are most often used in elderly men who have severe prostate enlargement and whose overall health is poor, meaning more-involved surgery would be risky. In many cases, urinary obstruction gradually returns, and additional procedures may be required in some instances.

**Drug-coated balloon procedure (Optilume).** During this procedure, a doctor threads a catheter tipped by a balloon through the urethra into the prostate. The balloon is then inflated. After approximately five minutes, the catheter is removed, leaving an open channel. This relieves pressure on the urethra, allowing urine to flow. The catheter is coated with a drug called paclitaxel, which is used as a coating on heart stents to prevent the formation of scar tissue around the stent.

Optilume was approved by the FDA in 2023 for treating enlarged prostates that weigh up to 80 grams. During clinical trials, the system provided relief of LUTS (see "Lots of LUTS: Symptoms of BPH," page 14) lasting up to four years while preserving erectile and ejaculatory function.

**ROUNDTABLE DISCUSSION:**

# Benign prostatic hyperplasia: How new treatments and procedures are helping patients overcome urinary symptoms caused by an enlarged prostate

*Benign prostatic hyperplasia (BPH), or non-cancerous enlargement of the prostate, is incredibly common among older men. Roughly one in four men globally develop it. In the United States, BPH ranks among the most common causes of insurance claims in men over the age of 65.*

*BPH is best known for causing bothersome urinary symptoms. Left untreated, it can progress to chronic kidney disease and renal failure. To help our readers better understand the causes of BPH and how best to treat it, we convened a panel of experts from Harvard Medical School, Massachusetts General Hospital, and Beth Israel Deaconess Medical Center.*

**Michael Barry, M.D.,** is a professor of medicine at Harvard Medical School and a physician at Massachusetts General Hospital.

**Aria Olumi, M.D.,** is a urologist and professor of surgery at Beth Israel Deaconess Medical Center.

**Ruslan Korets, M.D.,** is a urologist and assistant professor of surgery at Harvard Medical School and Beth Israel Deaconess Medical Center.

**Marc B. Garnick, M.D.,** editor in chief of this guide, moderated the discussion.

***Q: What sort of symptoms do men experience when they develop BPH?***

**Barry:** We divide BPH symptoms into two general categories: storage symptoms and voiding symptoms, which are collectively referred to as lower urinary tract symptoms, or LUTS.

Storage symptoms have to do with the filling and storage of urine in the bladder. They include urinary urgency, which is a strong feeling that you need to pee right away, as well as frequent urination, including having to get up repeatedly to urinate at night.

Voiding symptoms have to do with emptying of the bladder. You might have to push to start the urinary stream, have a weak or intermittent stream, or feel that you're unable to empty your bladder completely.

***Q: Why do men develop BPH?***

**Olumi:** I tell my patients that the two most common risk factors for BPH are being a male and aging, neither of which we have any control over. Hormonal factors also come into play. Testosterone and its main byproduct, dihydrotestosterone (DHT), both stimulate prostate growth. Some men have unusually high levels of an enzyme called 5-alpha-reductase 2 that converts testosterone into DHT, which is more potent than testosterone at increasing the prostate's size. Metabolic syndromes, including obesity, also activate the gene that makes 5-alpha-reductase 2. That boosts DHT levels and makes BPH more likely.

***Q: Can men reduce their risk by exercising and keeping their weight down?***

**Olumi:** Plenty of research, including studies our group has done at Beth Israel, demonstrates that leaner individuals are less prone to urinary tract symptoms. We recently found that men with obesity have more circulating 5-alpha-reductase 2 and larger prostates.

***Q: Dr. Barry, you were involved in developing the American Urological Association (AUA) Symptom Index—also called the AUA Symptom Score—for BPH. Patients typically fill out a variation of this standardized questionnaire (see "Your urinary symptom score," page 17) before meeting with a doctor. Can you describe it for us?***

**Barry:** Sure. The AUA Symptom Index was developed roughly 30 years ago to objectively assess LUTS severity. Patients respond by estimating how often they've experienced each of seven different urinary symptoms during the preceding month. Responses for each symptom range from 0 (never) to 5 (very often), and then the AUA score is tallied by summing those values together.

**ROUNDTABLE DISCUSSION** *continued*

Total scores of 0 through 7 are considered mild. Men in this category generally don't seek treatment. Scores of 8 through 19 are considered moderate, while scores ranging from 20 to 35 are considered severe. The index also asks the patient about how bothered they are with these symptoms. Some men with low scores are bothered, while others who have much higher scores are not bothered at all.

The AUA Index has since been adopted for global use under a different name, the International Prostate Symptom Score, and it's now available in over 50 languages.

***Q: Can BPH and prostate cancer have overlapping symptoms?***

**Barry:** They can. But men with BPH generally have both storage and voiding symptoms that develop slowly over time. Red flags for prostate cancer, or perhaps a condition affecting the bladder, would be having mainly storage symptoms or urinary symptoms that develop very rapidly. These would be unusual for LUTS caused by BPH.

***Q: If a patient reports bothersome symptoms on the AUA Index, what happens next?***

**Barry:** Some other basic tests follow. A urinalysis checks for substances that can rule out bacterial infections and undiagnosed diabetes as potential causes of symptoms. I'll typically do a digital rectal exam (DRE) to assess the prostate's size. Sometimes a prostate that feels normal during a DRE can turn out to be quite large, so I might also measure the gland with a transabdominal ultrasound scan.

In some cases, I'll also refer a patient to a urologist for a post-void residual urine test, which uses ultrasound to measure how much urine remains in the bladder immediately after a man uses the bathroom.

***Q: Dr. Barry, as a primary care physician, you'd likely be the first to start treating a patient for BPH. What goes into that process?***

**Barry:** Shared decision making with the patient is important when choosing among the options—or whether to treat at all. Most men will pick medical therapy first [meaning medication, rather than immediately undergoing a minimally invasive procedure].

We tend to start with a group of medications called alpha blockers. These drugs [which include tamsulosin, or Flomax, and alfuzosin, or Uroxatral] relax muscles in the prostate and bladder neck so that urine can flow more easily through the urethra. Patients who respond to the drugs usually do so fairly quickly, and we'll aim for the highest dose they can tolerate without side effects.

***Q: Dr. Korets, what's your approach to selecting medication for a patient with BPH?***

**Korets:** I also utilize alpha blockers as a first-line medication. Another class of drugs, known as 5-alpha-reductase inhibitors [which include finasteride (Proscar) and dutasteride (Avodart)], is also effective in larger prostates over the size of 40 to 50 grams [as measured via ultrasound]. So knowing the prostate's size is helpful when deciding on a medication.

**Olumi:** An important caveat is that 5-alpha-reductase inhibitors take six to 12 months and sometimes longer to become effective. But once they start working, they tend to continue being effective longer than alpha blockers, which may lose effectiveness over time.

***Q: Which side effects from these medications should men be aware of?***

**Barry:** Alpha blockers can cause orthostatic hypotension—a drop in blood pressure after standing from a sitting position that can cause dizziness and lightheadedness. Older alpha blockers, such as doxazosin and terazosin, are most apt to cause this problem, and we don't use those much anymore for BPH. Those drugs are more often used for high blood pressure, because they widen blood vessels in muscles and tissues throughout the body.

Newer alpha blockers for BPH—such as tamsulosin and alfuzosin—target cell receptors in the prostate and bladder neck selectively, making hypotension less of a worry.

**Olumi:** Another common side effect with alpha blockers is retrograde ejaculation. That's when men orgasm, but semen flows backward into the bladder instead of out through the urethra. It occurs more often in younger men than in older men because their prostate and bladder muscles are more relaxed.

**ROUNDTABLE DISCUSSION** *continued*

**Barry:** Alpha blockers have another odd complication, in that they can make cataract surgeries more difficult. So I usually make sure that no one has a cataract surgery scheduled before starting on them. If someone having cataract surgery is taking these drugs, they should talk to their ophthalmologist and will probably be advised to stop the medications before the procedure.

***Q: What about side effects of 5-alpha-reductase inhibitors?***

**Olumi:** Around 10% of men who take 5-alpha-reductase inhibitors experience decreased libido and erectile dysfunction (ED). But, for the most part, these drugs are very well tolerated. [Mood changes are also possible when taking a 5-alpha-reductase inhibitor such as finasteride, but these are more commonly reported in younger men using the drug for hair loss.]

***Q: What about PDE4 inhibitors? These drugs are ordinarily used for ED, but one of them, tadalafil (Cialis), also has FDA approval for treating BPH.***

**Korets:** PDE4 inhibitors could potentially improve both conditions.

**Olumi:** In my practice, I haven't found tadalafil to be very effective at improving urinary symptoms, even though it is approved for that purpose.

***Q: Can you recommend some practical strategies for managing BPH symptoms?***

**Korets:** I advise my patients to avoid diuretics like caffeine or alcohol before and during air travel. These agents stimulate the bladder and can worsen urinary frequency and urgency. Plan ahead when traveling. Choose aisle seats if you know you're going to be getting up frequently, and use the restroom before boarding to prevent your bladder from becoming overdistended.

Such measures help reduce the risk of acute urinary retention, which happens when you can't urinate at all despite having severe urgency. More than being extremely uncomfortable, urinary retention is a medical emergency that can cause kidney damage if it isn't addressed quickly. Treatment entails draining the bladder with a catheter at a urologist's office or an urgent care center. Urinary retention is sometimes exacerbated by inflammation or an infection in the prostate or urinary tract.

***Q: What about double-voiding? What is it, and how does it help?***

**Korets:** Double-voiding simply means waiting 20 to 30 seconds after urinating and then trying to urinate again. It can help reduce the post-void residual, which is the amount of urine remaining in the bladder after urinating. A timed voiding pattern where you try to urinate every two to three hours, even if you don't feel the urge, can also limit overdistension of the bladder and reduce the risk of urinary retention.

The bladder is actually a hollow muscle, and with age its contractions increasingly aren't strong enough to empty everything out, especially when there's blockage from the prostate. Double voiding, or a timed voiding, helps to "reset" the bladder muscle so that emptying happens more efficiently.

***Q: Dr. Barry, what would lead you to refer a patient to a urologist?***

**Barry:** I would certainly refer someone to a urologist if they had blood in the urine or microscope hematuria (blood cells detected in urine under a microscope.) Those could signal something other than BPH, such as an infection, kidney problems, or cancer. A prostate that feels abnormal during a DRE might also warrant a urology consult.

Additionally, someone who has bothersome BPH symptoms after trying medication could benefit from seeing a urologist to learn about other options.

***Q: Drs. Olumi and Korets, what would prompt you to initiate a discussion about surgical options?***

**Korets:** Someone who has LUTS that isn't relieved by medication might benefit from surgery. I would also bring surgery up with patients who develop complications from BPH, such as urinary tract infections, bladder stones, and hematuria or blood in the urine. These can be signs of incomplete emptying, which can lead to chronic kidney disease or renal failure over time. An episode of urinary retention would mark a turning point where we should escalate beyond medications and consider something with more durable benefits.

***Q: BPH can now be treated with an array of minimally invasive procedures as well as more invasive ones. How do you help patients decide?***

**ROUNDTABLE DISCUSSION** *continued*

**Korets:** The two main factors that determine which procedure is suitable for a patient are its invasiveness and prostate size. Office-based procedures are performed under local anesthesia. One such procedure, called Rezum, uses steam to shrink the prostate. It's ideal for glands measuring 80 grams or less. [Normal prostates weigh about 25–30 grams; large ones can weigh 150 grams or even more.] Rezum preserves normal ejaculation, which is important for men who want to avoid sexual side effects.

Prostate artery embolization (PAE) is another office-based option. It delivers tiny particles into the main artery feeding the prostate, thereby reducing the gland's blood supply. PAE can be suitable for older patients who may be unfit for surgery. And because it has low bleeding risk, it's appropriate for men on blood thinners.

Lastly, I'll mention UroLift, which opens the prostate canal with implanted clips. It's best for glands measuring 80 grams or less. But it may not be suitable for men with a large median lobe—this is the central part of the prostate that can intrude into the bladder.

***Q:** And the more invasive options?*

**Korets:** We perform them under general or spinal anesthesia. Among them, transurethral resection of the prostate, or TURP, still stands the test of time as the gold standard BPH surgery. It's ideal for prostates ranging up to 80 grams. A more recent option is to destroy prostate tissues with laser energy. It's associated with less bleeding and a quicker recovery and can be suitable for larger glands weighing over 100 grams.

One of the newest procedures, called aquablation, uses a high-pressure water system to remove prostate tissue. The advantage is that it can be done in prostates ranging between 60 to 150 grams in size. Aquablation is very precise, doesn't take long to complete, and it also preserves ejaculatory functioning.

I try to make sure our trainees gain exposure to as many BPH procedures as possible so they can then decide which ones they want to offer. But, in practice, urologists tend to specialize in two or three of them.

***Q:** How long do symptom improvements with these procedures last?*

**Korets:** The less-invasive options typically need to be repeated every three to five years. With procedures like TURP or the laser-based methods, benefits can last a decade or longer.

***Q:** I'd like to shift gears now and talk about prostate-specific antigen (PSA) testing in men with BPH. PSA levels typically increase when the prostate grows in size. Is that a concern?*

**Barry:** The first point to make is that BPH does not elevate the risk of prostate cancer. In fact, some studies show a lower risk of prostate cancer among men who have urinary symptoms and an elevated PSA. That said, men can have BPH and prostate cancer at the same time, so they should know about the pros and cons of PSA screening in order to make informed decisions about whether they want to be tested.

***Q:** How should we interpret PSA values that are outside the normal range?*

**Barry:** We can adjust the levels for age, since PSA generally increases as a man gets older. A mildly elevated level that could be alarming for a man in his 50s might be less so for someone in his 70s or 80s. We can also look at PSA stability, or the rate of PSA increase over time. This is called PSA velocity.

**Olumi:** I consider age and PSA velocity, but also results from imaging. A magnetic resonance imaging scan of the prostate can be extremely helpful when we're considering a biopsy for cancer.

**Korets:** We'll use PSA as a way to rule out more concerning findings like prostate cancer. Aa general rule, if the PSA level is less than 1.5 nanograms per milliliter (ng/mL), then the risk of significant prostate enlargement and prostate cancer are both low. PSA levels beyond 10 ng/mL, which are highly suspicious for cancer, suggest the need for further diagnostic workup. Levels between 4 and 10 ng/mL fall into a gray zone—we interpret those values cautiously in accordance with a patient's symptoms.

Treatment also factors into the interpretation. Since 5-alpha-reductase inhibitors typically lower PSA by about 50%, you'll want to repeat the PSA test about six months after initiating therapy. If the levels don't fall substantially, or even rise, then a biopsy may be necessary.

***Q:** What do you do if the biopsy in a man with BPH and an elevated PSA shows small amounts of Grade*

**ROUNDTABLE DISCUSSION** *continued*

***Group 1 prostate cancer, which has a very low risk of further progression?***

**Korets:** We know that men are more likely to die with very low-risk prostate cancer than they are from it. It's important to talk with patients about how worried they might be over a cancer diagnosis. You can educate and reassure them that these cancers are often slow-growing, and that we can monitor the disease with active surveillance while treating BPH with medication or surgery.

***Q: If surgery is an option, would you consider a radical prostatectomy or a lesser intervention?***

**Korets:** I would emphasize that radical prostatectomy—while it would eliminate the cancer—likely represents over-treatment. It would improve urinary symptoms, but potentially lead to many other downstream problems. So, my preference in such cases is to offer treatment geared toward BPH. The selection of a given procedure again depends on prostate size, urinary symptoms, and what's important for the patient in terms of side effects. But the focus should be on managing the patient's symptomatic problem—BPH—and monitoring a low-risk cancer that isn't causing him any problems.

***Q: Thank you for an amazing roundtable. Any parting thoughts?***

**Barry:** I'd like to highlight the proliferation of currently available BPH treatments. Sometimes patients try medication, it doesn't work for them, and then they don't want to see a urologist because they know someone whose prostate surgery didn't go well 30 years ago. There are many more options these days.

**Korets:** And those options can quickly get overwhelming! Urologists and other physicians can play an important role in helping a patient understand what each option really means for his body and lifestyle. We need to prioritize what's important and help by translating jargon into real-life terms.

**Olumi:** BPH is an extremely common problem globally that affects almost all men as they get older. I look forward to the day when we can treat BPH with better-targeted drugs, as well as actually prevent urinary symptoms from occurring in the first place.

4

# Prostate cancer

***What you need to know at every stage of the disease***

According to the American Cancer Society (ACS), the risk of dying from prostate cancer has fallen by roughly half since the mid-1990s, mostly because of advances in treatment. Still, prostate cancer remains the second most commonly diagnosed cancer in men in the United States, and the second leading cause of cancer death among men (after lung cancer). Although definitive numbers won't be available for a couple of years, since it takes time for scientists to gather and analyze data, the ACS estimates that 209,010 American men were diagnosed with the disease in 2024, and 35,250 died of it. According to the ACS, the 10-year survival rate for all stages combined is 98%, while the 15-year survival rate is 95%.

Nine out of every 10 cases of prostate cancer are detected at the local or regional stage (see "Prostate cancer terminology," page 34). When the disease is discovered at these early stages, the five-year survival rate approaches 100%.

## What causes prostate cancer?

No one knows precisely what causes prostate cancer. But that doesn't mean it's a total mystery, either. Genetic defects play a role in the development of any cancer, as do carcinogens (substances that cause DNA damage). In some instances, the defects are inherited, meaning they affect DNA in a parent's sperm or egg cells (also called germ cells) and carry through into a developing baby. These inherited (or germline) defects will be present in every cell of the body, but their cancer-causing effects tend to be selective for specific organs, including the prostate.

For example, germline defects in the BRCA genes that boost the risk of breast and ovarian cancer in women have also been linked to aggressive, hard-to-treat prostate cancers that affect younger men. BRCA genes ordinarily repair DNA damage. When those genes are defective, DNA damage can accumulate inside cells that, in turn, grow abnormally and form tumors. Roughly a quarter of all men who have aggressive prostate cancer have defects in one or both of the BRCA genes (BRCA1 and BRCA2), but most commonly in BRCA2 alone. Men who carry a BRCA2 mutation have a risk of prostate cancer that's two to five times higher than the general population.

However, DNA repair defects aren't limited to BRCA: investigators have found dozens of inherited mutations affecting other genes that could potentially be involved in prostate cancer. Indeed, more than 50% of prostate cancer risk can be attributed to genetic factors. Fortunately, many gene defects that have been found so far in advanced prostate cancer can be targeted with existing drugs or drugs that are now in clinical trials.

## Risk factors

Risk factors are characteristics or conditions that are associated with higher odds of getting a disease. Some risk factors for prostate cancer—such as age, race, and a family history of the disease—are things



Any man can develop prostate cancer, but having a father or brother with the disease significantly increases your risk.

you cannot change. Others—such as smoking and a diet high in processed foods—are things you can control. In fact, a recent Harvard study published in *European Urology* found that a healthy lifestyle can help to reduce the odds of developing prostate cancer (and also lower the likelihood of cancer progression), even among some men who are genetically predisposed to it.

Here are some well-documented risk factors.

**Age.** The risk of prostate cancer increases with advancing years. The disease rarely occurs among men under 40. About 90% of cases are diagnosed in men over age 55, and the median age for diagnosis is 66, according to data from the National Cancer Institute. Diagnoses taper off in men ages 75 and older, partly because men in that age group aren't screened as often.

**Family history.** Prostate cancer runs in families. A man who has a father or brother with a history of prostate cancer is two to three times more likely to have the disease—or to develop it in the future—than a man with no first-degree male relatives who've had it. If two or more first-degree relatives have a prostate cancer history, the risk is five to 10 times greater than for a man with no affected first-degree relatives. The age at which relatives are diagnosed also has some bearing on the risk calculations. Diagnosis before age 60 increases the risk, probably because early-onset prostate cancer is more likely to be caused by inherited mutations.

**Race.** Black men have the highest prostate cancer incidence and death rates of any group in the United States. The incidence of prostate cancer among Black men is about 62% higher than it is among white men (191.5 vs. 114.5 per 100,000 men, according to an analysis of cases from 2017 to 2021 reported by the ACS in 2025). Moreover, Black men are more likely to be diagnosed with the disease at younger ages and are

## Prostate cancer terminology

Experts classify prostate cancer according to its propensity to spread and how it responds to treatment.

**Cancer grade** is determined by how tumor-tissue samples look under a microscope. Low-grade prostate cancer has cell features that predict slow growth, whereas high-grade cancer is more likely to grow and spread.

**Cancer risk** incorporates additional factors, including PSA. High-risk prostate cancer is therefore defined as high-grade prostate cancer accompanied by high PSA levels. Conversely, low-risk prostate cancer is low-grade cancer accompanied by low PSA levels.

**Localized prostate cancer** is contained within the prostate gland. It is typically treated with surgery or radiation and has the most favorable prognosis.

**Advanced prostate cancer** has spread from its original location in the prostate gland to other parts of the body. Treatment in some instances includes androgen deprivation therapy (ADT). ADT induces a form of chemical castration that blocks the production of testosterone and therefore testosterone's growth-promoting effects on prostate cancer cells. This will ideally eliminate the cancer or slow its growth.

- **Locally (or regionally) advanced** prostate cancer is cancer that has spread into nearby tissues. **Metastatic prostate cancer** is advanced cancer that has spread to more distant locations, such as the lymph nodes or bones.
- **Oligometastatic prostate cancer** is an early form of metastatic cancer defined by the presence of five or fewer metastatic tumors that appear on imaging.

**Biochemical recurrence** refers to a rise in PSA levels following initial treatment for local or regionally advanced prostate cancer, but without any visible metastases on imaging scans. This suggests that cancer cells lurk unseen somewhere in the body. If subsequent treatment with ADT causes PSA levels to fall—indicating that the therapy is working—the condition is called **nonmetastatic castration-sensitive prostate cancer (nmCSPC)**. If PSA levels continue to climb despite the use of ADT—indicating that the therapy is not working—the condition is called **nonmetastatic castration-resistant prostate cancer (nmCRPC)**. In recent years, more potent therapies have become available for treating this condition. These treatments suppress testosterone in ways that differ from the frontline forms of ADT generally used initially.

**Metastatic prostate cancer** is divided into two subcategories:

- metastatic castration-sensitive prostate cancer (mCSPC), which responds to ADT.
- metastatic castration-resistant prostate cancer (mCRPC), which has become unresponsive to ADT.

twice as likely to die from it as their white counterparts. This discrepancy probably reflects multiple factors, including disparities in health care.

Genetic risk factors may also play a role. A 2023 study in *European Urology* identified nine genetic variants for prostate cancer, seven of which were found either primarily or exclusively in men of African descent.

**Nationality.** Prostate cancer incidence varies greatly among countries. The highest rates are in Australia, New Zealand, Western Europe, Canada, the United States, and the Caribbean, while the lowest rates are in south central Asia (Thailand and India) and northern Africa.

**Obesity.** Obesity seems to increase the risk of developing and dying from aggressive prostate cancer, particularly among men who are overweight during their 50s and 60s. One potential explanation involves insulin, the hormone that enables cells in the body to use energy from glucose and fatty acids in the blood. Excess weight causes people to develop insulin resistance, a condition in which cells become less sensitive to insulin's effects. To compensate for this resistance, their bodies produce higher and higher levels of insulin over time. Insulin is a growth factor, so, as insulin level rises, it may help drive the out-of-control cell growth characteristic of cancer directly or through the action of related hormones called insulin-like growth factors.

**Diet.** Another factor that can increase a person's insulin levels is diet. Greater consumption of plant-based foods appears to protect against aggressive prostate cancer, especially in men older than 65. By contrast, diets that prompt greater secretion of insulin—those that are high in sugary sweets, fried foods, processed snacks, saturated fats, and starchy vegetables—also trigger chronic inflammation, which is a risk factor for a number of diseases, including prostate cancer, according to a 2023 review paper published in *Prostate Cancer and Prostatic Diseases.*

Men who eat a lot of red meat or high-fat dairy products also seem to have a higher risk of developing the disease. Scientists have linked diets high in cholesterol and saturated fat—the type of fat found in fatty beef and cheese—to prostate cancers that are more aggressive, while diets rich in fruits, vegetables, legumes, nuts, and fish are protective against aggressive prostate cancer.

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Eating plenty of plant-based foods, including vegetables, may help lower the risk of developing aggressive prostate cancer.

**Alcohol.** As for drinking and prostate cancer risk, the evidence is mixed. Overall, it suggests that excessive alcohol use—and binge drinking in particular—may elevate prostate cancer risk, while alcohol use in moderation poses little to no risk of prostate cancer. Dr. Marc Garnick, editor in chief of this guide, cautions patients to avoid alcohol altogether, or to at least curtail their drinking during the first two months of starting a cancer medication to limit the chances of liver damage. Such damage might be mistaken for a drug side effect, and the drug would then have to be stopped.

**Smoking.** Smoking isn't as strongly associated with prostate cancer as it is with cancers of the lung, kidney, and bladder. But results from a large 2024 analysis published in *Cancer Causes and Control* show that smokers do have a higher risk of a more aggressive form of the disease than men who never smoked. Another 2023 study in *Tobacco Induced Diseases* supports these conclusions: Swedish investigators, reviewing health and smoking data from more than 350,000 men, found that smokers were more likely than nonsmokers to die from prostate cancer, especially if they were overweight or obese.

**Ejaculation frequency.** Harvard researchers have found that men who ejaculate frequently have a lower risk of prostate cancer. During a large study, men who

ejaculated more than 21 times per month had a 20% lower prostate cancer risk than those who ejaculated seven or fewer times per month. It's not clear why frequent ejaculation is protective, although some experts believe the release of semen flushes harmful substances from the prostate.

## Can prostate cancer be prevented?

Prostate cancer development is incredibly complex, and there's no surefire way to prevent the disease. That said, certain lifestyle habits and medications called 5-alpha-reductase inhibitors might help tip the odds in your favor. (Note that the information in this section focuses on primary prevention, meaning the prevention of prostate cancer in men who have never had it. For information on reducing the chances of a cancer recurrence, see "Make smart lifestyle changes," page 92.)

### Diet

"What can I eat—and what foods should I avoid—to reduce my risk for prostate cancer?" This is one of the most common questions physicians hear from men concerned about prostate health. There is evidence that certain foods or dietary patterns, especially plant-based diets, can help to lower the risk of prostate cancer progression in men who already have the disease. However, the evidence that dietary choices can help prevent cancer, while compelling, is not definitive.

**Fruits and vegetables.** Diets rich in fruits and vegetables may reduce the risk of prostate cancer. Carotenoids—compounds that occur naturally in certain plants—have antioxidant properties that may protect the body against unstable molecules that damage DNA. One frequently studied carotenoid is lycopene, the compound that gives tomatoes their bright red hue. Epidemiologic research has shown a correlation between eating tomato-based foods and lower prostate cancer risk. Pasta lovers will like this: two servings of tomato sauce a week seem to be enough to give some protection. But lycopene supplements have flopped in studies.

**The Mediterranean diet.** Prostate cancer death rates are much lower in the Mediterranean countries of southern Europe than in Scandinavia, Great Britain, and other parts of Europe. Any number of reasons could explain the difference, but the foods people eat might be one of them. The classic Mediterranean diet includes lots of fruits and vegetables, whole grains, nuts, olive oil rather than butter, and fish and poultry instead of red meat.

The Mediterranean diet is healthy, but its impact on prostate health is unclear.



Many studies show that this dietary pattern limits chronic low-grade inflammation and contributes to good health, especially when it comes to preventing heart disease and stroke. But the evidence regarding prostate cancer is inconclusive. A 2025 review published in *European Urology* concluded that consuming a Western diet high in processed foods, red meat, high-fat cheese, and added sugars elevates prostate cancer risk. But the results also showed that consuming a Mediterranean diet was not protective against the disease.

### Exercise

Some evidence suggests men can lower their likelihood of getting prostate cancer with regular exercise. Indeed, Harvard researchers have published findings suggesting that men who engage most frequently in vigorous activity might lower their risk of developing advanced prostate cancer by as much as 30%. Participants in the study also had a 25% lower risk of dying from prostate cancer compared with men who exercised the least.

A study in the *British Journal of Sports Medicine* provided additional evidence of protective effects from exercise. Published in 2024, the study followed 57,652 men for nearly seven years. Findings showed that men who had worked to improve their cardiovascular fitness had a 35% lower risk of developing prostate cancer than men with lower fitness levels. Why exercise might lower cancer risk isn't entirely clear, but researchers behind this study noted that cardiovascular fitness is associated with lower levels of cancer-promoting inflammation in the body.

### 5-alpha-reductase inhibitors

No medications have been approved by the FDA for the purpose of preventing prostate cancer. However, drugs known as 5-alpha-reductase inhibitors, or 5-ARIs—which include finasteride (Proscar) and dutasteride (Avodart)—are sometimes prescribed off-label to men at high risk of developing prostate cancer for this reason.

Finasteride and dutasteride are more commonly used to treat benign prostatic hyperplasia (BPH; see page 12) or hair loss. They inhibit an enzyme called 5-alpha-reductase type 2, which the body uses to convert testosterone into a more potent hormone, dihydrotestosterone (DHT). DHT not only promotes the growth of normal prostate tissue but also fuels the growth of tumors. For that reason, doctors and scientists long hoped that men who took one of these 5-ARIs would be less likely to develop prostate cancer.

A 2022 analysis with over 20 years of follow-up bore out that hope, finding that men who took a 5-ARI were less likely to be diagnosed with prostate cancer as well as less likely to die of the disease if they developed it. The catch: other research has found that men diagnosed with prostate cancer while taking these drugs have a slightly higher risk of developing aggressive forms of the disease. These medications have carried a black box warning about this risk since 2011.

If your physician suggests taking finasteride or dutasteride for BPH, Dr. Garnick advises having a baseline PSA test and then another five to six months later. If PSA doesn't decrease by at least 50%, consult a urologist, who may recommend a biopsy.

The latest data on 5-ARIs and cancer, published in 2024 by a Canadian research team, is somewhat reassuring. After reviewing health records from nearly 20,000 prostate cancer patients, the researchers found that 5-ARI users did not have an elevated risk of dying from the disease. These drugs can safely be used to treat BPH and prevent prostate cancer, they concluded, and suggested the black box on their labels be removed.

Men who take 5-ARIs for any reason should be aware that these drugs lower PSA levels in the blood by about 50%. Anyone taking finasteride or dutasteride should have their PSA levels monitored closely. That includes men who use either drug to treat BPH, as well as those who use finasteride to treat baldness (finasteride is the active ingredient in Propecia). A Propecia pill contains just 1 mg of the drug, versus 5 mg for the BPH medication, but even this small dose can decrease PSA by 50% over the course of a year. Your doctor will need to compensate for the effect of the drug by doubling your PSA measurement. If PSA levels go up, remain steady, or fail to decline by at least 50%, a referral to a urologist and a biopsy may be in order.

It's important to note that some men experience mood changes and persistent problems with sexual function after taking finasteride. The condition even has a name—post-finasteride syndrome—and among its many reported symptoms are libido loss, erectile dysfunction, panic attacks, anxiety, and depression, especially early in treatment. A 2023 study published in *Scientific Reports* of nearly 300,000 men even found an association between finasteride and suicidal thoughts, although this was only evident in men with a history of psychiatric disorders. However, a more recent meta-analysis of studies enrolling a combined total of over 2 million men, which was published in *European Urology Focus* in 2024, found no evidence linking 5-ARIs with depression or suicide.

### Other potential preventive agents

Other drugs and vitamins have been proposed as potential cancer-prevention agents, but there's not much evidence to support such claims. Rigorous studies have debunked the once-popular notion that vitamin E supplements reduce prostate cancer risk. (Instead, they appear to increase it.) What might help?

**Vitamin D.** A number of studies have correlated low vitamin D levels with various cancers, including higher risks of high-grade, more-advanced prostate tumors. Sufficient intake of vitamin D might therefore be one potential way to reduce your overall risk. However, the evidence is not conclusive, and some studies have shown no prostate cancer prevention or treatment benefits from vitamin D supplements.

**Statins.** Some evidence suggests statins may exert anti-cancer effects. These cholesterol-lowering drugs also lower levels of testosterone, a hormone

## Do vasectomies raise the risk of prostate cancer?

A vasectomy is a surgical procedure in which the tubes that carry sperm are cut and sealed. Some data have suggested this procedure could increase the risk of prostate cancer, but the evidence is mixed. A review of 53 studies with a total of more than 2.5 million men found no evidence linking the birth control procedure to high-grade or advanced prostate cancer. The authors of the study emphasized that worries over prostate cancer should not preclude men from getting a vasectomy.

A later study with more than two million men linked vasectomy to small increases in prostate cancer risk over time, which the authors said was similar in magnitude to the risk of breast cancer among women who use oral contraceptives.

However, many specialists, including Dr. Garnick, editor in chief of this publication, say risks of prostate cancer from vasectomy have not been conclusively shown.

that's required for cholesterol synthesis. Testosterone also drives prostate tumors to grow, and studies have found statin users have a lower risk of advanced and fatal prostate cancers than non-users.

## Screening

There are two types of screening for prostate cancer. The first one—the digital rectal exam (DRE)—is well accepted among doctors. PSA testing, the second type, is common but controversial.

### Digital rectal examination

In case you had any doubt, the word "digital" here doesn't have anything to do with computers or data. Rather, the digit in the DRE is the doctor's lubricated, gloved finger inserted into the rectum. Because the prostate sits in front of the rectum, the doctor can feel part of it through the rectal wall. A normal prostate is small—about an inch and a half from side to side—and feels smooth and rubbery. Swelling, lumps, firm knots, or abnormally textured areas may indicate prostate cancer or another condition.

Early cancerous tumors are often too small to detect during a DRE, and some are located in areas a doctor's finger can't reach. Only the back of the gland can be felt, but this is where most prostate cancers develop. For these reasons, clinicians who use DRE alone to screen for prostate cancer may miss the smallest and most treatable tumors. At the same time, small tumors that can't be felt by the physician may be less likely to cause future problems.

### Prostate-specific antigen test

Most men with prostate cancer don't have any symptoms in the initial stages of the disease (see "Symptoms of prostate cancer," page 39). And the DRE doesn't find small cancers or those in the front (anterior) portion of the gland. So when the prostate-specific antigen (PSA) test was introduced as a screening test during the 1990s, it took off. The idea of catching cancer early, when it's more treatable, is a powerful one, and studies show that PSA tests save roughly one life for every 1,000 men screened over 10 years.

These tests measure the amount of PSA in your blood. All prostate cells make PSA, a protein that helps to dissolve semen so that sperm cells can more easily reach and fertilize an egg. Normal and cancerous cells in the prostate each make PSA in similar amounts. But since cancer cells are leakier, they release more of the protein into the bloodstream.

What constitutes a high PSA reading? Most experts agree that a PSA level is abnormal once it rises above 4 nanograms per milliliter (ng/mL) of blood. Studies have suggested that a man who has a PSA of 4 to 10 ng/mL has a 25% chance of having prostate cancer; if his PSA is greater than 10, the likelihood increases to more than 50%. But other research suggests the traditional cutoff point of 4 ng/mL may be too high. So we should probably think of PSA values as being on a continuum, with higher values associated with a greater likelihood of having prostate cancer.

Because PSA is not solely produced by cancer cells, however, an elevated score doesn't always point to cancer. The prostate leaks more PSA, not just when cancer is present, but also when the gland is irritated or damaged. As a result, elevated PSA levels can accompany other noncancerous conditions, including BPH and prostatitis. Levels can also rise after recent

sexual activity, bike riding, recent urinary infections, or recent urinary catheterization (see "What causes PSA levels to rise or fall?" on page 40). And some men's prostates naturally release more of the protein into the blood than others.

That means a high PSA level can cause a false alarm. The opposite problem also exists, in that the PSA test misses cancer about 15% of the time. To help get a sense of what's normal for a particular patient, some experts argue that men should at least get a baseline PSA measurement during their 40s or early 50s and then have more tests later, depending on the initial results and other risk factors. Either way, men should be aware of the potential risks and benefits of PSA screening before making such a decision.

Even if the PSA test performs as desired and leads to further tests that confirm prostate cancer, that cancer may be very slow-growing (indolent), meaning it's unlikely to cause any harm. Doctors use the term "overdiagnosis" to refer to detection of a prostate cancer that wouldn't have caused any problems and would have gone undetected were it not for screening. According to Dr. Garnick, a disproportionate number of screening-detected prostate cancers fall into the overdiagnosis category, and the figures are highest for older men.

If overdiagnosis merely failed to deliver benefits, that would be one thing. But it can also lead to harm. If a man has an elevated PSA level, doctors often order a prostate biopsy, which can cause pain, bleeding, or other complications—the most worrisome being infection, which can be serious enough to require hospitalization. Furthermore, once diagnosed, many men choose to undergo treatment, prompting worries that an excessive number of them are being treated for prostate cancer that may never be life-threatening as well as risking serious treatment-related complications.

Accordingly, in 2012, the U.S. Preventive Services Task Force (USPSTF) issued guidelines recommending against routine PSA screening, regardless of age, race, or family history. Prostate cancer screening rates fell by roughly 25% after those guidelines were published. Initially, cancer cases also fell, presumably because many cases weren't being detected. But studies have since shown that new diagnoses of advanced prostate cancer rose after that recommendation. A 2025 study found that the incidence of metastatic prostate cancer in the United States increased by 3% annually between 2014 and 2021, especially among men younger than 55. Diagnoses of early-stage cancer also increased among men 70 and older during the same time period.

The USPSTF did soften its anti-testing stance in 2018, largely because men with low-risk prostate cancers flagged by PSA screening are increasingly opting for active surveillance rather than immediate treatment, thereby avoiding unnecessary cancer therapies and their associated harms, perhaps indefinitely. The revised guidelines recommend that clinicians inform men ages 55 to 69 about the potential risks and benefits of PSA screening, but advise against screening men over 70 and give no recommendation for men younger than 55. New PSA screening guidelines from the USPSTF were being prepared as of this writing.

The true long-term effects of reduced PSA screening will not be known until researchers can assess its impact on survival. Given that prostate cancer is in many cases a slow-growing disease, this will take years to ascertain. In the meantime, other expert groups have

### Symptoms of prostate cancer

Many men with prostate cancer have no symptoms. But because the prostate gland is enlarged both in cancer and in nonmalignant conditions such as BPH, these very different conditions share many of the same symptoms. Contact your physician if you notice any of the following signs or symptoms:

- a need to urinate frequently, particularly at night
- difficulty starting or stopping urination
- a weak or interrupted urinary stream
- an inability to urinate
- pain or burning when you urinate
- painful ejaculation
- blood in your urine or ejaculate
- frequent pain or stiffness in your lower back, hips, or upper thighs.

weighed in with their own screening recommendations. Among them:

- Guidelines from the American Urological Association (AUA) recommend that doctors offer a baseline PSA test and then further testing every 2–4 years to men ages 45 to 50. But routine screening starting at age 45 should be reserved for men with Black ancestry, certain inherited mutations, or a strong family history of prostate cancer. For all men ages 50 to 69, the AUA advises regular prostate cancer screening every two to four years. The guidelines further advise doctors to work with each patient to make a joint decision based on the individual's values and preferences.
- The ACS recommends against screening until men discuss the associated uncertainties with their doctors. The ACS position is that these discussions should begin at age 50 for men at average risk, at age 45 for men at higher risk (such as Blacks or men with a father, son, or brother who had prostate cancer), and at age 40 for men who have more than one first-degree relative who developed prostate cancer at an early age.

### What causes PSA levels to rise or fall?

These factors typically produce a substantial or sustained rise in PSA:

- benign prostatic hyperplasia
- prostatitis
- urinary tract infections
- prostate biopsies
- prostate cancer.

These factors sometimes produce a small or temporary rise in PSA:

- ejaculation
- a digital rectal examination
- a urinary catheter and bladder examination
- vigorous bike riding
- warm climates
- changes in laboratories or testing methods
- hepatitis
- bypass surgery.

These factors typically produce a substantial or sustained decrease in PSA:

- therapy with finasteride (Proscar) or dutasteride (Avodart)
- use of finasteride in a smaller-dose formulation (Propecia) as a treatment for hair loss
- prostate cancer surgery.

These factors sometimes produce a small or temporary decrease in PSA:

- therapy with a statin (for cholesterol) or a thiazide diuretic (for blood pressure)
- therapy with a nonsteroidal anti-inflammatory drug, such as ibuprofen
- obesity
- changes in laboratories or testing methods.

## Should you be tested?

Choosing whether to be tested is a decision that should be informed by discussions with your doctor. Importantly, slow-growing, non-aggressive cancers detected by PSA screening may pose no immediate threat, especially to older men who may die of other causes long before the prostate cancer would have progressed. An elevated PSA level may cause needless worry and unnecessary treatment, but it can also lead to early cancer detection and better outcomes. Your doctor can help you understand the varied uncertainties and potential benefits of getting a PSA test (see "Take-home messages about PSA screening," page 43).

Your race and family history are two key factors to consider. Since Black men are at higher risk of developing and dying from prostate cancer than men of other races, for example, they might consider screening more often. A 2022 study in *JAMA Oncology* supports that advice. The investigators reviewed health records from nearly 46,000 male U.S. veterans gathered between 2004 and 2022 and found screening lowered the risk of prostate cancer mortality for all participants, but that annual screening was especially beneficial for Black men.

Men of any race who have first-degree relatives with prostate cancer might also consider early screening, especially if testing has identified they also have genetic risk factors for the disease. Studies have shown that prostate cancer patients with close relatives who also had the disease are more likely to survive it, possibly because they are more aware of their own risk and therefore more likely to be screened and diagnosed during early stages.

If you decide to have a PSA test, keep in mind that PSA levels can vary for reasons unrelated to cancer. Before acting on a surprisingly high PSA, consider repeating the test in a month or two to confirm the result.

### Variations on the PSA test

Rather than subject everyone with an elevated PSA reading to a biopsy, sometimes doctors will order additional tests, described below, that involve more-detailed interpretations of PSA levels.

**Free PSA.** PSA circulates in the blood in two forms—either bound to other proteins or unbound (free). Several studies suggest that men with elevated PSA levels who have a very low percentage of free PSA are more likely to have prostate cancer. By contrast, higher circulating levels of free PSA are typically associated with benign prostate conditions.

Measuring the free PSA level may be useful when considering whether a biopsy is the appropriate next step. Many doctors recommend biopsies in men with a free PSA level of 10% or less and advise men to consider a biopsy if the free PSA level is between 10% and 25%.

**PSA density.** Dividing the total PSA level (in ng/mL) by the volume of the prostate gland in milliliters yields a measure known as PSA density. PSA densities higher than 0.15 ng/mL may be associated with prostate cancer. A 2024 study in *JAMA Open Network* showed that combining PSA density tests with magnetic resonance imaging (MRI) is helpful for diagnosing aggressive cancer in the prostate and may help some men avoid unnecessary biopsies.

**PSA velocity.** Some physicians rely on a measure known as PSA velocity, which tracks how much a PSA reading increases from one test to the next. In order for your doctor to calculate PSA velocity, you will need at least four PSA tests, which are typically taken over an 18-month period (at baseline, 6 months, 12 months, and 18 months).

PSA scores tend to rise more rapidly in men with cancer than in those with BPH, and some research has shown that men with prostate cancer who have rapid increases in PSA are more likely to die from the disease than those with slower-rising levels. However, PSA velocity is controversial, and evidence shows it can lead to large numbers of unnecessary biopsies. According to Dr. Garnick, PSA levels rise normally as men get older, so you should check with your doctor to be sure any increases are within normal bounds for your age group.

**Prostate Health Index.** The Prostate Health Index (PHI) is a single test that combines three different measurements: total PSA, free PSA, and an "isoform" of PSA called proPSA. Isoforms are variants of a given protein—in this case PSA—each made from the same gene, but with a slightly different mix of building blocks called amino acids.

The PHI incorporates these three measurements into a formula to generate a combined score that indicates the likelihood of cancer. It is FDA-approved for use in men 50 and older with PSA levels between 4 and 10 ng/mL whose rectal exams do not show evidence of cancer. About 25% of men with PSA levels in this range have cancer; the other 75% do not.

Some evidence suggests PHI scores are better at predicting prostate cancer than PSA by itself, especially when the cancer is aggressive. Incorporating the PHI into cancer screening could therefore reduce unnecessary biopsies without sacrificing the detection of high-grade cancers that need treatment. The PHI test is also being used to check for tumor growth among men on active surveillance, which is an alternative to immediate treatment for low-risk prostate cancer (see page 49).

More recently, researchers have developed a value called PHI density, or PHID, which is the PHI divided by the prostate volume as measured on MRI. Evidence published in 2023 suggests this test can help to reduce unnecessary biopsies more so than PHI by itself.

**IsoPSA Assay.** The IsoPSA assay is a test that analyzes PSA isoforms in a blood sample, focusing on those linked to prostate cancer while ignoring benign ones unrelated to the disease. Unlike the PHI, which measures just one isoform (proPSA), IsoPSA examines many different isoforms at once. The resulting isoform pattern helps to distinguish more aggressive cancers from less aggressive ones, and gives doctors additional guidance for determining which men with abnormal results on a PSA test should consider a prostate biopsy. The FDA approved this test in 2025 for men aged 50 and over with elevated PSA levels.

## PSA and prostate cancer in transgender women

Anyone with a prostate has the potential to develop prostate cancer. That includes transgender women. Gender-affirming medical care lowers the risk, but does not eliminate it.

Many transgender women take hormones that suppress testosterone, a male hormone that can fuel the growth of prostate cancer. Some opt for surgery, which also drops testosterone (if the testes are removed). However, genital reconstruction surgery doesn't mean losing your prostate. Because removing this gland can cause urinary incontinence and other complications, doctors usually leave it in place.

How to screen for prostate cancer in the transgender population isn't totally clear, as no official guidelines exist. Monitoring PSA levels can be helpful, but hormone treatments that block testosterone interfere with the body's ability to make PSA. Studies have shown that PSA levels in transgender women with prostate cancer are much lower than they are in cisgender males with the disease.

A 2023 review published in *European Urology* recommends that people meeting age criteria for PSA screening get tested before they start gender-affirming treatment. This measurement can serve as a baseline and be used to help interpret future test results. However, most doctors recommend further evaluation if PSA value is greater than 1 ng/mL.

**4Kscore.** The 4Kscore is another combination test. It combines total PSA, free PSA, intact PSA (bound to proteins, making it the opposite of free PSA), and an enzyme called human kallikrein 2, which is secreted by prostate cancer cells and ordinarily found at very low levels in the blood of men who do not have prostate cancer

Several studies have shown that the 4Kscore correlates with the outcome of a prostate biopsy. It therefore might help men decide whether to proceed with a biopsy or choose active surveillance. A study in 2023 in *Urologic Oncology* also found the 4K score is more informative when combined with MRI.

## Imaging

Many prostate cancers today are diagnosed at the earliest stages, when a tumor may be no bigger than a pea. Radiologists are continually trying to improve the imaging techniques that enable physicians to better understand how extensive a prostate cancer is and where it is located in the gland—details that can be used along with other clinical information, such as the biopsy findings that confirm a cancer diagnosis, to help predict how aggressive a tumor is.

### Transrectal ultrasound

Doctors use transrectal ultrasound (TRUS) when they suspect prostate cancer based on an abnormal DRE or an elevated PSA. To conduct the test, a small, lubricated probe is placed in the rectum. It emits sound waves that enter the prostate and create echoes, which a computer turns into black and white images of the prostate. These images can also guide biopsies of the prostate, helping to delineate the gland's anatomy and pinpoint any suspicious areas.

### Micro-ultrasound

Micro-ultrasound uses higher-frequency sound waves than conventional ultrasound, thereby visualizing anatomic structures with up to 300% better resolution. Imaging results may rival those of MRI for detecting aggressive prostate cancer, which potentially makes it a good option for men who are unable to undergo MRI because of claustrophobia or surgically implanted medical devices. The catch is that it's not yet widely available. Late-stage clinical trials investigating its use for prostate cancer diagnosis are now ongoing.

### Magnetic resonance imaging

An MRI machine uses a very large magnet, a radiowave transmitter, and a computer to construct detailed pictures of structures inside the body. Cancerous tissue has a different set of magnetic properties than normal tissue, and MRI can capture these differences.

MRI of the prostate can be done with or without an endorectal coil, a thin wire covered with a small inflated balloon that's inserted in the rectum. Once the MRI machine is turned on, the coil receives the magnetic waves. The closer the coil is to the target tissue, the stronger the signal and the clearer the images. The endorectal coil can be uncomfortable, so your doctor may inject a muscle relaxant to help muscles in the rectal wall

## Take-home messages about PSA screening

- Screening doesn't lower your risk of having prostate cancer; it increases the chance you'll find out if you have it.
- PSA testing can detect localized or microscopic cancers that a digital rectal examination would miss.
- A "normal" PSA level of 4 ng/mL or below doesn't guarantee you are cancer-free; in about 15% of men with a PSA below 4 ng/mL, a biopsy will reveal prostate cancer.
- PSA levels can increase after ejaculation or other activities that stimulate or jostle the prostate, such as bike riding, horseback riding, or riding an all-terrain vehicle. Men who choose to get a PSA test should abstain from such activities for three days prior to getting tested.
- An elevated PSA level may prompt you to seek further diagnostic tests and, if cancer is found, lead to treatment, resulting in possible urinary and sexual side effects.
- Conditions other than cancer—BPH and prostatitis, for example—can elevate your PSA level.
- PSA levels are generally lower in obese men than they are in lean men.
- Levels of free PSA (PSA that is not bound to proteins in blood) tend to fall in men who have prostate cancer as opposed to more benign conditions. A separate test of free PSA is most helpful when the regular PSA test level is between 4 and 10 ng/mL.

relax. Some patients also receive a mild sedative to ease any anxiety.

Doctors use MRI in the following scenarios:

- to determine whether an elevated PSA, abnormal DRE, or both, point to cancer. If the MRI is negative, you might not need to have a biopsy.
- to generate images to guide a biopsy procedure (called an MRI-guided biopsy)
- to assess how far cancer may have spread in men who already have an established diagnosis
- to determine whether someone is a good candidate for active surveillance instead of immediate treatment (provided they have low- to medium-risk prostate cancer).
- to monitor potential changes in the prostate that may need to be treated.

One of the reasons MRI is so valuable is that it provides high-resolution images of the entire prostate. That's a significant advantage, given that prostate cancer in most men is multifocal, meaning it occurs in more than one part of the gland.

**Multiparametric MRI (mpMRI)** is a hybrid approach that improves diagnostic accuracy. Also called a three-part MRI, it combines three different images (also known as sequences):

- a traditional MRI image, which reveals the prostate's internal structures
- an image that tracks how freely water molecules move inside the prostate. Tumors have tightly packed cells, so water movements are more restricted.
- an image that tracks how an intravenously injected dye moves through the gland. The dye reveals abnormal blood vessel patterns associated with cancer.

This three-part approach is so accurate that many experts now advocate for using mpMRI instead of a biopsy to check for tumors in men suspected of having prostate cancer. In fact, guidelines issued by the European Association of Urology state that men with

**Avoiding biopsy when an MRI is negative**

Scan the QR code to read the *New England Journal of Medicine* study.

© simonkr | Getty Images

Your doctor might order an MRI to check for prostate cancer or find out whether the disease has spread.

elevated PSA levels can skip diagnostic biopsies if their mpMRI scans are normal, but only after discussing the pros and cons with a doctor. The aim is to reduce the number of unnecessary biopsies and the potential side effects that come with them. (If an mpMRI is positive, a biopsy would be warranted.)

Clinical trials investigating an mpMRI-first strategy are generating promising results. In a 2024 study reported in *JAMA Oncology*, researchers gave nearly 600 men with suspected prostate cancer an mpMRI. The 233 men with negative mpMRI results were then followed for three years; among them, just 4% developed aggressive prostate cancer. The researchers concluded that men with a negative mpMRI can safely avoid biopsy as long as they are monitored appropriately. Furthermore, a 2024 study in the *New England Journal of Medicine* showed that omitting biopsies in mpMRI-negative men with PSA levels of 3 ng/mL or higher cut the diagnosis of clinically insignificant cancers—the kind that likely don't need treatment—by more than half.

Additionally, evidence is increasing that mpMRI scanning may allow men on active surveillance for low-risk cancer to forgo repeat biopsies. During one study, mpMRI detected significant prostate cancer at least 92% of the time. When a biopsy is warranted, a skilled urologist can also use mpMRI images to target a biopsy in an area that appears abnormal.

The downside: mpMRI is an expensive and lengthy procedure that can take up to an hour to perform. However, a more streamlined version of the technology, called **biparametric MRI (bpMRI)**, might be just as effective. A bpMRI omits the injected dye and relies solely on the other two types of image sequences used in mpMRI.

According to a 2025 study published in the *Journal of the American Medical Association*, bpMRI and mpMRI are equally good at detecting aggressive tumors that need treatment. But bpMRI offers important advantages: it takes just 10 minutes to perform and avoids the allergic reactions some men have to injected dyes used in mpMRI.

At the moment, mpMRI and bpMRI are generally available only in academic teaching hospitals, but will likely become more widespread in the coming years: Dr. Garnick believes bpMRI will eventually become the preferred imaging test for prostate cancer screening.

Another MRI technique, called **MRI spectroscopy**, analyzes the chemical composition of tissue. This technique provides information that can help doctors distinguish between prostate cancer and benign prostate tissue. At this point, MRI spectroscopy is used only at research centers.

### Positron emission tomography

Where MRI and ultrasound are used mainly for localizing and characterizing tumors within the prostate gland itself, positron emission tomography (PET) scans are used to look for prostate cancer that may have already metastasized, or spread, to other parts of the body, such as lymph nodes or bones.

PET scans differ from other types of imaging in that, instead of revealing physical structures in the body, they look for high rates of metabolic activity. Cancer cells are more metabolically active than normal cells. They grow and divide rapidly and therefore consume glucose, a sugar, in high amounts.

During a PET scan, a small amount of a minimally radioactive substance, called a radiotracer, will first be injected into a vein in your arm. The radiotracer travels in the bloodstream and collects in areas with high metabolic activity—including cancer cells.

The most selective PET tracers for prostate cancer bind to a protein called prostate-specific membrane antigen (PSMA) in the prostate cancer cell membrane. Three such tracers have been approved by the FDA:

- Gallium-68 PSMA-11 (Illuccix, Locametz), which uses gallium as the radioactive element, won FDA approval in 2020. Studies have shown it can detect prostate cancer metastases with greater than 90% accuracy. The tracer is approved specifically for the initial diagnosis and staging of prostate cancer patients with biochemical recurrence who might be curable with radiation or surgery.
- Piflufolastat F18 (Pylarify) was approved by the FDA in 2021, also for use in detecting metastatic or recurring prostate cancer. It uses fluorine as the radioactive element.

- Flotufolastat F18 (Posluma) was approved in 2023, similarly for use in men who are suspected of having metastatic prostate cancer or a recurrence of a previously treated cancer. It has properties that allow for higher and clearer resolution of very small tumors.

PSMA scans are particularly useful for diagnosing oligometastatic prostate cancer, which is defined by the presence of five or fewer metastases in the body that may not yet be visible with older imaging tests. Men who have this condition can be treated with a new approach called metastasis-directed therapy, which focuses highly targeted radiation directly on tiny cancerous deposits, sparing healthy surrounding tissues. Dr. Garnick says that PSMA scanning and other advanced imaging techniques are revolutionizing prostate cancer diagnostics and treatment, especially for oligometastatic disease (see "Treating oligometastatic prostate cancer," page 69).

## Biopsies and diagnosis

If your doctor suspects you have prostate cancer on the basis of an elevated PSA level, an abnormal DRE, or one of the imaging tests described above, the next step may be a biopsy. This procedure entails removing small pieces of tissue from the prostate and sending them to a laboratory to check for cancerous cells. If cancer is found, the characteristics of the biopsied cells, along with findings from other tests, enable the doctor to classify its severity.

### The biopsy procedure

Doctors may choose among several approaches for taking prostate biopsies, depending on such factors as the purpose of the biopsy, the location of the suspicious area, and your health.

**Transrectal biopsy (TRUS biopsy).** The most common biopsy procedure is the transrectal ultrasound–guided biopsy, usually called a TRUS biopsy. While you lie on your side, the doctor inserts an ultrasound probe into your rectum and scans the prostate. A separate spring-loaded device rapidly inserts a needle through the rectal wall into the prostate and retrieves a tiny tissue sample. The doctor uses the ultrasound image as a guide in taking biopsies from specific areas. The standard used to be six samples, or cores, but now 10 to 12 cores are often taken. Some medical centers perform "saturation" biopsies that involve retrieving 20 to 30 samples, but the optimal number of cores remains uncertain.

After the ultrasound probe is introduced and before the biopsies are taken, the doctor may inject an anesthetic into the prostate, guided again by the ultrasound image. Even with anesthesia, you may feel a slight pinch when each tissue sample is taken. The procedure itself usually takes less than 15 minutes.

TRUS biopsies are quick, relatively inexpensive, and safe the vast majority of the time. But they also have some drawbacks and risks. Some men have blood in their semen for about four to eight weeks afterward. This can be alarming, but it is usually harmless. To avoid excessive bleeding, you may be instructed not to take aspirin or similar drugs, such as ibuprofen (Advil, Motrin) or naproxen (Aleve), for a week before the biopsy. Additionally, up to 25% of men experience lower urinary tract symptoms (having to urinate often, poor stream, dribbling, and so on), although this is almost always temporary. Repeat biopsies can increase the likelihood of erectile dysfunction, especially in older men.

TRUS biopsies can also have more serious consequences. The needle to collect the specimen goes through the rectum, so there's a chance that fecal bacteria from the rectum will be introduced into the prostate gland or escape and spread to the bloodstream (septicemia); this happens about 1% to 2% of the time. These sorts of biopsies also come with a risk of urinary tract infections, especially for men who have had such infections before.

It's now accepted practice to take antibiotics before and after transrectal biopsies to guard against infections, but they can occur anyway—and, though still rare, serious infections from bacteria that can't be treated with conventional antibiotics are increasing. Strategies for reducing infections include cleansing the rectum with povidone iodine (the same iodine solution you can buy at the drugstore) and enemas. Doctors can also culture bacteria obtained from a rectal swab to screen in

advance for antibiotic-resistant strains. Targeting antibiotics to the specific bacteria in the patient's rectum has been proposed, and 2024 guidelines from the European Association of Urology recommend this approach, suggesting it can help reduce infectious complications.

**Transperineal biopsy.** Another way to minimize the risk of infection is to bypass the rectum altogether. With an alternative approach, doctors insert the biopsy needle through the perineum (the area between the anus and the base of the scrotum) under guidance from ultrasound. Recent clinical trials have consistently found that transperineal biopsies lower rates of infection without compromising cancer detection. A 2025 review of 10 clinical trials found that transperineal biopsies lowered the risk of hospitalization for infectious complications by 77% when compared with TRUS biopsies.

Some evidence also suggests transperineal biopsies are better than standard TRUS biopsies at detecting high-grade tumors, including those located in the anterior (front) of the prostate that may not be identified by prebiopsy MRI. In 2025, British researchers reported findings from a clinical trial in *The Lancet Oncology* showing that, when compared with TRUS biopsies, the transperineal method detected more high-grade cancer in men flagged by PSA screening or abnormal DRE.

Transperineal biopsies are now favored in many countries and are becoming more widely adopted in the United States, where the TRUS method still predominates. In 2023, for the first time, the AUA and the Society of Urologic Oncology issued guidelines endorsing the alternate approach.

Transperineal biopsies may be especially appropriate if antibiotic-resistant bacteria are detected in a rectal swab. They are also performed for patients who have had colon or rectal cancer surgery, for whom access through the rectum may be difficult. In addition, the transperineal approach may also be used during a mapping biopsy (see Figure 5), when cancer has already been diagnosed and the surgeon plans to remove only the affected area of the prostate rather than the entire gland.

Transperineal biopsies require general as well as local anesthesia, and doctors who perform them need additional training.

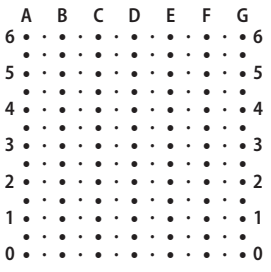
**MRI-guided biopsy.** MRI scans generate detailed images of the prostate that can help doctors find cancers they might otherwise miss with ultrasound imaging. One approach is to take an MRI scan of the prostate before the biopsy and then, with computer software, fuse that high-resolution image with the real-time images generated by ultrasound during the biopsy procedure. These MRI-guided biopsies help doctors pinpoint suspicious areas better and thereby make the biopsies more accurate.

The AUA and the Society of Abdominal Radiology both recommend that men undergo an MRI-guided biopsy if high PSA levels suggest prostate cancer but a TRUS biopsy does not find any. A 2023 study published in *Cancers* provided support for this, showing that MRI-guided biopsies detected more intermediate- and high-grade tumors than TRUS biopsies alone.

Experts are continuing to study how to use MRI imaging and MRI-guided biopsy to increase the likelihood of detecting cancer. Some research suggests that, in certain cases, it may be better to use both the TRUS and MRI-guided methods together. MRI-guided and TRUS biopsies combined have been shown to detect high-grade tumors more effectively than either method alone.

Meanwhile, a newer alternative to MRI-guided biopsy is emerging. Guided by micro-ultrasound instead

### *Figure 5: Mapping biopsy*




During a mapping biopsy, prostate tissue samples are taken every 5 millimeters, front to back and side to side. The radiologist places a grid over the perineum to aid the process. Each dot on the grid represents a hole through which a needle can be inserted. This allows doctors to map the location of tumors in three dimensions and determine if a patient might be a candidate for focal therapy (see page 62).

of MRI, this newer approach also generates high-resolution images of the prostate, but at less cost. In a 2025 study of 677 men published by the *Journal of the American Medical Association*, researchers found that microsound-guided and MRI-guided biopsies were equally effective when it came to detecting high-grade prostate cancer.

## Staging

If inspection of the biopsied tissue confirms prostate cancer, more tests may be ordered to find out if the cancer has spread to other parts of the body. CT or MRI scans help detect the spread of malignant cells to surrounding tissue, including the lymph nodes. A bone scan can reveal areas of bone that contain cancer. But these tests are not always accurate for detecting cancer that has spread beyond the prostate, and not all men need them, particularly if they have tumors with lower Gleason scores (see "How fast is it growing?") and lower PSA levels. In some situations, however, doctors use imaging tests to help assign a stage to the cancer.

Recently, doctors have begun using PSMA scans (see "Positron emission tomography," page 44) to search for small, newly formed tumors that may be too small to see with older imaging techniques. This type of scanning is crucial for diagnosing a stage of cancer known as oligometastatic prostate cancer, which occurs when five or fewer metastases have developed.

Ultimately, a prognosis and decisions about treatment depend on staging. A staging system is a common way of describing how far a cancer has progressed. There are different staging systems for prostate cancer, but the most widely used is the TNM system, short for tumor-node-metastasis (see Figure 6, page 48). It describes the extent of the primary tumor (T), whether the cancer has spread to nearby lymph nodes (N), and whether it has spread to distant sites (M).

## How fast is it growing?

Doctors use another assessment scale, known as the Gleason scoring system, to predict the behavior of a prostate tumor. The **Gleason score**, which is based on a microscopic evaluation of biopsied tissue cells, describes the cancer's aggressiveness and potential to spread (metastasize).

To determine your Gleason score, a pathologist examines the architectural pattern of cells in your sample and gives them a grade based on how similar or different they are compared to normal prostate tissue. Gleason patterns are graded from 1-5. Pattern 1 cells look very similar to those in normal prostate tissues, while Gleason 5 patterns have the most aggressive features.

Prostate tumors often consist of multiple types of cells (see Figure 7, page 49), so the pathologist assigns a grade to the pattern found in the most common and second most common cells in your biopsy sample. Those two grades added together equal your Gleason score. The higher the score, the faster the malignant cells are multiplying (see Table 5, page 49).

Say, for instance, that the most common cell pattern in a biopsy sample is grade 3, and the second most common pattern is grade 4. The Gleason score would in this case be expressed as 3+4=7.

Though it's been widely adopted, the Gleason scoring system has some drawbacks. For instance, doctors today are debating whether tumors with a score lower than 3+3=6 should even be classified as cancer, given their slow-growing nature and the likelihood that they will never cause trouble. By the same token, the Gleason system makes a 3+3 tumor appear to be in the middle of the risk scale, when it's actually in the low-risk category. Moreover, since the first number in the system carries more weight than the second, a Gleason 4+3=7 tumor is actually more dangerous than a Gleason 3+4=7 tumor, even though the final scores for each are the same.

To simplify matters, scientists have developed a five-tier grading system that ranks tumors from Grade Group 1 (the least dangerous) to Grade Group 5 (the most dangerous). Using this approach, a Gleason 3+4=7 tumor is classified as Grade Group 2, while a Gleason 4+3=7 tumor is classified as Grade Group 3. The system also distinguishes more clearly between high-grade cancers that would traditionally be scored as Gleason 8, 9, or 10.

*continued on page 49*

## Figure 6. Stages of prostate cancer

The TNM system for classifying tumors (illustrated here) captures basic information about a cancer in a few letters and numbers—namely, the extent of the primary tumor (T), whether the cancer has spread to nearby lymph nodes (N), and whether it has spread to distant sites (M).

### Stage T1

Your doctor can't feel these tumors during a DRE or see them with an imaging test such as a transrectal ultrasound.

- **T1a:** Tumor is found incidentally during transurethral resection of the prostate (TURP) for BPH; less than 5% of the tissue removed is cancerous, and is usually of low grade.
- **T1b:** Like T1a, but more than 5% of the tissue removed is cancerous, or the cancer is high grade.
- **T1c (not shown):** Detected when an elevated PSA leads to a needle biopsy.

### Stage T2

These cancers can be felt during a DRE and seem confined to the prostate.

- **T2a:** The cancer fills less than half of one side (left or right) of the prostate.
- **T2b:** Like T2a, but the cancer fills more than half of one side (left or right) of the prostate.
- **T2c (not shown):** Like T2a, but cancer is detected in both sides (left and right) of the prostate.

### Stage T3

These cancers have broken through the prostate's fibrous capsule.

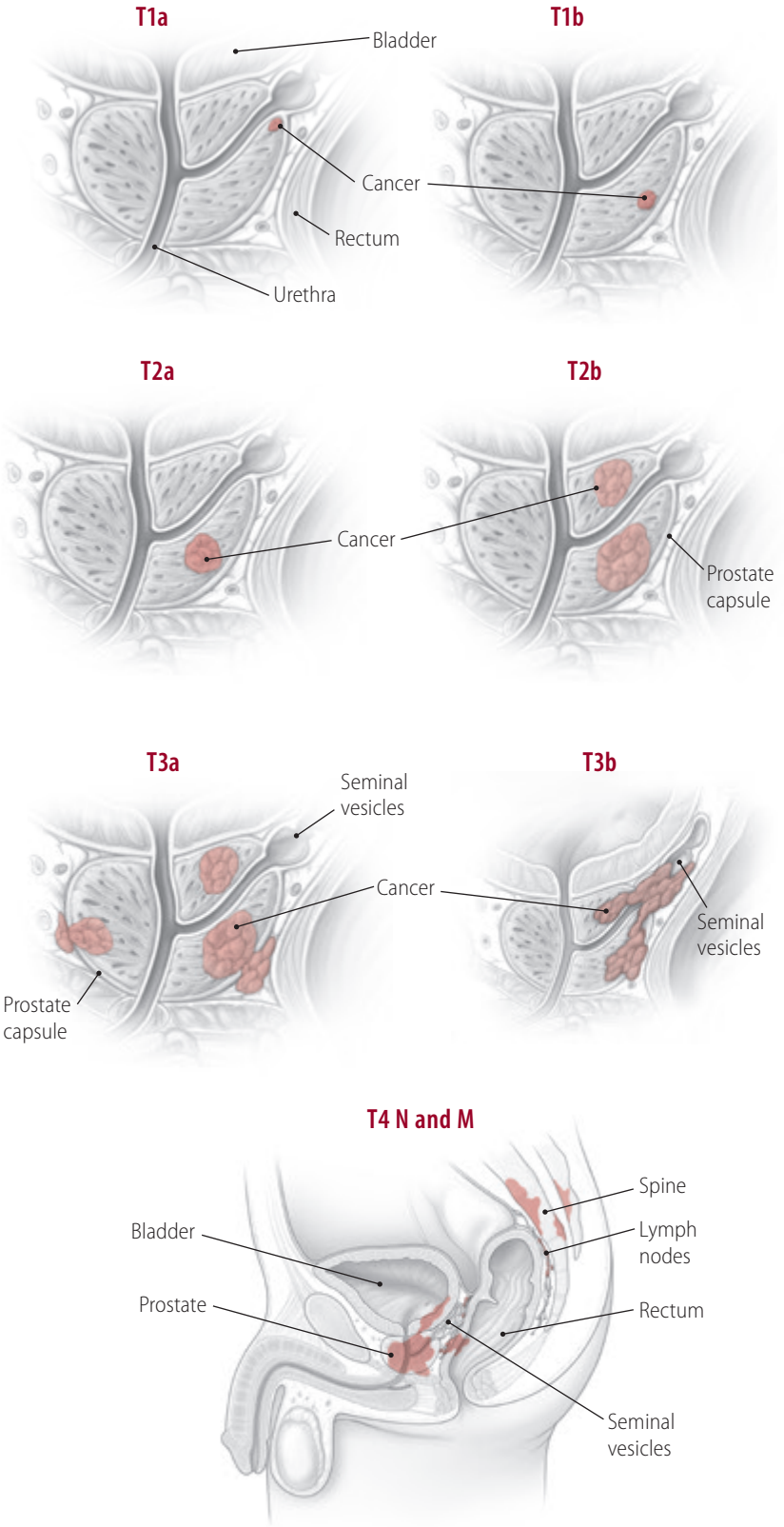
- **T3a:** The cancer extends outside the prostate, but has not spread to the seminal vesicles.
- **T3b:** The cancer has spread to the seminal vesicles.

### Stage T4

Like T3 disease, but the cancer invades other nearby structures, such as the bladder or rectum.

### Stages N and M

These cancers have metastasized to the pelvic lymph nodes (N1) or to other parts of the body (M1). Cancers that have spread to distant lymph nodes are classified as M1a, while cancers that have spread to the bones are M1b. Cancers that have spread to other sites—such as the lungs, but not the bones—are classified as M1c.



*continued from page 47*

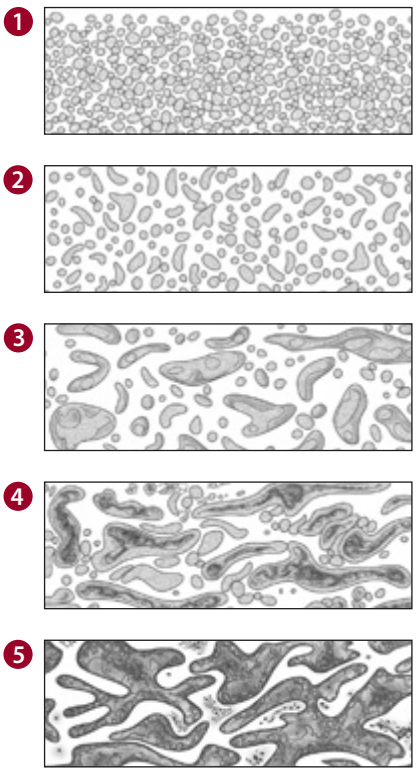
The Grade Group system has some obvious benefits: being more accurate than the Gleason score, it's less likely to lead to overtreatment. That's because men diagnosed with Grade Group 1 cancer might be less anxious to begin treatment than men who've been assigned a Gleason score of 6 out of 10, even though it is the same grade.

## Active surveillance

Some men diagnosed with prostate cancer need no treatment: for example, a man with a small, slowly progressing stage T1 cancer with a Gleason score of 5 or 6 who also has another serious medical condition, or a man with a life expectancy of less than 10 years. Prostate cancers often take 15 to 20 years, or even more, to grow to a detectable size and cause symptoms; in the meantime, they cause little harm. Many older men, especially those over age 75, are more likely to die of another condition before their prostate cancer becomes troublesome or dangerous, and they may face greater risks from surgery or other treatments than from the cancer itself.

At the other end of the spectrum are younger men—those ages 50 to 60, with an aggressive cancer in the early stages and a family history of prostate cancer. Virtually all doctors agree that these men require treatment. Treatment might also make sense for men

### *Figure 7. Gleason patterns*




**Well-differentiated cells**

**Grade Group 1 (Gleason 3+3=6 or lower).** Cells are small, of fairly uniform shape, and tightly packed together.

**Grade Group 2 (Gleason 3+4=7).** Cells display more varied and irregular shapes and are loosely packed.

**Moderately differentiated cells**

**Grade Group 3 (Gleason 4+3=7).** Cells are even more irregular in size and shape and are more dispersed; some cells are fused, and cell borders are less distinct.

**Poorly differentiated cells**

**Grade Group 4 (Gleason 4+4=8).** Many cells are fused into irregular masses; some cells (those darkly shaded) have begun to invade the connective tissue that separates cells.

**Grade Group 5 (Gleason 4+5=9 or higher).** Most of the tumor consists of irregular masses that have invaded the connective tissue.

**Table 5. Criteria for classifying new localized prostate cancer as low, intermediate, or high risk**

| Risk | PSA level | | Gleason score | | Cancer stage | | Percentage of positive biopsy cores |
|---|---|---|---|---|---|---|---|
| **Low** | under 10 ng/mL | and | 3+3 (Grade Group 1) | and | T1–T2a | | less than 34% |
| **Intermediate favorable** | 10–20 ng/mL | or | 3+4 (Grade Group 2) | or | T2b–T2c | and | less than 50% |
| **Intermediate unfavorable*** | 10–20 ng/mL | and/or | 4+3 (Grade Group 3) | and/or | T2b–T2c | and/or | 50% or higher |
| **High** | over 20 ng/mL | and/or | 4+4 or higher (Grade Group 5) | and/or | T3+ | | Only one core is needed if the Gleason score is 4+4 or higher |

*Must be 4+3 or have at least two of the other characteristics listed here.

Sources: D'Amico AV. "Risk-Based Management of Prostate Cancer," *New England Journal of Medicine* (2011), Vol. 365, No. 2, pp. 169–71. Zhang H, et al. "Risk of Adverse Pathological Features for Intermediate Risk Prostate Cancer: Clinical Implications for Definitive Radiation Therapy," *PLoS One* (2021), Vol. 16, No. 7, e0253936.

### Active surveillance vs. watchful waiting

In the past, doctors used the term "watchful waiting" to describe any strategy that involved following a prostate tumor to see if it worsened. Testing was done, not on a set schedule, but only when symptoms developed or worsened. And while some patients eventually had their cancer treated, others had no intention of doing so.

Today, patients who monitor their cancer closely and plan to have treatment when its activity increases are said to be engaging in active surveillance. Many doctors now reserve the terms "watchful waiting" and "observation" for cases in which patients don't plan to have treatment for prostate cancer because of their age or health, and in which they will intervene only if symptoms related to the cancer develop.

with prostate cancer who also suffer from BPH. That's because removing the prostate through surgery—or reducing its size with other therapies—not only treats the cancer but may also improve urinary symptoms.

But a significant number of men fall into a gray area, where the decision whether to treat isn't clear-cut. Estimates vary, but by some measures, up to 40% of men diagnosed with prostate cancer—as many as 100,000 Americans each year—have low- and intermediate-risk tumors that meet the criteria for active surveillance. This is a strategy that involves monitoring the cancer closely (with a regimen of prostate biopsies, DREs, PSA tests, and imaging scans) and choosing to start treatment if the cancer advances or shows evidence of increasing activity.

## Is active surveillance safe?

Yes, for appropriately selected candidates. A widely cited study by U.S. researchers published in 2015 showed that 93% of men with low-risk disease were still alive 10 years after being put on active surveillance, and nearly 70% of them were still alive after 15 years. A 2020 update on the same group of men found the risk of dying from prostate cancer or developing metastatic disease was only 0.1%, although half the men eventually wound up having surgery or radiation therapy.

Similarly, a Canadian study, first reported in 2015, found that out of 993 men with either low- or intermediate-risk prostate cancer who were put on active surveillance in 1995, only 15 (just 1.5%) died from the disease over the following two decades. Most of the 30 men who developed metastases were in the intermediate-risk group. The authors put the 15-year risk of metastases at 15% to 20% for that group—but close to zero for men in the low-risk group.

Studies show that men who choose active surveillance report significantly better urinary function, sexual function, and sexual satisfaction than men who chose surgery or radiation therapy. Patients are likely to have initial worries about the future course of their cancer when they first go on active surveillance. But evidence shows that cancer-specific stress and anxiety levels also decrease significantly with time if monitoring shows the disease is remaining stable.

Black men were advised for years to approach active surveillance cautiously, not just because they're at higher risk for aggressive disease, but also because favorable outcomes with active surveillance have mainly been documented in white populations. Black men are therefore significantly less likely to choose active surveillance than white men are. Yet research increasingly shows that Black and white men on active surveillance fare equally well. One study found that Black and white men on active surveillance had similar rates of metastasis (1.5% and 1.4%, respectively) as well as death from prostate cancer (1.1% and 1.0%) after nearly eight years of follow-up. A more recent 2025 study found no difference in prostate cancer death rates among more than 100,000 Black and white men after 10 years on active surveillance. Black men accounted for just 16% of the entire group, however. The authors of this study concluded that active surveillance is safe, but also underutilized in Black populations.

## Criteria for active surveillance

Is active surveillance right for you? If your cancer has been deemed low or very low risk, it might be worth considering. The criteria for determining which cases are eligible for active surveillance are not uniform or strict. Several research groups and medical centers have developed their own standards. But the important elements of commonly used criteria include the following:

- PSA less than 10 ng/mL

- Grade Group 1 or Gleason score equal to or less than 6
- tumor stage of T1c (typically found by PSA testing) or T2a (a small nodule that can be felt during a DRE).

Active surveillance may also be considered for men with "favorable" intermediate-risk features, according to guidelines published by the National Comprehensive Cancer Network (NCCN), an alliance of 33 cancer centers throughout the United States. The NCCN criteria for active surveillance include the following:

- Grade Group 1 or 2, with Gleason scores no higher than 3+4=7
- PSA in the range of 10–20 ng/mL
- detectable cancer in fewer than half a man's biopsy cores.

Tools such as PSA density, MRI, and some genomic tests can help to identify candidates with intermediate-risk cancer for whom active surveillance may be suitable. Your age and overall health should also factor into the decision. All other things being equal, the older a man with low-risk prostate cancer is, the more suitable he is for active surveillance, because it's likely that other health conditions will cause illness and death before his prostate cancer would. But research also suggests that active surveillance can be appropriate for men younger than 60. Your doctor can provide guidance in this area.

Active surveillance isn't right for everyone. Specifically:

- Men with BRCA2 and possibly ATM gene mutations have higher risks for aggressive disease and should approach active surveillance cautiously, the NCCN warns.
- Evidence of perineural invasion in biopsy samples puts men at higher risk of progression. Perineural invasion means that cancer cells are migrating into spaces surrounding nerve fibers.
- Men who suffer from anxiety and stress before and after monitoring tests might find that active surveillance impacts negatively on their quality of life.
- Logistical burdens may make it hard to keep regular appointments, especially among men with limited access to health care.

But with mounting evidence of its safety for appropriately selected candidates, active surveillance rates are increasing steadily. Indeed, study results published in 2024 in *JAMA* showed that the percentage of men with favorable intermediate-risk tumors who chose active surveillance in the United States has quadrupled, rising from 2% in 2010 to 8.6% in 2020.

### Monitoring during active surveillance

During active surveillance, it's important to undergo regular monitoring to determine if the cancer has become more aggressive. If it has, it's time to consider treatment.

Monitoring recommendations vary. At a minimum, monitoring should consist of regular DREs to assess tumor growth and periodic PSA tests to check for increases in blood levels that might indicate a progression of the cancer. These follow-up tests should be scheduled every four to 12 months, depending on your age, biopsy results, and anxiety level.

Biopsies are also done periodically. Experts recommend an early repeat biopsy to rule out the presence of high-grade cancer that might have been missed during a man's initial diagnosis, followed by repeat biopsies every two to four years. The frequency depends on certain risk factors, including the number of positive cores in a biopsy (higher numbers are more concerning) and how fast PSA increases over time. Some guidelines recommend annual biopsies. But a number of experts, including Dr. Garnick, believe that annual prostate biopsies shouldn't be recommended automatically because they can lead to complications, including erectile dysfunction, infection, and other problems.

Moreover, doctors are increasingly relying on other tests that can provide key information without subjecting a man to a biopsy. Multiparametric MRI (mpMRI; see "Magnetic resonance imaging," page 42), for instance, can generate information about a cancer that makes some biopsies unnecessary, especially when combined with repeated PSA measures and other tests such as the PHI and the 4Kscore (see "Variations on the PSA test," page 41). To reduce the risk of complications, Dr. Garnick integrates informa-

tion from genetic testing, previous biopsies, and MRI to determine when and how often to do biopsies.

That said, there's no question that regular monitoring of some kind is necessary while you are on active surveillance; without it, you run the risk that the cancer may grow and spread to a stage that makes it much more difficult to treat. Once on active surveillance, men should stick with their monitoring plan. Various clues—such as a sharp increase in PSA, a new lump found during a DRE, or a change in urinary habits—can signal whether cancer may be advancing and if treatment should be reconsidered.

© Halfpoint Images | Getty Images

Active surveillance entails regular monitoring so you and your doctor will know when it's time to consider treatment.

### Signs it may be time to consider treatment

Men on active surveillance can change their minds and, in consultation with a doctor, opt for treatment. You're not locked in.

But, more often, a treatment recommendation is triggered when a low-risk cancer begins to exhibit features of an intermediate- or high-risk one. Active surveillance hasn't been standardized, and recommendations for exactly what should trigger treatment vary. Most doctors would recommend treatment in any of the following circumstances:

- The Gleason score on a follow-up biopsy is equal to or greater than 7, especially if the primary score is a Gleason pattern 4 or higher.
- The Grade Group is 3 or higher.
- PSA doubling time (the time it takes for PSA levels to double) accelerates.
- There is increased evidence of disease, such as finding more cores with cancer during a follow-up biopsy or discovering that the percentage of cancerous cells in individual cores is increasing.
- Significant changes are noted during a DRE.
- Significant changes are noted on a multiparametric MRI scan.
- You have a change in urinary habits. The doctor will need to determine if the cause is BPH or cancer (or both).

## Treating prostate cancer

One thing is certain about prostate cancer: it's complicated. Often there is no obvious choice when it comes to treatment, and you will need to weigh your options carefully and base your decision, with the help of your doctor and loved ones, on many factors—not only the stage of your cancer, but also your age, lifestyle, and risk of side effects such as urinary incontinence and erectile dysfunction. You might even opt for no treatment at all, preferring active surveillance.

If you choose treatment, there are several options:

- radical prostatectomy (surgically removing the prostate gland)
- radiation, including external beam or implanted pellets (brachytherapy)
- focal therapy (which focuses treatment on the cancer and leaves most of the gland intact)
- hormonal therapy (which suppresses testosterone, a "fuel" for prostate cancer)
- other medications, including targeted therapies and radionuclides.

Each of these treatments has pluses and minuses, and—despite years of research and efforts to improve results—complication rates remain stubbornly high. That's especially true in the case of sexual complications. Men often report difficulty achieving erections for one to two years after radical prostatectomy, even when surgeons try to avoid damaging the nerves and blood vessels in the prostate that control erectile functioning. Sexual complication rates tend to be lower with radiation than they are with surgery, but radiation is associated with higher rates of long-term urinary incontinence and irritation, and impotence rates also tend to rise with time.

Prostate cancer treatments therefore involve complex trade-offs. They can be used alone or in combination depending on a man's age, the stage of the cancer, and personal preferences regarding the side effects of treatment and the lifestyle changes they may entail.

Numerous medications have been approved over the past 15 years, and the wide variety can be confusing for patients and doctors alike. But it isn't simply a question of variety. No one treatment has emerged as preferred. With this in mind, the following sections describe available treatments with the aim of helping you make a decision based on your doctor's recommendations and how a particular treatment is likely to affect your quality of life.

### Radiation vs. surgery

Most men being treated for non-metastatic prostate cancer have a choice between surgery and radiation. Which one should you pick? Your age, cancer stage, concerns about common side effects, and willingness to undergo additional treatments should all be factored into the decision. Whether you have other health problems also matters. For example, men with inflammatory bowel disease that affects the lower bowel are generally advised to have surgery, since radiation can exacerbate preexisting bowel symptoms.

For many people, having the cancer removed immediately via surgery provides a sense of relief. It also gives the surgeon a clearer understanding of the cancer's extent. However, surgery is associated with higher rates of erectile dysfunction (ED) and urinary complications, especially in the first few years after treatment.

Radiation, on the other hand, carries a higher risk of bowel problems, such as diarrhea, blood in the stool, and rectal pain. However, newer techniques can help to minimize risks to the bowel and urinary system. Importantly, radiation delivery has become more precise, making it easier for doctors to spare the urethra. For instance, doctors can also inject a gelatinous substance called a perirectal spacer between the prostate and rectum to protect rectal tissues and avoid harm to the bowel. Still, side effects can occur.

A 2025 paper in *The Lancet Oncology* reported that men who experience bowel or urinary problems soon after treatment are more likely to have those same kinds of problems months or years later—even if their symptoms get better for a while. Studies have also shown a small but definite increased incidence of rectal cancer after radiation therapy.

**Surgery vs. radiation vs. active surveillance**

Scan the QR code to read the *New England Journal of Medicine* study comparing survival rates among men being treated for localized prostate cancer.

What about differences in survival between the two treatment methods? An important long-term study published in 2023 in the *New England Journal of Medicine* provided encouraging data. The investigators followed 1,610 men with localized prostate cancer who were treated with either surgery or radiation. Fifteen years later, 2.2% of the radiation-treated men had died from prostate cancer, compared with 2.9% of the men who got surgery. Remarkably, survival rates with active surveillance were nearly the same, at 3.1%.

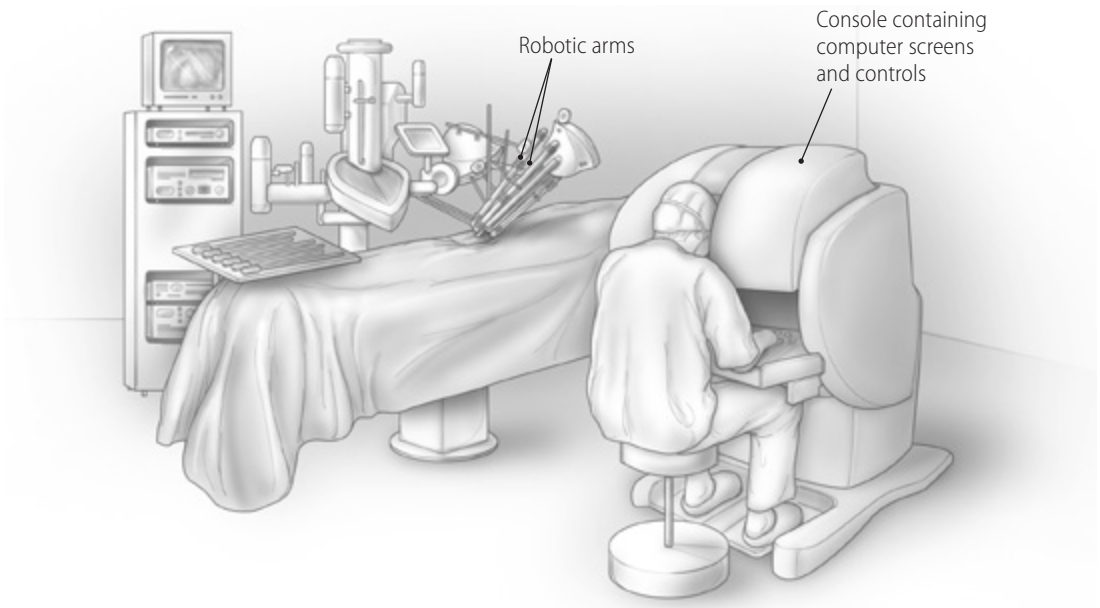
## Surgery

The best candidates for surgery are men whose disease is confined to the gland itself (stages T1 and T2), who are under age 70, and who are in good general health.

Surgery that removes the entire prostate gland is called radical prostatectomy, and it's long been the standard surgical treatment for prostate cancer. In this context, radical has nothing to do with politics: instead, it means removing affected tissue and any surrounding tissue that might also be affected. A radical prostatectomy almost always involves removing the seminal vesicles—slender, saclike glands that, along with the prostate, release fluid that becomes part of semen. In most cases, the surgeon also removes pelvic lymph nodes.

Radical prostatectomy was once offered routinely to men with low-risk prostate cancer. Today, this type of surgery is reserved mostly for men with intermediate- and high-risk prostate cancer. (Men with

***Figure 8. Operating robotically***




To perform a robot-assisted laparoscopic prostatectomy, the surgeon sits at a console several feet away from the operating table and manipulates robotic arms fitted with tiny cameras and surgical instruments to locate and remove the diseased prostate gland. The console contains two full-color computer screens that provide a magnified, three-dimensional view of the prostate and surrounding tissues. The surgeon guides the robotic arms by manipulating the controls while watching the screens.

lower-risk tumors are generally treated with other techniques or followed with active surveillance.)

Over the years, the way this surgery is performed has undergone a profound shift. In the traditional technique, called radical retropubic prostatectomy, the surgeon would make an incision from just below the navel to the pubic bone to gain access to the prostate. This open surgical technique has been supplanted by laparoscopic surgery—which involves inserting instruments and tiny cameras through much smaller "keyhole" incisions—and, in particular, by robot-assisted laparoscopic surgery.

In robot-assisted surgery, the surgeon sits at a console and uses remote controls to move robotic arms that hold laparoscopic instruments (see Figure 8).

The use of robotic surgery for prostate cancer has skyrocketed since its approval by the FDA in 2000; it now accounts for the vast majority of radical prostatectomies performed in the United States. Patients treated with robotic surgery often have less blood loss, less pain, fewer infections, and shorter recovery time than patients treated with traditional methods. Meanwhile, several international studies comparing the experience of patients treated with either robotic or traditional approaches show no difference in cancer outcomes, continence, sexual functioning, or quality of life.

Study after study has also shown that the most important determinant of surgical success is the experience and skill of the surgeon, not whether the surgery is open or robotic. The best results are obtained by surgeons who do large numbers of these procedures in high-volume hospitals.

## Leaving no cancer behind

Before taking out the prostate, the surgeon will remove lymph nodes that could have been infiltrated by the cancer. A pathologist will immediately examine the lymph nodes. If cancer is present, the operation usually will go no further because this means the cancer has spread beyond the prostate, in which case other treatments are more appropriate than removing the prostate. However, some surgeons do advocate going

ahead with the prostatectomy anyway. For that reason, it's important to discuss this possibility ahead of time with your surgeon so you can express your preferences regarding prostatectomy.

If the lymph nodes show no cancer, the surgeon carefully separates the prostate and the seminal vesicles from the surrounding tissues and removes them. Later, a pathologist examines these organs. If the cancer is confined to the prostate, it likely won't return. If the cancer has already spread beyond the capsule surrounding the gland, additional treatment may be necessary.

### Nerve-sparing surgery

Men have traditionally shuddered at the risks of radical prostatectomy—especially permanent impotence, which used to occur in nearly all cases. But that began to change in the early 1980s, when nerve-sparing surgery was developed. During this surgery, doctors protect the two bundles of nerves that lie on either side of the prostate gland and control erections. This type of operation may also reduce the likelihood of other serious side effects, such as urinary incontinence and significant blood loss.

Almost all men undergoing prostatectomy would prefer to have the nerve-sparing procedure, and it's available across the country. A newer method involves having a pathologist check flash-frozen samples of the prostate while the operation is underway. If that test shows no cancer cells around where key nerves are situated, then the surgeon can spare the nerves with greater confidence (see "Erectile dysfunction and prostate disease," page 79).

However, success with nerve-sparing surgery is not guaranteed. If the tumor is too close to a nerve bundle, the nerves can't be saved—and saving one nerve bundle is not as likely to preserve erectile function as saving both of them. Even if the procedure is successful, it can take a year or more for the tiny nerve fibers—which often stop transmitting impulses when they've been traumatized by the surgery—to heal sufficiently to restore sexual function. (For more on avoiding and treating these problems, see "Complications" at right.)

As for treating the cancer itself, the nerve-sparing surgery seems comparable to traditional surgery. For a study published in 2024 in *BJU International*, researchers evaluated long-term outcomes in men with high-risk prostate cancer who underwent either a standard open radical prostatectomy or a nerve-sparing procedure. There was no difference between them in either 10-year survival rates (84% for the entire cohort) or the need for additional treatments such as radiation and chemotherapy.

### Recovery

Depending on the technique used and your health, recovery usually spans one to three days in the hospital and several weeks at home. Men undergoing robotic surgery tend to go home faster than those undergoing open surgery. You will need to urinate through a catheter for a week or two while the urethra heals.

It is important to avoid everyday activities that can put a strain on the incision, such as lifting tools or groceries, and to be careful when coughing or sneezing. Give yourself time to heal, and be sure to consult your physician before you start to exercise. A physical therapist can put you on a gentle program designed to strengthen your abdominal muscles. You can resume sexual activity within four to six weeks.

### Complications

ED and urinary incontinence are the most common—and often most distressing—complications of prostatectomy.

**Sexual complications.** Estimates of the number of men undergoing radical prostatectomy who regain their ability to have erections range widely. That's at least partly because some research relies on patient reports, while other research relies on physicians' estimates. Patients are often reluctant to tell their doctors about such problems unless they are specifically asked.

For a 2020 study in *JAMA*, researchers compared long-term outcomes in more than 2,000 men ages 59 to 70 who selected surgery, radiation, or active surveillance for localized prostate cancer. Among the surgically treated men, 61% said they

were still unable to achieve erections sufficient for sexual intercourse five years later.

Investigators later reported in 2025 that the rate of sexual complications increases in men with higher-grade tumors who also receive additional treatments, including hormonal therapy. Published in *Clinical Oncology*, the findings showed that men with the most advanced cancers reported the highest levels of ED as well as a loss of libido. Men who do regain sexual activity often report decreased sensation during orgasm.

Dr. Garnick points out that ED occurs commonly in older men and is likely to worsen over time, regardless of whether they undergo active surveillance or are treated for prostate cancer. Being overweight, having diabetes, or having been a smoker are additional factors that are associated with a poor recovery of erectile function. (For more on ED, see page 79.)

**Urinary complications.** Research shows that many men who undergo prostatectomy develop some degree of incontinence requiring the use of a pad or absorbent underwear. A 2025 study of over 166,000 men aged 66 or older published in *European Urology* found that 23% of patients who underwent radical prostatectomy for localized prostate cancer developed urinary incontinence. Although these common side effects aren't always permanent, recovery can take several years.

The likelihood of a successful outcome—in terms of preserving potency, preventing incontinence, and, most importantly, curing the cancer—generally correlates with a surgeon's experience. The number of procedures a surgeon performs does not necessarily make them better than one who does fewer; however, a minimum of 15 to 20 prostatectomies per year is necessary to be sufficiently skilled at the operation.

## Radiation therapy

Radiation treatment can be delivered by aiming an external beam of radiation at a tumor or by surgically implanting small radioactive pellets in the prostate (an approach called brachytherapy; see page 61). Neither approach has emerged as the winner. Moreover, within those two broad categories of external beam radiation and brachytherapy, there are many variations and modifications. Table 6 (page 57) will help you compare them.

If you choose radiation therapy, your doctor will recommend a treatment approach that takes into account your risk profile. In men with low- or intermediate-risk cancer, radiation will likely be directed to the entire prostate plus the seminal vesicles. In men with higher-risk cancer, the pelvic lymph nodes may be radiated as well. The criteria for low-, intermediate-, and high-risk cancer vary, depending on the study, the doctor, and the medical center. Table 5 (page 49) gives one commonly used set of criteria. Online risk calculators can also be very helpful and are relatively easy to understand. However, the best way to assess your risk is to work with your doctor.

In the past, radiation was mainly used for men with localized prostate cancer (that is, cancer confined to the prostate itself). Now, many doctors are using radiation, in some cases along with hormonal therapy, to treat oligometastatic prostate cancer (an early form of stage 4 disease with just three to five metastases; see "Treating oligometastatic prostate cancer," page 69). The radiation treatments can target the prostate gland as well as cancerous deposits that have spread to other parts of the body (called metastasis-directed therapy).

### External beam radiation therapy (EBRT)

During EBRT (see Figure 9, page 58), rays of high-energy radiation are aimed directly at the entire prostate, the seminal vesicles, and possibly the nearby pelvic lymph nodes. Higher radiation doses are directed to areas of the gland that contain the most cancer.

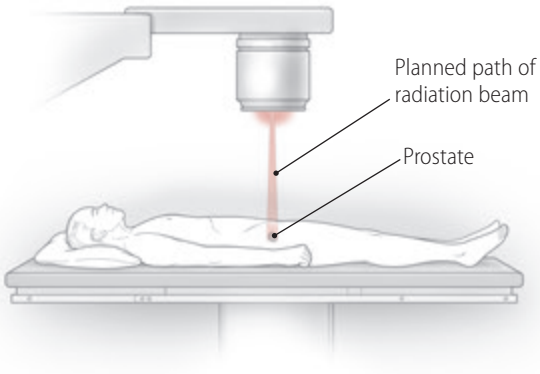
External beam radiation effectively destroys cancer cells, but it can also damage adjoining healthy tissue. To limit the collateral damage, a specialist determines the exact location of the tumor using a CT scanner. This technology relays images to a computer that constructs a detailed three-dimensional map of the prostate and seminal vesicles. The map allows the radiation therapist to precisely target the cancerous tissue while

*continued on page 58*

## Table 6. Forms of radiation therapy

| Treatment | Ideal candidates | Treatment time and recovery | Side effects | Advantages | Disadvantages |
|---|---|---|---|---|---|
| **Standard external beam radiation techniques: three-dimensional conformal radiation therapy (3D-CRT) and intensity-modulated radiation therapy (IMRT)** | Older patients or those with multiple medical conditions; patients whose cancer has spread outside the prostate capsule; men who have had a transurethral resection of the prostate (TURP), men with oligometastatic prostate cancer. | 35 to 45 treatments (five times a week for seven to nine weeks); each treatment takes about 15 minutes. | Bowel problems (diarrhea, blood in stool, rectal leakage, rectal pain), frequent urination, blood in the urine, urinary incontinence (increases over time), impotence (develops slowly), fatigue. | Both 3D-CRT and IMRT are very well-understood therapies with well-documented outcomes.<br>IMRT may, in theory, allow more accurate targeting of the tumor than 3D-CRT so that there's less damage to surrounding healthy tissue. The intensity of each of the beams can be adjusted. | Length of treatment makes it inconvenient, especially for men living far away from a treatment facility or those who travel frequently.<br>In rare cases, the radiation may miss part of the tumor if the beam is too narrowly focused. |
| **Proton beam therapy** | | | | May be able to deliver more radiation to the prostate and less to surrounding tissues, causing less damage to nearby structures; protons release their energy after traveling a certain distance, minimizing damage to the tissue they pass through. | Available at a limited number of sites in the United States.<br>Might not be covered by insurance.<br>More research is needed to determine whether it reduces side effects. |
| **Stereotactic body radiation therapy (e.g., CyberKnife, Gamma Knife)** | | Usually five outpatient treatments, each lasting 60 to 90 minutes. May require fewer treatments if combined with another form of radiation. | | Corrects for small movements and changes in the prostate during the course of treatment.<br>Shorter treatment regimen is important for some men. | Limited availability. |
| **Hypofractionated radiation therapy** | | Five outpatient treatments, which can be done in a single week or spread out over five weeks. | | The shorter treatment regimen is important for some men, especially those living in areas without easy access to radiation facilities. | Limited data available on outcomes after five years. |
| **Permanent seed implants (brachytherapy)** | Men with early-stage cancer and prostate volume of less than 60 ml. | Half-day to full-day outpatient procedure with anesthesia. | Impotence and urinary and bowel problems. Pain and rectal irritation usually resolve in about a month. | Radiation is concentrated in the prostate, potentially sparing the urethra, bladder, rectum, and nerves.<br>Can be used with external beam radiation in high-risk patients. | Small risk that unlinked seeds will migrate or be passed in the urine. Rarely, seeds enter the bloodstream and travel to the lungs or other parts of the body.<br>May cause severe urinary toxicity, which may last a long time. |
| **High-dose-rate brachytherapy** | Intermediate- and high-risk patients. | Usually three treatments over a few days; treatments last about 15 minutes. | | | Limited availability.<br>Needles remain in place until after the final treatment.<br>Requires a hospital stay. |

### *Figure 9: External beam radiation therapy*




During external beam radiation for prostate cancer, a patient will typically wear a gown or sweatpants that can easily be removed, allowing the area being treated to be aligned with a ray of light that matches the path of the radiation. The radiation beam itself is not visible. Marks on the skin or metallic gold implants (called gold fiducials) in the prostate help pinpoint the gland's location. The patient may also lie in a custom-made body "cast" to immobilize the pelvis.

*continued from page 56*

avoiding healthy tissue nearby. The clinician then places you on the procedure table in exactly the right position, checks the computer settings, and finally activates the device that delivers the radiation.

A 2023 study found that EBRT by itself is associated with fairly high rates of biochemical recurrence (when PSA levels rise after surgery; see "Prostate cancer terminology," page 34), especially among men with high-risk prostate cancer. The investigators evaluated five- and 10-year outcomes in 1,193 patients with low-, intermediate-, or high-risk disease. The biochemical recurrence rates at 10 years were 28.5%, 36.4%, and 61.5%, respectively.

Patients with biochemical recurrence typically require treatment. However, in 2025, researchers published evidence on a newer EBRT method that can help to minimize biochemical recurrence. With the newer technique—called a focal boost—doctors give a high dose that selectively targets only the most aggressive spot within a tumor. The goal is to increase the radiation dose without causing excess damage. The study, published in the *Journal of Clinical Oncology*, enrolled 557 men with intermediate- or high-risk prostate cancer. Results showed that 81% of the men who got a focal boost were still disease-free after 10 years, compared to 71% of the men who did not.

There are several types of EBRT, described in the sections below.

**Three-dimensional conformal radiation therapy (3D-CRT)** was once the standard form of outpatient EBRT. It involves taking three-dimensional pictures of the prostate and surrounding structures before treatment to pinpoint their locations. Using computer software, specialists determine the angles at which the beams of radiation should enter the tissue. In this way, the radiation field conforms to the shape of the treatment area while avoiding the bladder and rectum. Typically, 35 to 45 treatments are required, which take place five times a week over seven to nine weeks. Each treatment takes about 15 minutes.

**Intensity-modulated radiation therapy (IMRT)** is a form of 3D-CRT that allows doctors to change the intensity of the radiation within each of the radiation beams—increasing radiation to the prostate while reducing radiation to normal tissues. Because treatment conforms so tightly to the prostate, the gland's exact location must be determined at the start of each treatment. This is now the most commonly used form of radiation therapy in the United States. As with 3D-CRT, 35 to 45 treatments are typically used—five times a week for seven to nine weeks, with each treatment taking about 15 minutes.

**Proton beam therapy** offers the same precision as IMRT, but it uses protons (subatomic particles with a positive electrical charge) instead of photons (light particles), which are used in conventional radiation. During proton beam therapy, radiation is released in a very narrow band, thus theoretically minimizing damage to surrounding tissue.

Studies comparing proton beam therapy with IMRT have reached inconsistent conclusions. The latest clinical trial results, published in 2024 by investigators at Harvard Medical School and Massachusetts General Hospital, found no difference in five-year

survival and quality-of-life measures among 450 men with low- or intermediate-risk prostate cancer who were treated with either approach.

At this time, proton beam therapy is not widely available because it requires a cyclotron (a type of particle accelerator that is prohibitively expensive for many hospitals) to deliver the radiation. Because of the expense and limited supporting evidence, Medicare and private insurance coverage is often determined on a case-by-case basis.

**Stereotactic body radiation therapy (SBRT)** uses image guidance and computer-controlled robotics to deliver multiple beams of radiation to the tumor from almost any direction. Several devices are available to deliver this form of radiation, so you might hear this method referred to as the CyberKnife, the Gamma Knife, TomoTherapy, or other brand names.

While planning treatment, the radiologist implants tiny gold pellets called fiducials in the prostate gland to make it more visible for treatment purposes. The computer system tracks the tumor's position, detects prostate movement, and automatically adjusts the delivery of radiation, if necessary, to account for any change. SBRT is gaining in popularity because it's faster than other forms of radiation. Patients typically have five high-dose sessions over one to two weeks.

Several review studies have shown that the method is safe and that it delays disease progression in patients with localized prostate cancer.

Growing evidence shows that SBRT can also be a safe and effective treatment for tumors that spread beyond the prostate in men with oligometastatic prostate cancer. In one study, 54 men were randomly assigned to either SBRT directed at cancer sites outside the prostate (this is called metastasis-directed therapy, or MDT), or to an observation group that received no treatment. After six months, cancer had progressed in just 19% of the men in the radiation-treated group, compared with 61% of men in the observation group. Interim findings from the largest ongoing study of MDT in oligometastatic prostate cancer are similarly promising. In total, 199 men were treated with MDT during the study. After five years, 21.7% of the men had avoided the need for systemic hormonal therapy or chemotherapy, according to 2024 results published in the *International Journal of Cancer.*

Studies have also reported promising results with SBRT delivered to metastases in the lymph nodes and bones. For instance, during a 2023 study, 95 patients were treated for metastases located outside the spine. After three years, 89% of the men had avoided further progression in SBRT-treated areas.

**Hypofractionated radiation therapy** divides (or fractionates) the total dose of radiation into larger doses that are given in fewer sessions (fractions) than standard radiation therapy—typically, a total of five treatments over the course of one to five weeks. Long-term studies that compare hypofractionated and conventionally fractionated radiation therapy in men with early-stage prostate cancer have found virtually no differences in toxicity or survival.

A 2024 paper in the *New England Journal of Medicine* evaluated 874 men treated either with SBRT given over one to two weeks or conventional radiation given across four to 7.5 weeks. After five years, their outcomes were nearly the same. In total, 95.8% of the men given hypofractionated treatments avoided biochemical recurrence, compared to 94.6% of men on the other standard dosing schedule. There were no significant differences in side effects between the two groups. A longer-term study also published in 2024 found no differences in overall survival or late side effects up to 12 years after men were treated with hypofractionated or conventional radiation.

Clinical guidelines published by the American Society for Radiation Oncology, the American Society of Clinical Oncology, and the AUA concluded that, despite limited follow-up beyond five years, the accumulated evidence so far warrants the use of hypofractionated therapy for men who would prefer it. The evidence is strongest for men with low- to intermediate-risk prostate cancer, but mounting evidence supports the use of hypofractionated therapy for men with high-risk cancer as well. These guidelines say that hypofractionated radiation therapy can be offered to men in all risk categories after a discussion with a doctor about the risks and benefits.

The primary advantage of hypofractionated radiation is convenience, particularly for men who have to travel long distances for treatment. Some institutions will even provide housing for men while their treatment is under way. The criteria for selecting suitable candidates for hypofractionation vary by institution, and treatment protocols are continuing to evolve as researchers refine the technique.

For most of these types of external beam radiation, certain advanced imaging techniques can assist the radiologist:

- **Targeted delineation** uses imaging technology to pinpoint radiation therapy. MRI scans can be used to locate tumors and plan where radiation should be targeted for maximum effect. Currently, MRI scans require the use of an endorectal coil inserted into the rectum, but a more power-

## Radiation treatment after prostatectomy

Radiation can be first-line therapy for prostate cancer, but it is also used after radical prostatectomy (surgical removal of the prostate). There are two main categories of post-surgical radiation:

- **Adjuvant radiation** is radiation therapy given soon after surgery, when there is a high likelihood of residual cancer.
- **Salvage radiation** is radiation therapy given later. It is administered if cancer comes back after surgery, or if PSA levels rise after surgery (a condition called biochemical recurrence).

Doctors used to routinely recommend adjuvant radiation if post-surgical findings indicate some cancer is still present in the surgical margins (meaning the edges of prostate tissues that were removed), or if there's evidence of cancer in tissues next to the prostate. This additional treatment can reduce the risk of biochemical and local recurrence, as well as clinical progression, but the effects on the potential for spread (metastasis) and survival are less clear. Today, adjuvant therapy is used only under limited circumstances, such as when doctors encounter extensive amounts of Grade Group 5 cancer in surgical margins.

Adjuvant therapy rates are declining among men who have surgery for cancer with high-risk characteristics, and fewer than 20% of such patients opt for the additional radiation, given concerns about over-treatment, impotence, erectile dysfunction, and other side effects. Overall, doctors are moving steadily toward salvage radiation in response to clinical trial data showing little to no difference in cancer outcomes among men treated with either approach. One frequently cited study was published in *The Lancet* in 2024. Called the RADICALS clinical trial, it had approximately eight years of follow-up and showed no difference in overall survival between men with high-risk features who underwent adjuvant or salvage radiation. The men treated with adjuvant radiation developed worse problems with urinary and bowel functioning, however. Other large studies have produced similar findings.

The bottom line is that many patients never experience a biochemical recurrence after surgery. For these patients, salvage radiation amounts to a "watch-and-wait" strategy that could allow them to avoid additional treatments they may never need.

Scan this code to read the latest guidelines on salvage radiation.

In 2024, the American Urological Association, the American Society for Radiation Oncology, and the Society of Urologic Oncology issued updated guidelines for salvage radiation. Based on these guidelines, your doctor will likely recommend that you undergo salvage radiation quickly after your PSA levels start to rise. That's because the longer you wait for radiation, the greater the risk your cancer will spread. Salvage radiation does come with higher risks for ED, as well as urinary and bowel functioning, and these risks should be balanced with those from the cancer itself, with further consideration given to your age and other underlying health problems. If your PSA is higher than 0.7 ng/mL, or is persistently detectable after surgery, then the guidelines recommend a combination of radiation and hormonal therapy.

Several studies have shown that adding hormonal therapy to salvage radiation in such cases can lower your risk of progression and improve long-term survival. One study published in 2023 showed that salvage radiation given together with the hormonal drug enzalutamide (see page 65) kept further PSA increases at bay for longer than salvage radiation by itself. This is a promising finding, since enzalutamide has fewer metabolic side effects than conventional hormonal therapy (also called androgen deprivation therapy, or ADT).

Importantly, the guidelines highlight the growing role of prostate-membrane specific antigen, or PSMA, scanning, which can find tiny—and increasingly treatable—metastatic deposits that older imaging techniques might not detect (see "Treating oligometastatic prostate cancer," page 69) The guidelines also caution against delaying salvage radiation, even if your PSMA PET scan is negative after PSA starts to rise.

ful scanner (3-Tesla) allows MRI imaging of the gland without the coil.

- **Positron emission tomography (PET)**, which does not require an endorectal coil, can produce an image of the gland and the location of tumors so that treatment can zero in on the cancer and spare surrounding tissue. PET scans use radioactive tracers injected into the body that accumulate preferentially in cancer cells. Then, when the patient is placed under a PET scanner, the tracer signals the tumor's location. Newer tracers approved by the FDA bind specifically to the PSMA protein in the prostate cancer cell membrane. These tracers are also driving the development of new PSMA-targeted therapies that eradicate metastatic cells in the body before they have a chance to form new tumors.

### Brachytherapy

Rather than delivering radiation from an external source, brachytherapy delivers radiation from a source placed inside the body. *Brachy-* is Greek for "short," so brachytherapy refers to the radiation source being a short distance from the cancer. Sometimes brachytherapy is called internal radiation therapy or interstitial radiation therapy. The most common form of brachytherapy is permanent brachytherapy, also known as low-dose-rate brachytherapy or seed implantation. This form of brachytherapy involves placing 50 to 150 radioactive pellets, or "seeds," in or near the prostate tumor. The number of seeds depends on the size of the gland.

In this procedure, a patient receives either general or spinal anesthesia. Next, the doctor places an ultrasound probe in the man's rectum and a catheter in his bladder. Viewing a computerized map of the prostate, the doctor guides the placement of the seeds, using a template and a needle to insert them through the perineum. Doctors leave the seeds, which are smaller than grains of rice, in place permanently. Over time, the seeds emit less and less radiation until they become nonradioactive. Depending on the type of seeds, the loss of radioactivity may take three months to a year.

To date, most studies of brachytherapy have been in men with low-risk prostate cancer. In those with intermediate-risk cancer, researchers once speculated that brachytherapy might be more effective if it were combined with EBRT. However, clinical trial results reported in 2023 showed that the combined treatment resulted in more side effects, but not more effective treatment, than brachytherapy alone.

Permanent brachytherapy is usually an outpatient procedure, with most men going home as soon as the anesthesia wears off. However, it may cause severe urinary tract side effects, such as bleeding, incontinence, and the urgent and frequent need to urinate. Although this is rare, the problem can last a long time—even after the seeds are no longer radioactive—because of damage done by the initial radiation. The use of brachytherapy is steadily decreasing, partly because more men are choosing active surveillance for low-risk prostate cancer. Brachytherapy is also being superseded by SBRT, which is increasingly seen as a convenient alternative with a reduced risk of side effects. Dr. Garnick rarely, if ever, recommends brachytherapy as a first-line treatment for patients with localized prostate cancer.

### Radiation complications

Radiation treatment for prostate cancer can cause side effects like frequent or painful urination, bowel problems such as diarrhea or rectal bleeding, and fatigue (see Table 7, page 62). It may also lead to sexual difficulties, including ED. Most side effects improve after treatment, but some can last longer or become permanent, so it's important to report any symptoms to your doctor.

## Focal therapy

Unlike radical prostatectomy and radiation—which treat the entire prostate gland—focal therapy focuses only the part of the prostate where cancer is located. It has been likened to a lumpectomy for breast cancer, in which only the cancerous mass and the margins around it are removed while sparing the rest of the breast. However, focal therapy does not refer to a specific procedure, and it does not typically involve

surgery. It is best understood as a treatment approach used to home in on the cancer while minimizing damage to nearby tissue.

Different technologies can be used in focal therapy. Those used most often are **cryotherapy**, which involves freezing tissue, and **high-intensity focused ultrasound**, a more powerful version of the harmless sound waves used to create diagnostic images of the prostate. A review of studies on these and other techniques, published in 2023, could not point to any one approach as being the best, in part because studies so far have not made head-to-head comparisons between types of focal therapy procedures. Another option is to use water vapor to ablate cancerous tissue. The Vanquish System—which is a transurethral, ultrasound and electromagnetically guided, thermal water vapor device—was cleared by the FDA in late 2025.

Focal therapy isn't an option for everyone. Joint guidelines from the AUA and the American Society for Radiation Oncology advise using it only in men with intermediate-risk prostate cancer, since low-risk disease can be managed with active surveillance. In contrast, high-risk cancer calls for treating the whole prostate. Additionally, it is not usually recommended for treating multifocal cancer (cancer that appears in more than one spot within the prostate).

If you're considering focal therapy, you should know there's a lack of high-quality data comparing it with standard approaches (active surveillance, radiation, or radical prostatectomy). However, there's reason to be cautiously optimistic about it. A 2018 study in *European Urology* found that 88% of 625 men treated with focal therapy for prostate cancer had avoided a cancer recurrence after five years. Dr. Garnick cautions that the risk of recurrence rises for men who were initially diagnosed with more aggressive cancers. If the disease does recur, patients can undergo other therapies, such as cryotherapy, surgery, radiation, or even high-intensity focused ultrasound (see page 63), depending on the cancer's location in the prostate.

Whichever method is used, focal therapy requires additional training and expertise on the part of the surgeon. It begins with a mapping biopsy (see Figure 5, page 46) to pinpoint the "index lesion"—that is, the part of the tumor with the highest cancer grade. This biopsy also determines whether a cancer has spread to the seminal vesicles.

After focal therapy is used (with cryotherapy, high-intensity focused ultrasound, or another technique), regular monitoring is crucial so that you can promptly have other treatment in the event of a recurrence.

### Focal therapy with cryotherapy

Cryotherapy, also called cryosurgery or cryoablation, kills cancer cells by freezing them. It appears to work well when treating a small, newly diagnosed tumor. In a study published in the journal *Urology* in 2025, 70% of men treated with cryotherapy for intermediate-risk prostate cancer hadn't experienced a recurrence after five years of follow-up.

Side effects from cryotherapy may include urinary stress incontinence and ED. ED is especially common because the freezing process can destroy nerves that are essential for achieving erections. In rare cases, complications, including rectal fistula (an abnormal

**Table 7: Percentage of patients with side effects three years after radiation**

| Type of radiation therapy | Percentage of men with urinary incontinence | Percentage of men with erectile dysfunction |
|---|---|---|
| High-dose-rate brachytherapy | 7% | 72% |
| Low-dose-rate brachytherapy | 5.4% | 36% |
| External beam radiation therapy (generally 3D-CRT, IMRT, and stereotactic) | 2.7%<br>(7% after 12 years) | 68%<br>(73% after seven years) |

Sources: Donovan JL, et al. "Patient-Reported Outcomes After Monitoring, Surgery, or Radiotherapy for Prostate Cancer," *New England Journal of Medicine* (2016), Vol. 375, No. 15, pp. 1425–37. Hamdy FC, et al. "Fifteen-Year Outcomes After Monitoring, Surgery, or Radiotherapy for Prostate Cancer," *New England Journal of Medicine* (2023), Vol. 388, No. 17, pp. 1547–58. Smith DP, et al. "Quality of Life Three Years After Diagnosis of Localized Prostate Cancer: Population Based Cohort Study," *BMJ* (2009), Vol. 339, b4817.

### Biochemical recurrence: An early signal of recurring prostate cancer

A man's PSA should plummet after he's been treated with surgery or radiation for localized prostate cancer. An increase in PSA after treatment is called a biochemical recurrence, and it means that prostate cancer still lurks in the body. However, the threshold that defines biochemical recurrence depends on how a man was treated.

- If a man has a radical prostatectomy, his PSA level should drop to zero, since PSA-releasing cells should all have been removed from the body. Biochemical recurrence would be diagnosed if PSA rises by any amount after surgery. However, it takes time for PSA to be cleared from the blood. Experts recommend waiting up to three months before testing PSA after surgery to avoid misdiagnosing a biochemical recurrence.
- If a man was treated with radiation, then his PSA levels will not fall to zero. Instead, PSA will decline toward a nadir, which is the lowest level reached after treatment. Ideally, the PSA nadir will be less than 0.5 ng/mL. Biochemical recurrence is diagnosed if the PSA level rises to 2 ng/mL or more over the nadir. It typically takes 18 to 24 months for PSA levels to reach a nadir after radiation.
- What defines biochemical recurrence after focal therapy remains an active area of investigation.

opening in the skin near the anus that leads to the rectum), may be severe.

### Focal therapy with high-intensity focused ultrasound

This method of delivering ultrasound generates intense, precisely targeted heat to destroy cancer tissue. A study published in *BJU International* in 2023 followed 1,391 men treated with high-intensity focused ultrasound (HIFU) in the United Kingdom between 2010 and 2018. It found that 80% did not require further cancer treatment during a median follow-up period of five years.

HIFU for prostate cancer can cause side effects such as urinary problems and ED. Some men may experience pain, blood in the urine, or urinary tract infections shortly after treatment. Most side effects improve over time, but some urinary or sexual issues can persist.

## Androgen deprivation therapy

Androgens, the family of male sex hormones that includes testosterone, function as a fuel for growth in normal development. However, in some men they can also drive the progression of prostate cancer. Androgen deprivation therapy (ADT; also called hormonal therapy) treats prostate cancer by dramatically reducing levels of testosterone and other androgens or by blocking them from working. ADT is a treatment option for men who

- have cancer that has spread beyond the prostate gland (metastatic disease)
- have a rising PSA after initial treatment with surgery or radiation therapy, indicating a possible recurrence of cancer that may not yet be visible with standard imaging
- are frail and unable to tolerate surgery or radiation as their initial treatment.

In such cases, ADT is typically taken by itself. But it can also be used in combination with other treatments, such as radiation or chemotherapy (see "Combined ADT and chemotherapy," page 68).

ADT uses drugs to lower androgen levels and slow prostate cancer. The older method of lowering male hormones—namely castration, or surgical removal of the testicles, which produce 90% of a man's testosterone—is rarely used today. ADT reduces hormonal levels by an equal amount, but its effects are reversible if men stop taking the drugs. If cancer continues to progress after treatment, it is referred to as castration-resistant prostate cancer; if the cancer responds to the therapy, it is called castration-sensitive.

There are many possible drug options and regimens for this type of therapy. For a complete listing of hormonal therapy medications, see Table 8 (page 64).

### ADTs that affect the pituitary gland

A class of ADT drugs known as luteinizing hormone–releasing hormone (LHRH) agonists stimulate the pituitary gland—the "master gland" at the base of the brain that helps orchestrate the activity of other glands and hormones throughout the body. The result is a

*continued on page 65*

**Table 8: Hormonal therapy medications**

| Drug name | Side effects | Comments |
|---|---|---|
| ***LHRH agonists*** | | |
| goserelin (Zoladex)<br>histrelin (generic only)<br>leuprolide (Eligard, Lupron Depot)<br>triptorelin (Trelstar) | Hot flashes, impotence, decreased libido, fatigue, weight gain, anemia, osteoporosis. | Injected or implanted. |
| ***GnRH antagonists*** | | |
| degarelix (Firmagon) | Hot flashes, sleep disturbances, pain, dizziness, headache, nausea, fatigue; for degarelix, large welts at the injection site. | Given monthly via injection. |
| relugolix (Orgovyx) | | Taken orally once a day. |
| ***Anti-androgens*** | | |
| apalutamide (Erleada) | Fatigue, high blood pressure, rash, diarrhea, nausea, weight loss, joint pain, hot flashes, falls, decreased appetite, skeletal fractures, and swelling of extremities. | Taken orally. Approved for use in men with nmCRPC and mCSPC. |
| bicalutamide (Casodex) | Hot flashes, impotence, decreased libido, breast tenderness and swelling, nausea, diarrhea; rarely, liver failure. | Taken orally. Liver function should be checked periodically. |
| darolutamide (Nubeqa) | Fatigue, pain in extremities, and rash. | Taken orally twice daily with food. Approved for nmCRPC and mCSPC. Men should also take an LHRH agonist. |
| enzalutamide (Xtandi) | Fatigue, musculoskeletal pain, hot flashes, diarrhea, tissue swelling, respiratory infections, dizziness, difficulty sleeping, blood in urine, anxiety, high blood pressure. Seizures occur in about 1% of men. | Taken orally. Approved for mCRPC, nmCRPC, and mCSPC. |
| flutamide (generic only)<br>nilutamide (Nilandron) | Hot flashes, impotence, decreased libido, breast tenderness and swelling, nausea, diarrhea; rarely, liver failure. | Taken orally. Liver function should be checked periodically. |
| ***Other*** | | |
| abiraterone (Zytiga) | Joint swelling or discomfort, low levels of blood potassium, fluid retention in legs and feet, increased blood pressure, muscle aches, hot flashes, and urinary and gastrointestinal problems. | Used in combination with low-dose steroids. Approved as both first-line and second-line treatment for mCRPC. |
| estrogens | Blood clots and breast enlargement. | Once the main alternative to surgical removal of the testicles, these drugs have been largely replaced by LHRH agonists and anti-androgens. May be tried if other hormonal therapies don't work. |
| ketoconazole (generic only) | Dizziness, depression, headaches, loss of libido. | Used first for treating fungal infections, ketoconazole reduces testosterone levels quickly in men with advanced prostate cancer when other forms of hormonal therapy don't work. |

Note: For the cancer-type abbreviations in this table, see "Prostate cancer terminology," page 34.

*continued from page 63*

temporary surge in testosterone that generally lasts from three to four weeks, followed by a consistent suppression of the hormone to castration levels.

LHRH agonists are administered via injection or implant. During the initial surge, symptoms such as bone pain may worsen, a situation known as a clinical flare. To counteract the effect of high testosterone levels during this period, your doctor may also prescribe a drug called an anti-androgen (see "Anti-androgens" at right). This two-drug strategy helps to reduce bone pain and produces more rapid declines in PSA than using an LHRH agonist by itself.

**Gonadotropin-releasing hormone (GnRH) antagonists** also drop testosterone levels by acting on the pituitary gland. However, these drugs do not cause an initial testosterone surge.

Clinical trials comparing LHRH and GnRH drugs are still ongoing. Current evidence shows that one type of GnRH, degarelix (Firmagon), and LHRH agonists have about the same PSA-lowering effect in patients with advanced prostate cancer, although the declines may at first be more pronounced with degarelix treatment.

Some evidence suggests that switching to degarelix after LHRH agonists fail will stabilize or reduce PSA levels in about 30% of patients within three months. However, these data are insufficient to determine how long that reduction lasts or whether it has a bearing on long-term outcomes.

A second GnRH antagonist, called relugolix (Orgovyx) comes in a convenient pill form (versus the monthly injection for degarelix). In a late-stage trial, it suppressed testosterone to optimal levels within four days.

Both LHRH and GnRH drugs carry an FDA-mandated warning stating that they slightly increase the risk of a heart attack, sudden cardiac death, or stroke. Of the two, LHRH drugs seem to be safer, according to a 2024 study co-authored by Dr. Garnick. Published in the *Journal of Urology*, the study evaluated outcomes in over 45,000 ADT-treated patients. According to the results, 7.0% of men who started on a GnRH antagonist developed significant cardiovascular problems within a year, compared to 3.8% of men treated with an LHRH agonist. Risk factors that predicted greater effects on the heart among men taking the drugs included a higher age, the extent of baseline metastases, pre-existing cardiovascular disease, and a prior history of smoking.

### Anti-androgens

These drugs prevent testosterone (produced in the testicles as well as the adrenal glands) from attaching to receptors in prostate cells. They also block testosterone's close relative, dihydrotestosterone (DHT), from attaching to receptors in prostate cells. Enzymes in the prostate convert testosterone into DHT. Left unchecked, DHT plays an even greater role in fueling prostate cancer than testosterone.

Anti-androgen drugs are considered part of "conventional" ADT, but they have a different mechanism of action, so are generally discussed separately.

Anti-androgens can be used in various situations. Some men take an anti-androgen for a few weeks before treatment with an LHRH agonist. Others take one for the duration of LHRH treatment. Anti-androgens are generally not taken together with GnRH antagonists.

The anti-androgens include three older drugs: bicalutamide (Casodex), flutamide (generic only), and nilutamide (Nilandron). They also include three newer ones—apalutamide (Erleada), darolutamide (Nubeqa), and enzalutamide (Xtandi)—which are discussed in more detail below. The newer drugs were approved on the basis of their ability to delay the appearance of metastases in men with rising PSA levels after initial prostate cancer treatment (therefore increasing what's called metastasis-free survival). They have also been shown to delay worsening of pain, bone problems, and the need for subsequent chemotherapy.

Anti-androgen drugs include the following:

- **Apalutamide.** FDA-approved for nmCRPC and mCSPC in combination with ADT.
- **Darolutamide.** Approved for nmCRPC in combination with ADT and for mCSPC in combination with ADT, either with or without chemotherapy.

- **Enzalutamide**. Approved for men with nmCRPC, mCRPC, and mCSPC, all in combination with ADT. It is also approved for men with nmCSPC who have a high risk of biochemical recurrence, as well as in combination with talazoparib for men with mCRPC who have certain mutations to DNA repair genes (such as BRCA). Enzalutamide causes seizures in a very small number of men (less than 1%).

### Abiraterone

Abiraterone (Zytiga) is another option for advanced prostate cancer. This drug lowers testosterone levels by inhibiting an enzyme that is essential to the synthesis of the hormone. Abiraterone is taken with prednisone, a powerful anti-inflammatory medication.

It was first approved in combination with prednisone for patients with mCRPC who had already been treated with docetaxel. But the FDA later approved earlier uses of the drug after research showed that early abiraterone treatment can delay the need for chemotherapy, which has more significant side effects.

### Duration of ADT

The amount of time patients receive ADT varies considerably depending on disease risk, treatment goals, and a man's other underlying health problems. Men with localized high-risk cancer are typically treated for 24 to 36 months, whereas intermediate-risk patients are treated for shorter durations of four to six months. Men with metastatic disease may require lifetime ADT to control cancer progression. Some patients, however, are candidates for intermittent ADT, or "drug holidays," where treatment is cycled on and off (see "Intermittent vs. continuous hormonal therapy," page 70).

### Side effects of ADT

Not surprisingly, because they involve blocking a major hormone, all forms of ADT have wide-ranging side effects.

**Sexual dysfunction.** Because ADT interferes with testosterone, sexual function is often a casualty of this type of treatment. Most men experience ED and a loss of sexual desire. When treatment is stopped, however, sexual function usually returns, especially in younger men who have been on the drugs for less than two years. Moreover, research indicates that men who exercise when starting hormonal therapy report fewer sexual side effects, more energy, and less tendency to develop depression.

**Bone disease.** One of the side effects of ADT is loss of bone tissue, which increases the risk of fractures.

**Cardiovascular risks.** ADT can increase total cholesterol and triglyceride levels as well as blood sugar levels. All these changes can potentially increase your risk of developing diabetes and cardiovascular disease, which is the leading non-cancer cause of death in men with prostate cancer. In 2021, the American Heart Association issued a statement recommending that men undergoing hormonal therapy for prostate cancer should be closely monitored for potential cardiovascular complications, especially if they already have risk factors such as high blood pressure, high cholesterol, smoking, and a family history of heart disease.

**Liver disease.** Men who received ADT were 54% more likely than the men who did not use hormonal therapy to be diagnosed subsequently with nonalcoholic liver disease, according to a study published in the *Journal of Urology*. The investigators reviewed national cancer registry data for a total of 82,938 men with localized prostate cancer (including just over 31,000 who received ADT) and followed them between 1992 and 2009. The longer these men took hormonal therapy, the more their risks for liver cirrhosis, liver necrosis, and other types of liver disease increased. Anti-androgens, in rare cases, cause a condition called transaminitis, characterized by high blood levels of certain liver enzymes known as transaminases. Dr. Garnick checks liver function every two weeks during the first eight weeks of anti-androgen therapy, since this is when liver injury from treatment is most likely to occur. If left untreated, transaminitis can result in severe liver injury and possibly death.

## Cancer and bone weakening

Cancer or its treatments can cause bone loss and increase the risk of fractures. However, there are medications that can help. Bisphosphonates such as zoledronic acid (Zometa)—most commonly used to treat osteoporosis—directly target osteoclasts, the cells that break down bone. These cells become overactive when cancer metastasizes, making the bones weaker and increasing the risk of pain, fractures, and spinal compression.

Current clinical guidelines from the National Comprehensive Cancer Network and the American Society of Clinical Oncology recommend limiting the use of zoledronic acid to men with mCRPC. Further support for those recommendations came from a 2025 study in *Prostate Cancer and Prostatic Diseases*, which showed that adding zoledronic acid to enzalutamide and androgen deprivation therapy did not improve bone health in men with mCSPC.

Another drug, denosumab (Xgeva), works in a different way. It blocks a substance known as a RANK ligand, which is necessary to activate the bone-destroying osteoclasts. By blocking the RANK ligand, denosumab prevents bone erosion. The FDA initially approved denosumab for men whose cancer had already spread to the bone. That approval was later expanded to include men at risk for bone fractures because they are taking hormonal therapy for advanced prostate cancer.

Interestingly, research has shown that taking denosumab or zoledronic acid to build bone mass also improves survival in men with mCRPC who are taking abiraterone. However, discontinuing denosumab after completing prostate cancer treatment can result in bone loss, according to a 2023 study. The research focused on men treated with radiation for nonmetastatic prostate cancer who took hormonal therapy for three years and denosumab for five years. Discontinuing denosumab led to bone losses of 2% to 5%, on average.

In rare instances, these drugs can cause a distressing problem known as osteonecrosis of the jaw, in which the jawbone dies after its blood supply is cut off. It is not clear who might develop this condition, although men who undergo invasive dental work—such as tooth extraction—while taking a bone-preserving agent seem to be more at risk. For that reason, it is important to maintain good oral hygiene by flossing and brushing and to complete any needed dental work before beginning treatment. Dr. Garnick recommends getting approval from your dentist before starting on any of these drugs.

**Cognitive decline.** Studies in healthy men have highlighted a possible connection between dementia and low testosterone levels. Might ADT pose a similar risk? It's possible. A 2023 review of 12 clinical trials enrolling a combined 13,524 men with prostate cancer found that abiraterone, apalutamide, darolutamide, and enzalutamide were associated with higher risks for cognitive problems, in addition to falls and fatigue. According to Dr. Garnick, however, conclusive evidence linking hormonal therapy with cognitive decline is still lacking. In his view, the benefits of ADT generally outweigh the potential risk of cognitive impairments for men with prostate cancer.

### Combined ADT and radiation therapy

ADT is sometimes used in conjunction with external beam radiation to boost the effectiveness of radiation. It may also be used to shrink large prostate glands (typically defined as those weighing more than 50 grams) before brachytherapy takes place, enabling proper placement of the radioactive seeds.

Experts generally recommend against this combined treatment for men with low-risk, localized prostate cancer. There is no evidence the combination improves survival rates in this group, so the side effects of ADT are not considered justified.

Whether to combine ADT with radiation in men with intermediate-risk cancer is a more nuanced question. Guidelines published in 2022 by the American Urological Association and the American Society for Clinical Oncology caution that ADT's side effects may outweigh any potential survival benefits for men with favorable intermediate-risk cancer (see Table 5, page 49). However, the guidelines state that men with unfavorable intermediate-risk disease can benefit from a short, four- to six-month course of ADT given together with radiation.

Combination hormonal/radiation therapy is a standard option for men with high-risk disease, with studies showing that it reduces the risk of dying from prostate cancer and other causes more than either treatment given alone. In a 2022 study from Spain, 355 men with high-risk prostate cancer were treated with radiation

given together with hormonal therapy for either four months or two years. The two-year regimen was ultimately more effective. After 10 years, men treated this way avoided cancer progression for longer durations, and they also had better survival. Based on these results, Dr. Garnick says two years of hormonal therapy should now be strongly considered for men with high-risk disease.

Combining ADT with radiation can also be effective for treating prostate cancer that returns after radical prostatectomy, especially in men with high-risk features such as a PSA of 0.7 ng/mL or greater, a PSA doubling time of less than six months, persistent PSA after surgery, a Gleason Grade of Group 4 or 5, or evidence of cancer in the seminal vesicles. Studies have shown that long-term survival is significantly better among men treated with a combination of salvage radiation (radiation given when cancer returns after radical prostatectomy) and ADT than it is in men who get radiation alone.

A particularly promising area of treatment with combined hormonal therapy and radiation involves oligometastatic prostate cancer, an early form of stage 4 cancer (see "Treating oligometastatic prostate cancer," page 69).

### Combined ADT and chemotherapy

Evidence has shown that patients with high-grade or highly advanced prostate cancer can benefit from combining ADT with chemotherapy. The combination is especially suitable if the cancer has spread beyond the prostate and nearby lymph nodes to other areas of the body. As a systemic treatment, chemotherapy circulates and targets cancer cells wherever they may be.

An early trial sponsored by the National Cancer Institute (NCI) showed that men with metastatic prostate cancer lived longer if they started chemotherapy along with ADT instead of going on ADT by itself. According to results published in 2015, men with the most advanced cancers benefited most from the combination: they lived roughly 49 months, which was 17 months longer than men who started on ADT alone. The trial investigators, noting the side effects of chemotherapy, cautioned that the ADT-chemotherapy combination should be used only in patients with high-volume cancer (occupying more than 25% of the prostate gland) that is also metastatic.

Further evidence supporting the combination for certain patients comes from the ongoing STAMPEDE clinical trial. STAMPEDE found that men with metastatic hormone-sensitive prostate cancer who received the chemotherapy drug docetaxel, in addition to ADT, lived longer than those who only got ADT. The same combination, however, did not extend survival rates in men with high-risk non-metastatic cancer, though it did slow the progression of the cancer.

Meanwhile, growing evidence suggests that men with metastatic cancer might survive longer with an approach known as triplet therapy, which combines a chemotherapy medication with two different types of hormonal therapy drugs (see "Darolutamide," page 65).

Research has shown no benefit from combining chemotherapy and hormonal therapy in men who have a biochemical recurrence after initial treatment with surgery or radiation.

## Chemotherapy

Chemotherapy is rarely used to treat early prostate cancer because prostate tumors tend to grow slowly. (Chemotherapy targets cells that proliferate rapidly.) It is used, however, to treat advanced cases of the disease that are no longer responding to other treatments. Chemotherapy drugs for prostate cancer are given intravenously. They are usually taken in cycles, with each period of treatment followed by an off period. Two chemotherapy drugs are officially FDA-approved to treat prostate cancer (see Table 9, page 71). Docetaxel (Taxotere) is the standard first-line drug for mCRPC. Cabazitaxel (Jevtana) is in the same class. Cabazitaxel carries a higher risk of a serious side effect—reduced numbers of blood cells in bone marrow—so it is typically reserved for men who stop responding to docetaxel.

### Side effects

Because chemotherapy drugs are absorbed by tissues throughout the body, healthy cells can also be harmed, especially those that are dividing quickly. Hair loss, one of the classic side effects of chemotherapy, occurs

## Treating oligometastatic prostate cancer

Oligometastatic cancer is an early form of stage 4 prostate cancer that has spread to other organs in the body, but only to a limited degree. It is generally defined as including no more than three to five areas outside the prostate gland, most commonly the lymph nodes or bones. Barely a decade ago, it was considered universally fatal, and treatment was limited to hormonal therapy. Today, exciting developments in the field are leading to new treatment strategies that are improving patient survival in clinical trials. Together with better, earlier detection, these approaches can potentially lead to cures in some groups of patients.

Oligometastatic prostate cancer can be classified in a couple of ways. Men who are found to have oligometastatic disease at their initial diagnosis are said to have *de novo* oligometastatic prostate cancer. If the disease is detected after a man has already been treated for prostate cancer, then the cancer is said to be oligorecurring. The initial sign is an increase in PSA, suggesting that new tumors exist somewhere in the body.

One technology driving advances in the field is PSMA PET scanning (see "Positron emission tomography," page 44), which can reveal newly formed tumors that are still too small to see with conventional imaging. This enables doctors to treat the tumors directly with radiation, either by itself or in combination with hormonal therapy. This approach is called metastasis-directed therapy (MDT) or sometimes site-directed therapy.

Studies have shown consistently that MDT can delay the need for systemic hormonal therapy. During one early trial published in 2018 in the *Journal of Clinical Oncology*, men treated with MDT for oligorecurring prostate cancer avoided hormonal therapy for eight months longer than men in an observation group. Other studies have shown even longer androgen deprivation therapy (ADT) delays with MDT. Indeed, during a clinical trial published in 2022 in the *Journal of Urology*, 20% of 116 men treated with MDT for oligometastatic prostate cancer remained cancer-free for four years or longer.

Mounting evidence shows that men can also benefit from MDT and hormonal therapy given together. A 2025 paper in *European Urology* showed that adding ADT to MDT significantly extends progression-free survival, meaning that men lived longer on the combined treatment without their disease getting worse. The study split 174 men with oligometastatic prostate cancer who had already been treated with ADT into four groups: One received ADT by itself given continuously (meaning on an ongoing basis until the cancer progressed or the hormonal treatments stopped working), another group got continuous ADT plus MDT, a third group got intermittent ADT by itself, and the fourth group got intermittent ADT plus MDT. Results showed that progression-free survival among men who got MDT plus continuous hormonal treatment was 47 months, compared to 22 months among the continual-ADT-only group. By contrast, progression-free survival in the intermittent-ADT-only group was 15.8 months versus 28.4 months among men who got the combined treatment.

Men with *de novo* oligometastatic cancer are also benefiting from new treatment strategies. In the past, they would have only hormonal therapy, while the prostate itself was left untouched. Doctors were generally reluctant to treat the prostate in men with metastatic cancer, since the benefits were unlikely to outweigh the side effects. Now, that's changing. Doctors are increasingly treating such cases with approaches that include giving ADT and MDT either by themselves or in combination. They may also watch the pace of cancer progression, then treat only if a man's disease begins to spread more aggressively. And other treatments are showing promise in clinical trials. Among them is a radioligand therapy called lutetium-177 vipivotide tetraxetan (Pluvicto) that targets and kills cancer cells—but not healthy cells—by delivering tiny particles of radiation (see "Radioligand drugs" below).

because the drugs damage the dividing cells of hair follicles. Cells in the bone marrow, mouth, stomach, tear ducts, and intestines are also commonly affected. Both toenails and fingernails can also be affected and sometimes fall off.

Chemotherapy may also cause fatigue, mouth sores, nausea, gastrointestinal disturbances, and infertility. The presence or absence of side effects, however, doesn't show how well the therapy is working. Most men find the side effects manageable, and the effects don't last very long. In a few months, the chemotherapy is finished, their bodies recover, and they steadily return to feeling normal.

## Radioligand drugs

Radioligands home in on PSMA, a protein that studs the surface of prostate cancer cells. (This is the same protein targeted by PSMA PET scans; see "Positron emission tomography," page 44). Currently, lutetium Lu-177 vipivotide tetraxetan (Pluvicto) is the only

## Intermittent vs. continuous hormonal therapy

Androgen deprivation therapy (ADT) can be delivered either continuously or, in an approach known as intermittent hormonal therapy, with periodic breaks in treatment. The regimens vary, but the basic plan is to stop hormonal therapy once a man's PSA falls below a certain level and begin again if his PSA starts to increase. The rationale is that on-again, off-again treatment may make ADT more effective by making prostate cancer cells more sensitive to the withdrawal of testosterone and related hormones. Intermittent therapy also gives men a "drug holiday" from side effects.

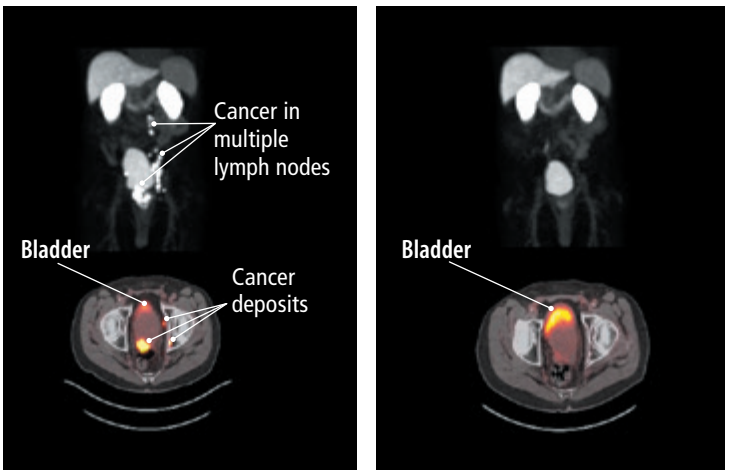
A number of large studies have compared intermittent with continuous therapy, but the jury is still out. Dr. Garnick urges extreme caution in using intermittent therapy in patients with metastatic disease, since some studies have shown better results with continuous treatment.

drug in this class. It zeroes in on metastatic cells like a guided missile.

Pluvicto is made up of two parts: a molecule that finds and attaches to PSMA on prostate cancer cells, along with a minimally radioactive particle. Prostate cancer cells that absorb the drug will then be killed by its radioactive cargo (see Figure 10).

The FDA initially approved Pluvicto for men with mCRPC who had already been treated with an anti-androgen and chemotherapy. During the clinical trial leading to this approval, overall survival among Pluvicto-treated men was 15.3 months, compared to 11.3 months among men who received standard care. In 2025, the FDA expanded its approval to mCRPC patients who hadn't yet been treated with chemotherapy. The FDA took that step after findings published in *The Lancet* in 2024 showed the drug slowed the progression rate by 50% in treated patients (11.5 months among Pluvicto-treated men compared to 5.6 months in men who did not get the drug).

***Figure 10: PSMA imaging and targeted radioligand therapy***




Radioligand therapy targets cancer with great precision. In the scan on the left, cancer is visible in the prostate as well as in several lymph nodes and bone. After treatment, cancer is nearly eradicated, as shown in the scan on the right.

## PARP inhibitors

About 10% of men with metastatic prostate cancer test positive for a BRCA gene mutation, and some of those who do may benefit from drugs known as PARP inhibitors.

All cells, including cancer cells, have various mechanisms to repair routine damage to their DNA. Cancer cells are especially reliant on enzymes called poly (ADP-ribose) polymerases, or PARPs. PARP inhibitors prevent cancer cells from fixing DNA damage. Instead, damage accumulates until the cancer cells die.

In 2020, the FDA approved a pair of PARP inhibitors—olaparib (Lynparza) and rucaparib (Rubraca)—specifically for BRCA-positive prostate tumors that no longer respond to other treatments. During the clinical trial leading to rucaparib's approval, tumors shrank in 44% of treated men for up to two years. Olaparib similarly delayed cancer progression for an average of 7.4 months, which was just over twice as long as the delay achieved with ADT in the control group.

*continued on page 72*

**Table 9: Chemotherapy, targeted therapy (PARP inhibitors), and immunotherapy for advanced prostate cancer**

| Drug name | Side effects | Comments |
|---|---|---|
| ***Standard chemotherapy (FDA-approved for prostate cancer)*** | | |
| cabazitaxel (Jevtana) | Drop in blood cell counts, diarrhea, fatigue, nausea, vomiting, constipation, weakness, kidney failure. | In combination with the steroid prednisone, cabazitaxel is approved for use in men who no longer respond to docetaxel. It can extend survival. |
| docetaxel (Taxotere) | Hair loss, nausea and vomiting, drop in blood cell counts, numbness and tingling (usually in the feet). | This anti-cancer drug may be used alone or in combination with other chemotherapeutic agents, such as estramustine and carboplatin. It may also be used initially with hormonal therapy for men with extensive metastases. Docetaxel can extend survival. |
| ***Chemotherapy used "off-label" (not specifically approved for prostate cancer)*** | | |
| carboplatin | Low blood cell counts, nausea, vomiting, taste changes, hair loss, weakness, constipation, diarrhea. | Used as a single agent and in combination with paclitaxel and estramustine. Also used as a second-line therapy for patients who have become resistant to docetaxel. Although not specifically approved for the treatment of prostate cancer, it can ease symptoms. |
| paclitaxel | Hair loss, nausea and vomiting, fatigue, drop in blood cell counts, numbness and tingling in hands and feet (usually after long-term use). | Although not specifically approved for the treatment of prostate cancer, it can ease symptoms. |
| ***Other chemotherapy drugs*** | | |
| estramustine (Emcyt) | Blood clots, nausea and vomiting, fatigue, headache, drop in blood cell counts. | Often combined with other agents in clinical trials, but the risk of blood clots and other complications make estramustine unlikely to become a standard treatment. Approved for use in prostate cancer patients to ease symptoms. |
| mitoxantrone | Nausea and vomiting, hair loss, fatigue, drop in blood cell counts. | This drug is often used in men who do not respond to docetaxel; eases symptoms. |
| ***PARP inhibitors (FDA-approved for prostate cancer)*** | | |
| niraparib (Akeega, Zejula) | Bleeding gums, blood in urine or stool, irregular heartbeat, low back pain. | In combination with abiraterone, niraparib delays cancer progression in men with mCRPC who test positive for BRCA gene mutations. |
| olaparib (Lynparza) | Decreased hemoglobin, nausea, fatigue, drop in white blood cell count, abdominal pain, vomiting, anemia. | Used in men with a BRCA gene mutation to reduce PSA levels, shrink tumors, lessen pain, and improve quality of life. |
| rucaparib (Rubraca) | Fatigue, vomiting, nausea, anemia, drop in white blood cell count. | Used to extend survival in men with a BRCA gene mutation who no longer respond to other treatments. |
| talazoparib (Talzenna) | Bleeding gums, blood in urine or stool, bone pain or fracture, sore throat, mouth sores. | In combination with enzalutamide, talazaparib can delay cancer progression and extend survival in men with mCRPC who test positive for DNA repair gene mutations. |
| ***Immunotherapy*** | | |
| pembrolizumab (Keytruda) | Fatigue, cough, nausea, itching, rash, shortness of breath, pericarditis, colitis. | May help men whose tumors contain mutated mismatch repair genes. |
| sipuleucel-T (Provenge) | Fever, chills, fatigue, back pain, nausea, joint pain, headache. | Extends survival for men with minimally metastatic disease. However, survival data are controversial, in part because the drug did not lower PSA levels or change how tumors appear on imaging scans. |

**Note:** This is a partial list, reflecting the more promising chemotherapeutic agents in clinical practice and in clinical trials. It does not include all agents or those in early stages of development. Those that have not been approved by the FDA for the treatment of prostate cancer might not be covered by health insurance.

*continued from page 70*

Since then, the FDA has approved two more PARP inhibitors, both of them for use in combination with other treatments. Talazoparib (Talzenna) is approved for use with enzalutamide in men with mCRPC who test positive for mutations in BRCA and other DNA repair genes. Clinical trial data published in *The Lancet* found that the overall survival time in men who got this combination was 45.8 months, compared to 31.1 months among men in a control group who got enzalutamide and a placebo.

Niraparib (Zejula) is approved for use with abiraterone in men with mCRPC who also have BRCA mutations. This combination is marketed as a single pill under the name Akeega. During the clinical trial leading to the approval, the two-drug combination delayed further cancer progression by 16.6 months, compared with 10.9 months with abiraterone and a placebo. Other research published in the *Journal of Clinical Oncology* found that the niraparib/abiraterone combination is also effective in men with mutations in other DNA-repair genes, including BRIP1, CDK12, CHEK2, FANCA, PALB2, RAD51B, and RAD54L. However, the benefits were greatest for those with a BRCA mutation.

## Bone-targeting treatments

When prostate cancer metastasizes, it spreads to bone about 90% of the time. Often prostate cancer's most serious—and sometimes deadliest—consequences are those involving bone tissue, including a higher risk of fractures and associated complications.

Several options are available for controlling cancer once it enters bone tissue. One of them, lutetium Lu-177 vipivotide tetraxetan (Pluvicto), is approved for treating PSMA-positive cancer cells wherever they exist (see "Radioligand drugs," page 69). That includes bone. Studies show the drug can improve survival and help to keep fractures at bay.

Another option is radium-223 (Xofigo). Approved for men who have advanced prostate cancer that has spread to the bone (but not to other organs) and are no longer responding to hormonal therapy, radium-223 behaves like calcium in the body. The drug is delivered intravenously and is absorbed preferentially into areas of bone that are rapidly breaking down and rebuilding, which is typical for metastatic bone lesions. Once deposited in bone, radium-233 targets and kills cancer cells. Results of an industry-sponsored trial showed that men with metastatic cancer who received radium-223 lived longer than men who received a placebo (14.9 months vs. 11.3 months).

Radium-223 and abiraterone should not be used together, because research has found that this combination increased the rate of fractures and lowered overall survival rate. Dr. Garnick notes that if an abiraterone-treated patient starts on radium-223, then abiraterone should be discontinued and only resumed four to eight weeks after radium-223 treatments have finished.

However, in 2025, investigators reported more encouraging results with a different combination that pairs radium-233 with enzalutamide. Published in *Annals of Oncology*, results from this clinical trial showed the combination delayed cancer progression. It took 19.4 months for the disease to worsen among men who got both drugs, compared to 16.4 months among men treated with enzalutamide alone. Survival was also improved in the combination group: it was 42.3 months compared to 35 months in the enzalutamide-only group.

Other medications, including zoledronic acid and denosumab, can help control or relieve the pain of metastases in bone and reduce the fracture rate in bones weakened by cancer or its treatment (see "Cancer and bone weakening," page 67).

## Immunotherapy

Immunotherapies (sometimes called cancer vaccines) turn the body's own immune system against tumor cells. Although immunotherapy has proved successful against many different types of cancer, its success in prostate cancer has been limited. An FDA-approved immunotherapy for prostate cancer, sipuleucel-T (Provenge), doesn't induce a measurable clinical response, such as a decline in PSA, making its effects difficult for doctors to monitor.

That said, a review of Medicare claims data from 6,044 men treated for mCRPC detected a survival advantage from sipuleucel-T. Results showed that men who received the immunotherapy lived 14 months longer on average than those who did not. However, insurance claims data contain limited clinical information and are therefore less informative than clinical trials.

Other immunotherapy drugs are showing promise. One called pembrolizumab (Keytruda) has FDA approval for all metastatic cancers that test positive for mutations affecting the mismatch repair (MMR) genes, which ordinarily patch the DNA damage that occurs routinely when cells divide. As DNA damage accumulates, cells can become genetically unstable, and cancer often results. To protect themselves, cancer cells rely on proteins—called checkpoints—that can deflect an incoming attack by the immune system. Pembrolizumab is a checkpoint inhibitor that disables this protective mechanism.

When researchers tested pembrolizumab in prostate cancer patients whose tumors contained MMR defects, they found that PSA levels dropped by more than 50%. And in approximately 40% of the PSA responders, tumors also shrank visibly. Dr. Garnick recommends, per guidelines, that all patients with metastatic cancer be tested for MMR defects, since they may respond to pembrolizumab or other checkpoint-inhibiting drugs.

# Genetic and biomarker-based tests

***Aids to diagnosis and treatment***

If you've been diagnosed with prostate cancer—or if a PSA test suggests you might have it—you likely have many questions. So does your doctor. Fortunately, there are a growing number of tests that can help answer them.

Increasingly, diagnosing clinically significant prostate cancer (defined as cancer that is likely to progress if left untreated) and managing it appropriately relies on measuring various biomarkers. Biomarkers are molecules, genes, proteins, and other measurable substances that provide insights into your disease status or susceptibility to disease.

One biomarker related to prostate cancer, prostate-specific antigen (PSA), has already been discussed at length in this report (see "Screening," page 38). Others include:

- inherited gene defects (also referred to as germline mutations), which are found in every cell of the body.
- mutations found in the genes of tumor cells (also known as somatic mutations). These kind of mutations are acquired over the course of a person's life, and can result from various factors, including errors in DNA replication, environmental exposures, and aging.
- genetic material and other substances shed by tumor cells into the bloodstream.

This Special Section provides an overview of biomarker-based tests and how you and your doctor might use them to answer key questions related to your care.

## Do you have an inherited genetic defect?

Several inherited genetic mutations are associated with an increased risk of developing prostate cancer. Mutations in the BRCA genes top the list, but defects in other genes—including ATM and CHEK2, among others—are also important to consider.

Mutations in any one of these genes can increase your risk of developing prostate cancer as well as make it more likely the disease will grow and spread. Current guidelines recommend genetic testing for men with a strong family history of cancer or Ashkenazi Jewish ancestry (which raises the risk of BRCA mutations). If you test positive for such a mutation, you can opt to follow a more vigilant cancer screening regimen, or begin screening at a younger age. Genetic testing is also recommended for men who have been diagnosed with metastatic or nonmetastatic prostate cancer with a Gleason score of 7 or higher. These men could be eligible for targeted therapies that block a mutation's cancer-promoting effects (see "PARP inhibitors," page 70).

Blood tests for inherited mutations related to prostate cancer are now typically performed as a multi-gene panel, which checks for mutations to several different genes at once.

## Can you skip a biopsy, even if your PSA is elevated?

A definitive diagnosis of prostate cancer hinges on whether cancer cells are found in biopsy samples. But when PSA levels are only somewhat elevated—in the range of 4 to 10 nanograms per milliliter (ng/mL)—about three out of every four biopsies come back negative. A magnetic resonance imaging (MRI) scan of the prostate provides useful information that can help doctors decide if a biopsy is necessary (see "Magnetic resonance imaging," page 42). But tests that measure urinary biomarkers can also help in that decision by providing insights into whether cancer that may be present is likely to grow and spread.

According to the National Comprehensive Cancer Network (NCCN), which sets global standards for cancer care, the following tests may be useful:

**SelectMDx.** This test measures levels of HOXC6 and DLX1, two biomarkers that can predict high-grade cancer in men flagged by PSA screening. Both biomarkers are messenger RNA (mRNA) molecules—substances that carry genetic instructions for making proteins. SelectMDx is used along with evaluations of prostate size, family history of prostate cancer, DRE, and MRI findings to assess the need for an initial biopsy in men with elevated PSA levels.

Evidence suggests that SelectMDx is especially predictive when combined with an MRI. In a 2023 study in *Cancer Reports*, combining the two tests would have allowed 87% of 129 men to avoid an unnecessary biopsy.

**ExoDx.** Exosomes are tiny capsules that develop inside a cell and contain some of its RNA, DNA, and proteins. Released into the bloodstream by many cell types, including tumor cells, exosomes contribute to the spread of cancer in the body—for instance, by helping to build new blood vessels that supply tumors with oxygen and nutrients. An exosome's cargo is unique to the cell it came from. Therefore, exosomes secreted by prostate cancer cells can be readily identified by the proteins and genetic material they contain.

The ExoDx urinary prostate test looks for three exosome-associated cancer markers: ERG, PCA3, and SPDEF. This test is intended to help physicians determine the need for initial biopsy in men 50 or older with PSA levels ranging up to 10 ng/mL.

Pooled results from three validation studies reported in 2022 showed that, 90% of the time, the test correctly identified men who did not have high-grade tumors. A 2023 study in *Prostate Cancer and Prostatic Diseases* found that men with low scores remained at very low risk of developing Grade Group 2 or higher prostate cancer 2.5 years after they had the test.

**MyProstateScore 2.0 (MPS).** Developed by researchers at the University of Michigan, MPS looks for 18 mutations expressed in prostate cancer tissue. These mutations are linked to high-grade, clinically significant prostate cancer. A 2024 paper in *JAMA Oncology* by the University of Michigan team showed the test correctly rules out Grade Group 2 cancer 95% of the time and Grade Group 3 or higher cancer 99% of the time.

## Do you have cancer—even if your biopsy was negative?

Sometimes prostate tissue sampled via biopsy appears normal, even when cancer lurks nearby. Uncertainty regarding the possible presence of cancer leads to high rates of repeat biopsies, along with the threat of infection and other complications, in men who are actually cancer-free.

**ConfirmMDx** is a test that can help determine whether another biopsy is warranted after an initial negative result. Performed on biopsy tissue samples, it provides an "epigenetic" profile of three genes involved in the development of prostate cancer: GSTP1, APC, and RASSF1. Epigenetic changes influence how a gene works without altering its underlying DNA sequence. These changes interfere with how a cell reads its instructions for making proteins and other products.

During a multicenter study in the United States, the test correctly identified men who did not have cancer with 88% accuracy. The five participating U.S. urology practices reported that the test had allowed them to reduce repeat biopsy rates to less than 5%.

## Is active surveillance safe for you?

Once a prostate cancer diagnosis has been made, next steps can range from active surveillance (see page 49) to starting treatment. But active surveillance is only an option if you have low- to intermediate-risk prostate cancer. Several tumor-tissue tests are available to help determine if active surveillance is right for you.

**Decipher** is a tumor-tissue test that looks at 22 genes involved in cancer cell proliferation, hormonal signaling, and tumor growth (see Figure 11, page 76). The test assigns a score from 0 to 1 for each biopsy sample, with scores above 0.6 predicting more aggressive cancer and the likelihood that a cancer will metastasize within five years if PSA levels rise again after surgical treatment.

If your Decipher score is low, then active surveillance may be a reasonable strategy. The score

### *Figure 11: Tumor tissue testing with Decipher*

This sample Decipher test shows results for a patient with low-risk disease, making him a good candidate for active surveillance. A different patient might have an identical Gleason score yet be deemed high risk by Decipher; in that case, a further discussion about treatment may be advisable.


also provides useful information that can help your doctor determine how frequently to monitor you with biopsies.

Decipher has another use as well: it can help doctors predict which men are most likely to benefit from radiation after having a radical prostatectomy (see "Surgery," page 53).

**Oncotype DX** measures the activity of 17 genes in biopsy samples to generate a Genomic Prostate Score. Favorable scores mean the cancer is apt to be slow-growing and that active surveillance is worth considering. Evidence also shows that Oncotype DX scores tend to remain stable over time. So men on active surveillance who had a favorable score during initial testing may also have less need for future biopsies.

Doctors also use the Oncotype DX test for help in determining if men need additional treatment after radiation or a radical prostatectomy (see "Treating prostate cancer," page 52).

**Prolaris.** This test measures the activity of 31 genes in biopsy samples that control cell division. These measurements are used to generate a cell-cycle progression score, which describes how rapidly your tumor cells are dividing and helps your doctor determine if your cancer is low, intermediate, or high risk.

Studies have shown the Prolaris test can accurately assess the likelihood that prostate cancer will return and spread after initial treatment. The evidence so far indicates the test is better at detecting aggressive cancers than it is at finding low-risk tumors that may not become life-threatening for many years. A 2024 paper published in *JCO Precision Oncology* found that the test was a strong predictor of metastatic disease within three years after biopsy.

**ProMark.** The ProMark test measures eight proteins in cancerous prostate biopsy specimens that predict whether a cancer is likely to be aggressive or not. The test generates a score between 1 and 100, and, as the score gets larger, so does the likelihood a man has high-risk disease that could metastasize.

Updated guidelines from the NCCN issued in 2025 endorse the use of tissue-based gene assays, particularly for use in estimating the risk of metastasis among men with intermediate- to high-risk prostate cancer. According to the NCCN, these tests provide additional information when making decisions about active surveillance versus treatment, or whether treatments should be intensified or reduced. The NCCN advises against using the tests in men with low or very low-risk prostate cancer, since standard diagnostic procedures are generally adequate in such cases and using the tests may lead to unnecessary anxiety and increased health care costs without proven benefit.

## If you're having radiation, how intensive should your regimen be?

Radiation protocols vary in terms of the dose and number of sessions (see "Radiation therapy," page 56). The goal is to eradicate the cancer while minimizing side effects and damage to healthy tissue.

**Oncotype DX**, while more commonly used to guide decisions regarding active surveillance (see page 49), can be used to help your oncologist determine your radiation regimen. A 2023 study in the *International Journal of Radiation Oncology* showed the test

can predict poor outcomes, such as rising PSA levels or progression to metastatic disease after external beam radiation therapy for localized prostate cancer. According to the authors, these findings indicate Oncotype DX scores can therefore inform which patients should get more intensive radiation treatments.

## Do you need hormonal treatments in addition to radiation?

Is radiation alone sufficient, or should you also have androgen deprivation therapy (ADT)? The **Prolaris tumor-tissue test** (see "Prolaris," see page 76) can help you and your doctor decide.

In 2024, researchers reported that this test can be used to predict which men with an unfavorable, intermediate-risk cancer grade (which behaves more aggressively than a favorable, intermediate-risk cancer) or high-risk prostate cancer can safely avoid adding ADT to radiation. The researchers studied 554 patients who were given the test and then treated with either radiation therapy alone or in combination with ADT. Results showed that men with high test scores on biopsy samples had a 14% risk of metastases at three years, compared with a 3% risk among those with low test scores.

Skipping ADT might be safe in men with low Prolaris scores, but Dr. Garnick says results from this test should be considered in the context of other tests and clinical information, in addition to your personal preferences.

## Do you need radiation if you've already had surgery?

The **Decipher** test can help you and your doctor make better-informed decisions about whether to proceed with more treatment after surgery for radical prostatectomy, usually in the form of radiation. When used for this purpose, the goal is to determine if a surgically removed tumor has aggressive features and how quickly the cancer might metastasize.

A 2025 paper in *European Urology Oncology* showed that Decipher scores correlate with progression to metastatic disease among men treated with radical prostatectomy for intermediate- and high-risk localized prostate cancer. Each incremental increase in the Decipher score was associated with a corresponding increase in the risk of biochemical recurrence and metastatic disease over follow-up durations ranging up to four years.

**Oncotype DX** is another test that may be used to determine the likelihood a tumor is confined to the prostate, to ascertain the presence of high-grade cancer in tissues removed during surgery, and to estimate the likelihood of metastases or prostate cancer death within 10 years. Higher Oncotype DX scores are associated with more aggressive cancer and greater odds that PSA levels will increase.

For men who haven't yet had any treatment, Decipher and Oncotype DX can be used to help determine whether active surveillance is an appropriate option (see "Active surveillance," page 49).

## Which medication is best for you?

Many men with mCRPC (see "Prostate cancer terminology," page 34) benefit from abiraterone (Zytiga) and enzalutamide (Xtandi), which are both hormonal medications. But about a third of patients who get these drugs don't respond to them. To find out if they're a fit for you, your doctor might order a circulating tumor cell test (CTC test), which is sometimes called a liquid biopsy. CTC tests are blood tests that scan for cells, DNA, and other material that might have been shed by tumors and released into the bloodstream.

**MolDX: Oncotype DX AR-V7** is a CTC test that checks for an AR-V7 mutation, which affects a tumor cell's receptor for testosterone (the hormone that fuels prostate cancer growth). Scientists believe mutated AR-V7 blocks hormonal treatments from binding with the receptor, the result being that the drugs have no effect. If you test positive for an AR-V7 mutation, chemotherapy would be a better choice.

One study showed that men with metastatic prostate cancer whose tumor cells tested positive for an AR-V7 mutation lived nearly twice as long on chemotherapy using taxanes (a common class of cancer drugs, including docetaxel and cabazitaxel) as they did on enzalutamide (14.3 months compared with 7.3 months). The opposite was true in those whose

tumor cells tested negative; they lived seven months longer on enzalutamide compared with taxanes.

Another CTC test, called **CellSearch**, can detect a variety of molecular markers in the bloodstream, including prostate-specific membrane antigen (PSMA). A 2023 study showed that PSMA expression in CTCs increases rapidly in men with mCRPC whose cancer progresses despite treatment with abiraterone or enzalutamide. Such findings can help doctors identify patients who need different or additional therapies, including PSMA-directed treatments such as lutetium Lu-177 vipivotide tetraxetan (Pluvicto).

The **Liquid CDx test** is a different type of liquid biopsy. Known as a circulating tumor DNA test, it measures DNA released by prostate cancer cells into the bloodstream. Liquid CDx analyzes 324 genes in circulating tumor DNA and scans for acquired mutations. It can be used to predict whether abiraterone or enzalutamide will be effective. In addition, it's being used to identify men who are eligible for treatment with olaparib (Lynparza), which is approved for men with advanced prostate cancer who test positive for inherited mutations affecting the BRCA1 and BRCA2 genes, as well as mutations in another gene called ATM.

CellSearch and Liquid CDx can also be used to monitor treatment response (see next section.)

## Is your current treatment working?

If you have metastatic prostate cancer, your doctor will monitor you with regular imaging tests and PSA tests. But they also have other tools in their arsenal, including the **CellSearch** test.

CellSearch is a CTC test, also known as a liquid biopsy (see "Which medication is best for you?" on page 77). Currently, it is the only FDA-cleared test for detecting and counting CTCs, though researchers are trying to develop a more accurate test that costs less.

Cancer metastasizes when cells in the original tumor break away, get swept up into the bloodstream, and spread to other parts of the body. CellSearch measures the number of CTCs in a simple blood sample, which reduces the need for follow-up biopsies of the prostate and other tissues. If your treatment is effective, the number of CTCs should decline over time. If they remain high or increase, it suggests your current therapy is not working as well as it should.

A 2025 study of men with newly diagnosed metastatic prostate cancer showed that having five or more CTCs per milliliter in a blood sample predicts worse outcomes. Overall survival in such patients lasted roughly half as long as it did in men with four CTCs or fewer in blood samples. Based on these results, the authors concluded that CTC findings can help doctors decide among patients who should receive standard treatment versus possibly enrolling in new drug trials (see "Participate in a clinical trial," page 91).

The **Liquid CDx** test can also supply useful clues about how your cancer is responding to treatment. Levels tend to increase in men with prostate cancer that is rapidly progressing. Circulating tumor DNA is a lot more common in blood than CTCs themselves. It can also be used to determine whether you'll respond to the chemotherapy drug olaparib (see "Which medication is best for you?" on page 77).

### What is PTEN loss?

PTEN loss—loss of the function or expression of the PTEN gene—is among the most common of the acquired genetic changes that occur in prostate cancer, affecting roughly 40% of men who have the disease. PTEN is a tumor-suppressor gene. Without it, processes that keep cell division in check are missing, and cancer may develop.

PTEN loss correlates with the hallmarks of aggressive prostate cancer, such as high Gleason scores, a shorter time to metastases, and recurrences relatively soon after prostatectomy. A 2025 study in *Cancers Basel* showed that the odds of PTEN loss are greatest in men with Grade Group 2 and 3 tumors and correlate with higher risks for biochemical recurrence after treatment. Researchers have also found that PTEN loss is frequently detected in biopsy samples from men whose cancers are worsening on active surveillance. By contrast, PTEN loss tends to be rare in men with low-risk prostate cancer.

Measuring PTEN isn't easy. Cancer often appears in different spots—called foci—within the prostate gland, and PTEN levels within those foci can differ, complicating the analysis. Routine use of the test varies by institution, but with newer methods it could come into more widespread use.

5

# Erectile dysfunction and prostate disease

***Solutions for a troublesome complication***

When everything is working properly, an erection begins when a touch, a look, or even a thought nudges the brain to send signals of arousal down the spinal cord and into the nerves of the penis. The nerves "talk" to one another by releasing nitric oxide and other chemical messengers, which boost the production of other important chemicals. These, in turn, initiate the erection by relaxing smooth muscle cells lining the tiny arteries that lead to the corpora cavernosa, side-by-side flexible cylinders that run the length of the penis (see Figure 12). As the arteries relax, the tissues swell with blood. The small veins that would normally allow blood to flow out of the penis are compressed, so the blood is trapped. The result is an erection.

Because the prostate is so closely intertwined with the other reproductive organs, any prostate-related problem or procedure has the potential to impair this process. Many men with benign prostatic hyperplasia (BPH), as well as those impacted by prostate cancer, struggle with erectile dysfunction (ED), but help is available.

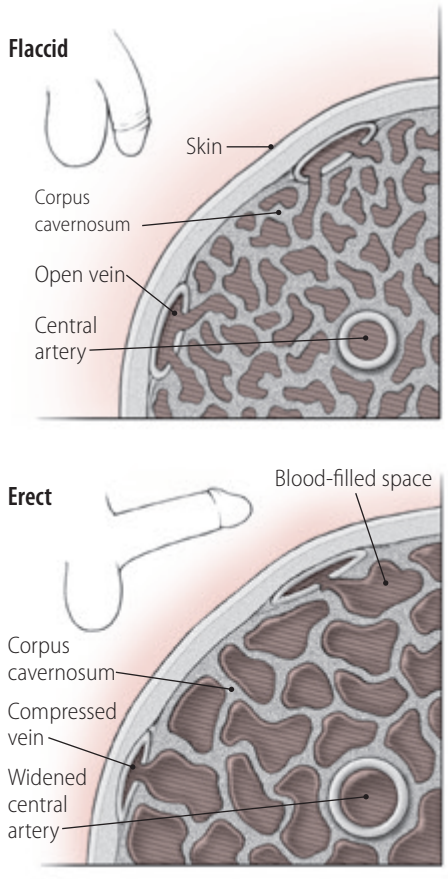
## Benign prostatic hyperplasia

BPH itself doesn't cause ED, but some of the medications used to address it can. In particular, finasteride (Proscar) and dutasteride (Avodart) are associated with this problem. These drugs shrink the prostate and alter hormone ratios within it (see "5-alpha-reductase inhibitors," page 18).

Clinical trials suggest that finasteride and dutasteride cause ED and lower libido in about 5% to 8% of men who take the drugs. But doctors report that, in real-world settings, the percent of men affected is much higher. In addition to impeding erections, these drugs can cause retrograde ejaculation, meaning semen flows back into the bladder rather than out of the penis during orgasm.

Surgery for BPH can also cause retrograde ejaculation. However, multiple studies have reported

***Figure 12: What happens during an erection***




Chemical signals from the brain cause arteries in the penis to widen, allowing more blood to enter the erectile bodies known as the corpora cavernosa. These tissues swell with blood, causing an erection. At the same time, blood-engorged tissues compress the veins, keeping blood in the penis and maintaining the erection.

no link between nonpharmaceutical BPH treatments and impotence.

### Prostate cancer

Surgery for prostate cancer can sever some of the nerves and arteries that are necessary for an erection, and some men also experience short-term (generally less than one month) reductions in erectile function after a prostate biopsy. Impairments in erectile function can be long-lasting, however, if cancer is confirmed and treated.

Reported rates of ED following prostate cancer surgery vary widely. While most men have ED immediately following surgery, some recover normal functioning within a few months, whereas others have problems that endure indefinitely. Factors that may impact whether ED persists include:

- **Your age.** Younger men tend to recover faster.
- **Your pre-surgery level of sexual potency.** Men who could easily achieve and maintain erections usually fare better.
- **Your health history.** Having diabetes, obesity, cardiovascular disease, and a history of being a smoker are all associated with a higher risk of persistent ED.

Surgical technique is also important. Robotically assisted surgeries are generally associated with better outcomes in sexual functioning than older surgical procedures, according to a 2024 review of 268 published trials enrolling a combined total of 131,500 men. Among the men who got robotic surgery, 35% reported erections sufficient for intercourse after three months, and 67% of the men had recovered sexual potency within three years.

Nerve-sparing prostatectomy (in which the surgeon tries to avoid damaging the nerves that control erectile function using either robotic or older methods) can also reduce the risk of prolonged post-surgery ED, but there are no guarantees.

A newer robotic approach to radical prostatectomy called NeuroSAFE incorporates an additional level of nerve-sparing guidance. During this procedure, a surgeon sends flash-frozen tissue samples from the edge of the prostate closest to the nerve bundles to a pathologist. The pathologist, in turn, supplies real-time feedback about the extent of a cancer's spread into the nerve bundles. With this additional guidance, doctors can more confidently preserve the nerves, or remove them, if necessary, to achieve cancer-free tissue margins. A 2025 study in *The Lancet Oncology* showed that 62% of men who had the NeuroSAFE procedure regained sexual potency within a year, compare to 44% men who had the standard surgery.

If you require radiation, keep in mind that the same beams that destroy cancer can also harm erectile tissues and the blood vessels that supply the penis and enable it to become erect. ED develops about 40% to 50% of the time when external beam radiation is used.

In its advanced stages, prostate cancer itself can spread to the nerves and arteries necessary for an erection.

## Assessing and treating ED

If you experience frequent or consistent ED after treatment for prostate disease, see your urologist or another qualified health professional. You may be asked to fill out a questionnaire about your erectile function, such as the International Index of Erectile Function (see Table 10, page 81). You should also expect to answer questions about your sexual history, medical condition, and any medications you take.

Next, your doctor may run tests to better understand what's happening physiologically. One such test sometimes used in men with ED related to heart disease or diabetes is a nocturnal penile tumescence test, which monitors erections while you sleep. During the test, a recording unit collects data on the number and duration of nocturnal erections, changes in the circumference of the penis, and penile rigidity. The measurements are made by two loops: one at the base of the penis, and the other at the tip. Rigidity above 70% produces an erection suitable for penetration during sex; below 40% represents a flaccid penis. During eight hours of sleep, it's considered normal to have three to six erections lasting 10 to 15 minutes each, on average, though definitions of "normal" vary.

The remedies for ED resulting from prostate treatment are the same as those for ED from other causes

**Table 10: The Abridged International Index of Erectile Function (IIEF) questionnaire**

The full-length IIEF questionnaire includes 15 questions to assess erectile function, orgasm ability, sexual desire, satisfaction with sexual intercourse, and overall satisfaction. An abridged version of the questionnaire with five questions, called the IIEF-5 and shown below, focuses specifically on erectile function and satisfaction. A higher point total means better erectile function, and therefore less ED. Because the answers to some questions are subjective, clinicians also rely upon your medical history, a physical exam, and lab tests to diagnose and treat ED.

| Rate your symptoms in the past six months: | 1 point | 2 points | 3 points | 4 points | 5 points |
|---|---|---|---|---|---|
| How do you rate your confidence that you could get and keep an erection? | Very low | Low | Moderate | High | Very high |
| When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering your partner)? | Almost never or never | A few times (much less than half the time) | Sometimes (about half the time) | Most times (much more than half the time) | Almost always or always |
| During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner? | Almost never or never | A few times (much less than half the time) | Sometimes (about half the time) | Most times (much more than half the time) | Almost always or always |
| During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse? | Extremely difficult | Very difficult | Difficult | Slightly difficult | Not difficult |
| When you attempted sexual intercourse, how often was it satisfactory for you? | Almost never or never | A few times (much less than half the time) | Sometimes (about half the time) | Most times (much more than half the time) | Almost always or always |

**Your score**

Add up your points from each question

_____ + _____ + _____ + _____ + _____ = _____

**What do the numbers mean?**

5–7: severe ED
8–11: moderate ED
12–16: mild to moderate ED
17–21: mild ED
22–25: no ED

Sources: Rosen RC, et al. "Development and Evaluation of an Abridged, 5-Item Version of the International Index of Erectile Function (IIEF-5) as a Diagnostic Tool for Erectile Dysfunction," *International Journal of Impotence Research* (1999), Vol. 11, No. 6, pp. 319–26. Rosen RC, et al. "The International Index of Erectile Function (IIEF): A Multidimensional Scale for Assessment of Erectile Dysfunction," *Urology* (1997), Vol. 49, No. 6, pp. 822–30.

(see Table 11, page 82). A treatment's effectiveness varies from individual to individual, and some men may benefit from a combination of treatments rather than just one. There may be some trial and error before you find an approach that works for you.

## PDE5 inhibitors: Viagra and other ED drugs

Avanafil (Stendra), sildenafil (Viagra), tadalafil (Cialis), and vardenafil (generic only) belong to a class of drugs called PDE5 inhibitors. These pills are easy to use and are effective for ED, helping 60% to 70% of men who take them. Success rates may be lower in men with diabetes, which can damage blood vessels.

PDE5 inhibitors can be used for ED related to prostate cancer treatment (both nerve-sparing radical prostatectomy and radiation therapy) and for ED related to BPH medications. Tadalafil is also approved as a treatment for BPH itself. However, after a prostatectomy in which the nerve bundles could not be spared or were seriously damaged, PDE5 inhibitors are ineffective and should not be taken.

Men are now routinely prescribed a PDE5 inhibitor immediately after nerve-sparing or partial nerve-sparing prostatectomy surgery in which the nerves were not too badly damaged. Small, daily doses of these drugs are thought to decrease the chances of developing ED by preserving smooth muscle function and oxygenation of tissues in the penis, and they may also help to limit or prevent what are usually minor reductions in penis size that can occur after surgery. Some studies show the PDE5 inhibitor sildenafil is

*continued on page 83*

## Table 11: Comparing ED treatments

How well ED drugs work can vary from person to person. Men should consider how quickly they take effect, how long they last, and possible side effects. Your insurance coverage may determine what therapies you are willing to try. Some are exceedingly expensive without insurance, whereas prices for others, such as PDE5 drugs, have dropped significantly as generics have become available and can now cost around a dollar per pill.

| THERAPY | ONSET OF ACTION | DURATION* | ADVANTAGES | DISADVANTAGES |
|---|---|---|---|---|
| **Oral medications** | | | | |
| avanafil (Stendra) | 15–30 minutes | Up to 6 hours | Very effective (about 70%); few side effects. | Cannot be used by men taking nitrates or those with unstable cardiovascular disease. |
| sildenafil (Viagra) | 30–60 minutes | 4–5 hours | | |
| tadalafil (36-hour Cialis) | 30–45 minutes | 24–36 hours | | |
| vardenafil (Levitra, Staxyn) | 15–30 minutes (Staxyn may work slightly faster) | 4–5 hours (Staxyn may last up to 6 hours) | | |
| tadalafil (Cialis for daily use) | Steady low dose in bloodstream | Any time sexual arousal occurs | Effectiveness varies depending on dose (2.5 mg or 5 mg) and ED severity, but may be as effective as taking a higher dose of the same drug on an as-needed basis. | |
| **Penile injections** | | | | |
| alprostadil (Caverject, Caverject Impulse, Edex) | 5–20 minutes | 30–60 minutes | Highly effective (about 80%); few side effects. | Requires training; injections unpleasant for many men; may cause penile pain or painful sustained erections. |
| papaverine and phentolamine (Bimix) | 5–10 minutes | 30–60 minutes | Highly effective (about 90%); may be more effective than a single-drug injection for those who don't respond (or respond well enough) to a single drug. | Must be made to order by a compounding pharmacy; not covered by insurance. |
| papaverine, phentolamine, and alprostadil (Trimix) | | | | |
| papaverine, phentolamine, alprostadil, and atropine sulfate (Quadmix) | | | | |
| **Penile suppository** | | | | |
| alprostadil pellets (MUSE) | 5–15 minutes | 30–60 minutes | Moderately effective (about 30%). | Requires training; may cause penile pain, usually mild; may cause dizziness. |
| **Devices** | | | | |
| penile band (Encore, Timm, many other brands) | Immediate | While in use | Effective when used properly; helpful for men with venous leakage who cannot sustain an erection. | May be awkward to use. |
| vacuum pump (various manufacturers) | Immediate | Until the band placed at base of penis after using the pump is removed | Highly effective (about 80%); no serious side effects. | Requires training; cumbersome and awkward; may cause penile numbness or bruising. |

*Duration refers to the window in which you should be able to get an erection. An erection that lasts more than four hours is an emergency that requires medical attention.

*continued from page 81*

especially helpful in regaining potency after prostate cancer surgery.

**How they work:** PDE5 inhibitors augment cyclic GMP, a chemical that relaxes smooth muscles in the penis, improving blood flow during sexual stimulation.

**Side effects:** Short-term side effects of PDE5 inhibitors include headache, flushing, upset stomach, and nasal congestion. Temporary disturbances in vision have been reported. Some men experience a bluish tinge to their sight. Vision loss and hearing loss are rare. Another possible, though relatively rare, complication is priapism, an erection that lasts too long. Any man who has an erection for more than four hours should go to the emergency room to receive a counteracting drug. Prolonged erections can damage penile tissues and result in permanent impotence.

**What else to know:** PDE5 inhibitors are unlikely to produce an erection during the first six months or so after surgery, so be patient. The delay is fortunate, because an erection too soon after surgery could cause surgical stitches that hold tissues together to break open, causing bleeding.

These drugs shouldn't be taken more than once a day, and you shouldn't take them if you are also taking nitroglycerin or another nitrate drug for heart disease. Men who take certain alpha blockers that tend to lower blood pressure also need to exercise caution; in fact, all men with heart disease should be careful using these drugs, because PDE5 inhibitors tend to lower blood pressure. If you take a PDE5 inhibitor and wind up going to the hospital with heart attack symptoms, be sure to tell the medical personnel there that you have taken an ED drug.

Some of these drugs are expensive, though costs for sildenafil and tadalafil have dropped sharply since their generic versions came on the market. Some health insurance plans don't cover ED drugs, or cover just a few pills per month. You may be able to get discount coupons from manufacturers or your pharmacist. Medicare generally doesn't pay for medications used in treating ED, although some Medicare Part D plans cover generic versions. Tadalafil—the only PDE5 inhibitor that also has FDA approval for treating BPH—may be covered if prescribed for that purpose. Check with your plan to be sure.

One unconfirmed study has suggested that PDE5 inhibitors may lead to an increase in PSA after surgery (a condition known as biochemical recurrence), but such claims have never been reproduced or substantiated. A large study with more than 4,000 men published in 2025 in the *Journal of Urology* found no evidence that biochemical recurrence was more common among those who took PDE5 inhibitors during the first year after a radical prostatectomy.

### Injectable drugs

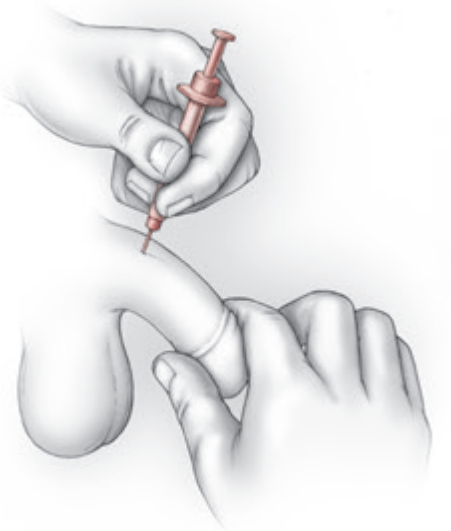
If you can't take a PDE5 inhibitor or don't respond to oral ED medication, injectable drugs are a good alternative (see Figure 13, page 84). The American Urological Association recommends that men try injectable agents as second-line ED therapies if PDE5 inhibitors don't work.

Injection therapy is often more effective than PDE5 inhibitors for men whose ED is related to radical prostatectomy, because the injected drug goes directly into the blood vessels that control erections. When you take a pill, the drug has to be metabolized and circulated throughout the body, and it may not reach the target tissue in high-enough concentrations to be effective.

**How they work:** In the United States, the only injectable drug specifically approved for ED is alprostadil (Caverject, Edex). Alprostadil is a potent vasodilator, meaning it widens arteries, allowing them to carry more blood. Other drugs used for injectable therapy include papaverine (another vasodilator) and phentolamine (an alpha blocker). Those two drugs are sometimes combined with alprostadil in a three-part mixture known as Trimix that is available off-label from compounding pharmacies.

**Side effects:** The main side effects of injectable ED drugs are mild to moderate pain, bruising, or scarring. But there can be more serious side effects, too. In some cases, the drugs cause priapism (an erection that can last for hours in the absence of stimulation). This constitutes a medical emergency, because blood is depleted of oxygen when it is trapped

### Figure 13: Injection therapy



In this treatment, you inject one or more prescription drugs into the side of the penis using a small needle. The drugs work by relaxing the smooth muscle tissue of the penis and allowing blood to flow into the tissue, producing an erection. However, they can also cause priapism (an erection that can last for hours in the absence of stimulation), which is a medical emergency.

in the penis, and the lack of oxygen can damage penile tissues.

**What else to know:** Patients who use injectable treatments while taking anticoagulant medications have a higher risk of bleeding complications, and men who use these agents may have also worse outcomes if they later opt for penile implants (see page 86). That's because repeated injections cause tiny injuries to penile tissue that can lead to higher rates of postoperative complications.

## Urethral suppositories

As an alternative to injection, alprostadil is also available as tiny pellets that can be inserted into the penis shortly before intercourse. These pellets are part of a therapy called the medicated urethral system for erection (MUSE). Some men find MUSE easier to use than injections.

**How it works:** This therapy involves inserting a pellet about an inch into the penis using a disposable plastic applicator. From there, the surrounding tissue quickly absorbs the drug (alprostadil, which dilates blood vessels).

**Side effects:** About 10% of men who try MUSE find the application mildly painful, and about 3% become dizzy and develop low blood pressure.

**What else to know:** You shouldn't MUSE more than twice in 24 hours, since doing so increases risks for priapism, a painful and prolonged erection that can last for up to four hours or longer A serious medical condition, priapism requires prompt medical treatment to prevent damage to penile tissues.

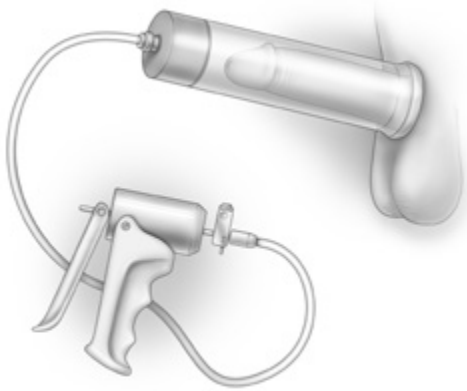
## Vacuum pump

A treatment that predates ED medication, vacuum pumps are noninvasive and highly effective when used correctly, working for about 80% of men.

**How it works:** This therapy involves lubricating your penis and putting it into an airtight plastic cylinder attached to a handheld or battery-operated pump that creates a vacuum (see Figure 14). The negative pressure draws blood into the corpora cavernosa, the columns of spongy tissue that fill with blood to

*continued on page 86*

### Figure 14: Vacuum pump



To achieve an erection, a man puts his lubricated penis into an airtight plastic cylinder attached to a handheld or battery-operated pump. Pumping air out of the cylinder creates a vacuum, which increases blood flow to the penis and causes an erection. An elastic band placed at the base of the penis maintains the erection.

## Figure 15: Penile implants compared

### Three-piece inflatable implant

**Advantage**

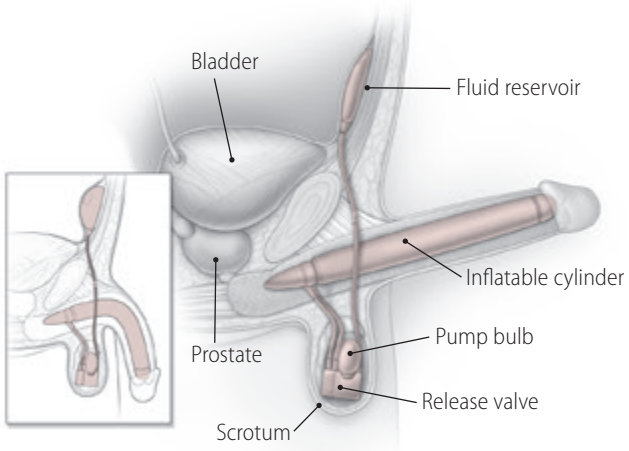
- Acts and feels more like a natural erection than semirigid models.

**Disadvantages**

- Requires more manual dexterity than other implants.
- Possibility of leakage or malfunction.
- Most expensive type of implant.
- Requires the most extensive surgery of all implants.

**Comments**

- The inflate/deflate device is implanted in the scrotum. Squeeze pump to inflate, then press the release valve to deflate.
- The fluid reservoir is implanted in the abdomen.
- Lock-out valve can prevent unintended inflation.




### Two-piece inflatable implant

**Advantages**

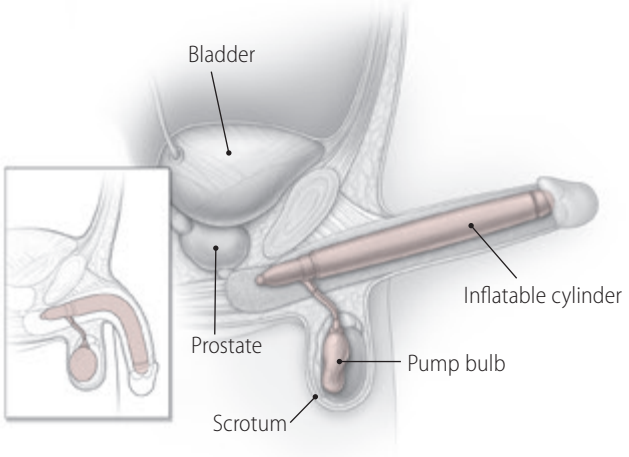
- Penis looks more natural in erect and flaccid states than with the semirigid implant.
- Easier to operate than the three-piece implant.
- No abdominal incision.

**Disadvantage**

- Possibility of leakage or malfunction.

**Comments**

- Squeeze and release the pump several times to move fluid into the penile cylinders. Bending and holding the penis causes the cylinders to soften.
- The penis does not deflate as fully as with the three-piece implant.




### Semirigid (malleable) implant

**Advantages**

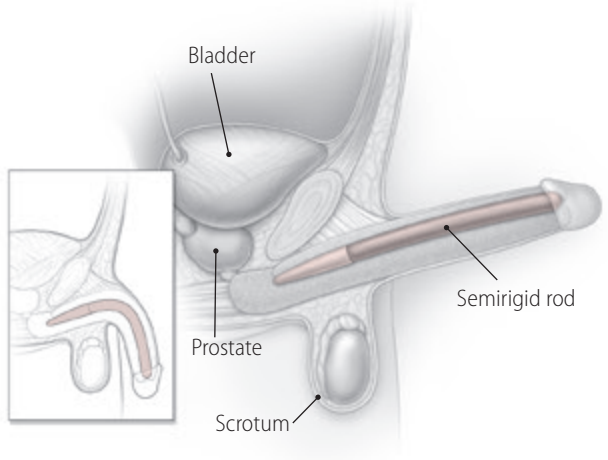
- Easy to use, especially for those with limited dexterity.
- Requires the least extensive surgery.
- Fewest parts, so less chance of malfunction.
- Least expensive type of implant.

**Disadvantages**

- Constantly firm.
- Somewhat harder to conceal than inflatable implants, but new designs make this less of a concern than in the past.
- Thinning of the penis and decreasing girth.

**Comment**

- For intercourse, lift the penis and make the rods as straight as possible.



*continued from page 84*

produce an erection. Once an erection occurs, which usually takes about five minutes, you remove your penis from the cylinder and fit an elastic band around the base of the penis to prevent blood from draining away. The erection lasts until the band is removed.

**Side effects:** About 10% of men have side effects from this treatment such as pain, bruising, or difficulty ejaculating, any of which can cause discomfort during sexual activity. Dr. Marc Garnick, editor in chief of this guide, cautions that men should be instructed in the proper use of a vacuum pump. In his experience, men who use it too soon after prostate cancer surgery can also pull their stitches out of place.

**What else to know:** A pump can be used as often as desired. However, using one requires a bit of manual dexterity, and having to fuss with the device can interrupt lovemaking. In addition, the erection doesn't feel as natural as one produced by a drug; although firm, it does not extend down into the base of the penis.

## Penile implants

Penile implants, which are surgically inserted into the penis, are a possibility for men who have tried ED medications and vacuum pumps with no success. With an implant, you can have an erection at any time—and maintain it for as long as you want—allowing for great spontaneity. Studies show the vast majority of men are happy with the results, and implants are typically covered by Medicare and most other forms of health insurance.

There are two basic varieties of implants: inflatable and non-inflatable (semirigid, or malleable, rods).

**Inflatable implants.** These may have a two- or three-piece design. Three-piece implants consist of a fluid-filled reservoir in the abdomen, a pump with a release valve in the scrotum, and two inflatable cylinders in the penis. Squeezing the pump transfers fluid from the reservoir into the cylinders, causing an erection. Pushing the release valve drains the fluid back into the abdominal reservoir. In two-piece implants, fluid-filled reservoirs are in the rear portion of the cylinders, while the pump is in the scrotum. Bending the penis returns the fluid to the reservoir.

© Kraig Scarbinsky | Getty Images

Many men struggle with erectile dysfunction due to a prostate condition. Medication, pumps, and implants can help.

One drawback to inflatable implants is the risk of mechanical trouble, such as a leaky reservoir that requires surgical repair. However, most devices are fairly durable and last 10 years or longer. Another is the possibility that the penis will get shorter, although a variety of techniques to increase penile length in men who undergo the procedure are available.

**Semirigid, or malleable, rods.** As the name implies, this type of implant consists of bendable rods, usually constructed of braided stainless steel wires or articulating plastic discs, covered with silicone. The rods are bent upward to have sex and pointed down at other times to conceal the penis under clothing. They are easier to manipulate than inflatable implants, and a single incision makes them simpler to insert surgically. But because the rods always remain firm, their presence is harder to disguise. Nearly 90% of the men who get one are able to have sexual intercourse. (For a more detailed comparison of semirigid and inflatable implants, see Figure 15, page 85.)

Regardless of the model chosen, patients and their partners report a high overall degree of satisfaction with penile implants. Still, it's important to consider penile implant surgery carefully. The infection rate is the same as it is for other surgical procedures—about 1% to 3%—though these rates are falling as surgical techniques improve and antimicrobial coatings are increasingly used.

The procedure to implant a penile device takes about one to two hours. Strenuous physical activities

should be avoided for about a month; sexual activity can resume in four to six weeks.

Patients and their partners are generally more satisfied with the results if they know what to expect from a penile implant. If possible, you and your partner should meet with the doctor together before surgery. Make sure you understand the risks and benefits of the procedure and how the device works.

### Topical gel

The FDA has authorized over-the-counter sale of MED3000 (Eroxon), a non-medicated topical gel treatment for ED. MED3000 is supplied in single-use tubes and rubbed onto the head of the penis immediately before sexual intercourse. The gel formulation includes volatile components (alcohol and water), which, when applied to the head of the penis, evaporate rapidly, stimulating nerve endings through an initial cooling effect, followed by a warming sensation. This reaction releases nitric oxide, relaxing the smooth muscle tissue inside the penis and increasing the blood flow needed to obtain an erection.

According to the company, the effect begins within 10 minutes—less time than it takes for a PDE5 inhibitor to kick in. However, no studies on this drug have been published, so experts are skeptical of these claims. Some doctors say there is not enough information available yet to start recommending the gel to patients.

6

# Help for urinary incontinence

***Treatments to stop embarrassing leaks***

The involuntary leakage of urine is a common and embarrassing side effect of prostate disease and its treatment. For many men, it is the most dreaded and unwelcome of all potential side effects from prostate cancer treatment—even more than erectile dysfunction.

Urine leakage is a frequent side effect of radical prostatectomy, particularly in older men who had large prostates. A 2024 study in the *Journal of the American Medical Association* that followed 2,455 men for 10 years after prostatectomy reported urinary incontinence rates ranging from 14% to 25%, compared with 4% to 11% of men treated with radiation. (Irritation and painful urination are the most common urinary side effects of radiation therapy.)

Men treated with minimally invasive techniques rather than radical prostatectomy report fewer urinary complications. A 2023 review in *Current Opinions in Urology* found that up to 10% of men treated with two such techniques—cryotherapy and high-intensity focused ultrasound—experienced transient urinary incontinence soon after surgery. However, men who received these treatments after having already been treated with radiation for prostate cancer had worse urinary outcomes. For instance, incontinence rates averaged 12.5% at 12 months for men who had cryotherapy after having had radiation, compared with 1.5% for those without the earlier radiation treatment.

Another factor that predicts higher odds of urinary incontinence after surgery is the length of the membranous urethra (the portion of the urethra surrounded by the sphincter muscle, which tightens to close off urine flow). A longer membranous urethra, visible in magnetic resonance imaging, tends to be more muscular, and that helps with continence after surgery.

If you experience urinary problems following prostate treatment, it might not be a permanent problem. Urinary incontinence tends to subside gradually over the first two years following prostatectomy. But it can be distressing in the meantime, and in some cases it never resolves.

If your incontinence doesn't improve within six months and is significantly impacting your quality of life, talk to your urologist. They may recommend a urodynamic evaluation—a group of diagnostic tests to help determine the nerve and muscle function of your bladder and urethral sphincter. This will help pinpoint the exact nature of the problem.

Before seeing your doctor, keep a written record of your urination patterns for at least three days. Note when the leaking occurred, what you were doing at the time, what appears to make the problem worse, and what appears to make the problem better. This will help your doctor determine the type or types of incontinence you have.

## Incontinence types and treatment options

There are three main types of urinary incontinence that may develop after treatment for prostate cancer. Treatment varies according to type.

### Stress incontinence

This type of incontinence is characterized by the leakage of small amounts of urine when you cough, sneeze, lift a heavy object, exercise, or otherwise put pressure on your bladder. One cause of stress incontinence is damage to the external urethral sphincter, a band of muscle tissue that controls "downstream" urine flow from the bladder and through the urethra. Surgery on the prostate, such as transurethral

resection of the prostate (TURP) or prostatectomy, can cause such damage.

**Treatments:** Pelvic floor exercises—also known as Kegel exercises—can help you control your pelvic floor muscles so you can delay voiding until you reach a toilet. The pelvic floor comprises the group of muscles spanning the pubic bone and the tailbone, or coccyx, in the back. Some research has found that pelvic floor exercises could have the added bonus of helping with ED after prostatectomy.

Sometimes, pelvic floor exercises are coupled with biofeedback, which utilizes sensors to provide real-time feedback about muscle activity. Electrical stimulation may also be used: in this treatment, electrodes are placed on the skin or in a probe inserted in the anus and used to electrically stimulate pelvic muscles and possibly strengthen them. Research shows some short-term benefits to this approach, but it's unclear whether it lasts.

Bulking agents, which have been used extensively in men who have undergone radical prostatectomy, are another option. In an outpatient procedure, a physician injects the bulking agent into the area once occupied by the prostate to support the urethral muscles. As a result, you don't lose urine as easily. The most commonly used bulking agent is collagen. (This protein gives skin its tone, and it's often used as a filler in cosmetic procedures.) You will likely need repeat injections, because your body typically absorbs the bulking agent within a few months.

### Urge incontinence

Urge incontinence occurs when the bladder develops a spasm, suddenly contracts, then expels urine. BPH seems to leave the bladder prone to such irritation.

**Treatments:** Some people with urge incontinence find that retraining the bladder is effective. Bladder retraining involves prolonging the interval between urinations. Over time, bladder storage capacity increases, and the bladder learns to suppress sudden urges to urinate.

The most effective drugs for urge incontinence are oxybutynin, tolterodine (Detrol), and some of the tricyclic antidepressants. For incontinence that results from treatments for prostate enlargement—such as TURP, which may produce bladder instability and urge incontinence—anticholinergic drugs such as dicyclomine (Bentyl) may help.

## Kegel exercises

The strength and proper action of your pelvic floor muscles are important in maintaining continence. Here's how to do basic pelvic muscle exercises, named for Arnold Kegel, the physician who first developed them:

1. Pretend you are trying to avoid passing gas. You will feel a contraction more in the back than in the front, as if you are pulling the anal area in.
2. Practice both short contractions and releases and longer ones, gradually increasing the strength of the contraction and holding it for up to 10 seconds.
3. Repeat multiple times, several times a day.

### Overflow incontinence

Overflow incontinence is the result of a partial obstruction, such as an enlarged prostate. Because the bladder cannot empty completely, it becomes overfilled or distended, and urine dribbles from the urethra. It can also occur when the bladder muscle becomes severely weakened—a problem that can develop as a result of BPH if the bladder muscle becomes thick from straining to urinate.

**Treatments:** Alpha blockers—such as alfuzosin (Uroxatral) and tamsulosin (Flomax)—may improve overflow incontinence caused by BPH. These drugs help relax urethral muscles, allowing full emptying of the bladder and therefore making leaking less likely.

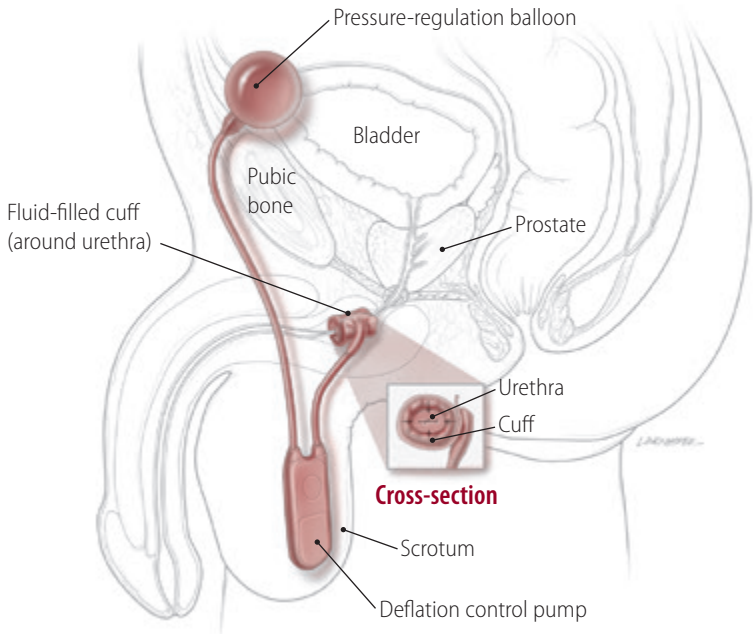
## Surgery for severe incontinence

For more severe incontinence, there are several surgical procedures that can be performed to achieve dryness. The leading therapy for severe stress urinary incontinence after prostate cancer surgery is the surgical placement of an artificial urinary sphincter (see Figure 16, page 90).

The procedure involves placing a small, fluid-filled inflatable cuff around the urethra and a small

### Figure 16. Artificial urinary sphincter

For men who have had prostate surgery, initial incontinence usually improves over several months. But for a man with intractable incontinence caused by sphincter weakness, the artificial sphincter is a possible solution. After it is surgically inserted, the fluid-filled cuff compresses the urethra to stop the flow of urine. To allow urination, the man squeezes a small pump in the scrotum to open the cuff and allow urine to pass. The cuff automatically refills.




pump in the scrotum. When it's inflated, the cuff squeezes the urethra so urine can't flow through it. When you're ready to urinate, you squeeze the pump, which deflates the cuff enough so that urine can flow. When you're finished, the cuff reinflates on its own.

Success rates for artificial sphincter surgery are relatively high. Continence isn't restored immediately, however. It may take four to six weeks to heal from the surgery, during which time the pump cannot be activated. Men who undergo this procedure may also experience complications such as infection, erosion of tissue around the implants, and device malfunction, which may require additional surgery.

## Living with urinary incontinence

Even if your urinary incontinence can't be cured, it can be managed. In addition to the treatments already described, absorbent underclothing is available that's no more bulky than normal underwear and can be worn easily under everyday clothing. Highly absorbent disposable pads are available in drugstores and online.

In another approach, a flexible tube (called an indwelling catheter) can be placed in the urethra to collect urine in a wearable container. However, long-term catheterization, although sometimes necessary, can create many problems, including urinary infections.

When a long-term catheter is necessary, one option to consider is a suprapubic catheter, which is inserted through the abdomen and then into the bladder. Although getting a suprapubic catheter requires minor surgery, it tends to be more comfortable and easier to keep clean, which may reduce the risk of infections.

Finally, an external collecting device (condom catheter or penile sheath) is another option. This device is fitted over the penis and connected to a drainage bag. It's noninvasive and can be removed as necessary, but it doesn't help with urinary retention (inability to completely empty your bladder).

Coping with incontinence can be frustrating, especially if the first few treatments you try don't yield the results you're seeking. But the good news is that there are many choices for managing incontinence. Through trial and error, you may be able to find an option that works well for you. Just remember that this process can take time, so you'll probably need to exercise some patience.

7

# Take charge of your condition

***A brief review of changes that may improve your health***

Coping with prostate disease isn't easy. If you have prostatitis, you may find that established treatments aren't particularly effective. You may become frustrated if medications for benign prostatic hyperplasia (BPH) don't alleviate the frequent urge to urinate. Prostate cancer treatment can be a long haul. You can, however, take steps to meet these challenges. This chapter offers some suggestions.

© MoMo Productions | Getty Images

Connecting with others who share your condition can help combat feelings of isolation and make you feel more hopeful.

## Participate in a clinical trial

Why should you consider a clinical trial? Doctors often suggest patients take part in clinical trials to gain access to promising treatments and medications. Importantly, joining one provides a way to access experimental therapies that might work better than existing treatments. Clinical trials offer close medical monitoring and sometimes cover costs related to care. And by participating, you also help to advance research that could benefit other patients in the future.

Your decision to enroll should be an informed one. Make sure you know why the study is being done, who is paying for it, what the experimental therapy entails, and how your participation might affect other aspects of your care. In addition, be aware that many clinical trials involve randomly assigning two or more groups of patients to various interventions so researchers can determine which delivers the best results. That means you might end up getting the standard therapy or even a placebo (sugar pill) rather than a new drug being investigated, and you probably won't be told which one you're taking.

The most effective way to find a trial that's right for you is to ask your doctor. Major hospitals and cancer centers often run these studies, and they can provide personalized recommendations or refer you to trial coordinators. Patient advocacy groups and government sites can also help. Here are some to check:

- The Prostate Cancer Foundation (www.pcf.org) lists clinical trials and connects patients with trial centers.
- ZERO Prostate Cancer has a clinical trial finder tool (https://zerocancer.org/help-and-support/find-clinical-trial).
- ClinicalTrials.gov is an online database (maintained by the U.S. National Institutes of Health) of clinical trials ongoing throughout the world.

## Join a support group

Some prostate diseases, especially prostatitis and prostate cancer, can make men feel demoralized or depressed. Joining a support group is a proven way to get help. These groups provide a safe space where you and others who share your condition can talk openly. Evidence shows that patients who join support groups feel less isolated and anxious. A sense of community can also foster hope and resilience.

Even if you don't feel the need for emotional support, these groups can be a great source of

information. To find a group in your area that deals with your condition, ask your doctor or check with your hospital. You can also find support groups through Zero Prostate Cancer at zerocancer.org.

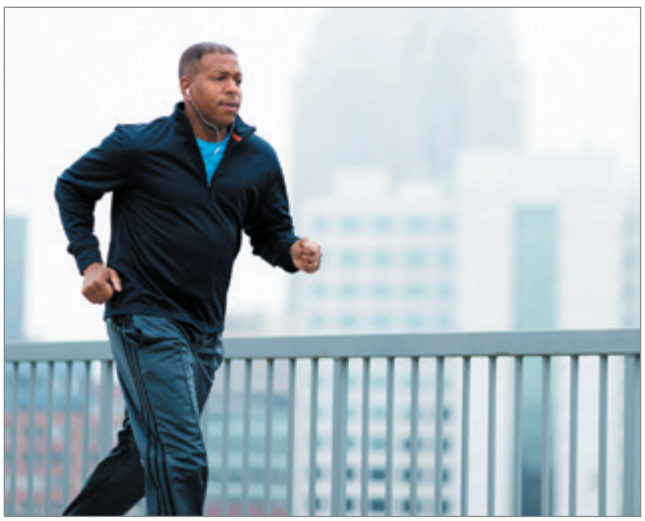
## Make smart lifestyle changes

Many of the same lifestyle changes that have been shown to help with overall health can improve quality of life for men with prostate disorders. They may also help prevent prostate cancer from recurring (secondary prevention). A number of observational studies indicate that eating a healthy diet, exercising, controlling your weight, and not smoking are all worthwhile.

### Eat well

Good nutrition is important for everyone, but it is especially a concern for men with prostate cancer. "Should I change my diet?" is probably the most common question men newly diagnosed with prostate cancer ask their urologists. For now, there are no definitive answers about whether food choices can affect the development or recurrence of prostate disease. We do know that prostate cancer, especially in its more aggressive forms, is more common in countries where men eat a Western diet containing relatively large amounts of red meat.

Some evidence also suggests that inflammatory compounds in spicy foods, coffee, and alcoholic beverages can irritate the urinary tract and possibly worsen symptoms of prostatitis and BPH.



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Exercise helps your physical and mental health. Find an activity you enjoy so you'll be motivated to stick with it.

While there's no one right way to eat, a Mediterranean-style diet—which is rich in fruits and vegetables, whole grains, nuts and legumes, healthy fats, and olive oil—may promote prostate health. This dietary pattern contains foods that are rich in antioxidants, vitamins, minerals, and other nutrients that help to reduce inflammation, which elevates risks for many prostate diseases.

To optimize prostate health, you might also consider adding some of these foods to your diet:

- fatty fish such as salmon, mackerel, sardines, herring, and trout, which are high in anti-inflammatory omega-3 fatty acids
- walnuts and soybeans, which are vegetarian sources of omega-3s
- tomatoes, watermelon, and pink grapefruit, which all contain lycopene, a powerful antioxidant.

It's also important to stay well hydrated. Water supports healthy urinary function and helps to flush toxins out of the body. If you have BPH, aim to get most of your fluids earlier in the day and cut back in the evening to reduce middle-of-the-night bathroom trips.

### Stay active

Although relatively few studies have directly assessed the impact of exercise on prostate health, those that have been done have concluded, for the most part, that exercise is beneficial. Some evidence suggests men who are more physically active are less likely to suffer from BPH, erectile dysfunction, or prostatitis. Other studies have found that exercise benefits men with prostate cancer. Those who engage in vigorous exercise for at least three hours a week are less likely to have their cancer progress.

Guidelines from the American College of Sports Medicine recommend cancer patients start exercising as soon as possible after, or even during, treatment. Exercising regularly can improve your physical state, helping you regain strength and conditioning you might have lost during cancer treatment. It reduces depression and fatigue and improves self-esteem.

Combined with a healthy diet, exercise can also help to boost metabolic health in men undergoing hormonal therapy.

The particular type of activity you choose is less important than finding one that you like, because you're more likely to stick with an activity you enjoy. The standard advice is to get at least a half-hour of physical activity on all or most days of the week. But any activity is better than none.

### Maintain a healthy weight

Evidence is accumulating that losing extra pounds, or avoiding weight gain in the first place, might help keep a prostate tumor in check. It is not yet clear why obesity might worsen outcomes of prostate cancer. Some research suggests that men with obesity tend to have lower PSA levels than those of normal weight, which can lead to a delay in diagnosis. Other research indicates that excess body fat may increase levels of hormones that fuel tumor growth.

### Don't smoke

If you're a smoker looking for another reason to quit, consider this: in addition to raising your risk of heart and lung disease, smoking could boost the odds that you will develop aggressive prostate cancer that metastasizes or recurs after initial treatment. One large study found that smokers have a 42% higher risk of death from prostate cancer than nonsmokers, and the risk is even higher for men with obesity.

## Use herbs and supplements with care—or not at all

Men with prostate conditions, including BPH and prostate cancer, often express interest in herbal or "natural" remedies. At the moment, strong evidence is lacking that any supplements are especially beneficial for prostate health. Some research has suggested saw palmetto might ease BPH symptoms, but two large studies funded by the National Institutes of Health determined saw palmetto was no more effective than a placebo. Meanwhile, evidence for using vitamin D for prostate cancer remains inconclusive, with a review of 22 studies finding no convincing evidence that the supplement lowers prostate cancer risk.

While some people assume there's no harm in trying a supplement, that's hardly the case. Some supplements, like saw palmetto and melatonin (which some men take hoping it will slow the progression of prostate cancer), increase the risk of bleeding when taken with aspirin, ibuprofen, naproxen, anticoagulants, or antiplatelet medications. A recent review of 27 clinical trials showed no improvement in urinary symptoms or quality of life from taking saw palmetto (alone or with other herbal supplements) over durations ranging up to 17 months. Other supplements may interact with other medications you take. In addition, research designed to determine whether vitamin E and selenium supplements might lower prostate cancer risk instead found the opposite: use of these supplements is associated with a higher risk of aggressive prostate cancer.

Generally speaking, the best reason to take a supplement is that your doctor has determined you are deficient in a particular vitamin or mineral. Your doctor may also recommend taking a certain supplement to protect against a specific problem. For example, you might need extra vitamin D if you're using hormone treatments that are known to weaken bones. If you're simply curious about a given supplement, ask your doctor to help you weigh the pros and cons as they pertain to your care.

# Resources

**American Urological Association (AUA)**
410-689-3700
www.auanet.org

The AUA is a professional association for the advancement of urologic patient care. It helps physicians and patients stay current on the latest research and practices in urology. The AUA also provides a range of services, including publications, research, meetings, and guidance on health policy.

**Harvard Health Publishing (HHP)**
www.health.harvard.edu

A division of Harvard Medical School, HHP publishes *Harvard Men's Health Watch* (www.health.harvard.edu/newsletters); in-depth reports on a variety of conditions, including erectile dysfunction (www.health.harvard.edu/reports); and online courses, including ones related to prostate diseases (www.harvardhealthonlinelearning.com). HHP also maintains a section on its website dedicated to prostate health (www.health.harvard.edu/topics/prostate-health), which features articles on prostate diseases as well as summaries of groundbreaking prostate research.

**National Cancer Institute (NCI)**
800-422-6237 (toll-free)
www.cancer.gov

This government agency, part of the National Institutes of Health, conducts and sponsors research on all types of cancer. Operators can answer questions, provide informational booklets and brochures on prostate cancer, and make referrals to local resources. The NCI also offers the latest information about cancer clinical trials, including their locations. The website provides online information for patients, health professionals, and the public.

**Prostate Cancer Foundation**
800-757-2873 (toll-free)
www.pcf.org

This philanthropic organization funds prostate cancer research. Its website offers general information about prostate cancer; a list of resources for patients needing financial assistance; help finding a doctor or treatment center; and support for patients, families, and caregivers.

**Zero Prostate Cancer**
202-463-9455
https://zerocancer.org

This nonprofit provides a comprehensive range of services for people with prostate cancer, including information on prostate cancer and treatment, support groups (both in person and online), a physician finder, and financial assistance in a number of states to help pay for transportation to and from appointments. Visit the website to find the chapter nearest you.

# Glossary

**active surveillance:** A strategy for managing prostate cancer in which a patient is regularly examined but is not treated until the disease shows signs of worsening.

**adjuvant radiation:** Radiation given shortly after initial surgery for cancer as an additional (adjuvant) treatment, when there is a presumption of residual cancer—even without a rise in PSA levels or signs of cancer on a scan.

**androgen deprivation therapy (ADT):** Treatment for prostate cancer (with either drugs or, in rare cases, surgery) that is intended to reduce or eliminate the supply of male hormones to the prostate and distant cancer sites, slowing cancer growth. Sometimes called hormonal therapy.

**androgens:** The male hormones, particularly testosterone and dihydrotestosterone (DHT).

**anti-androgens:** Drugs used in hormonal therapy that inhibit the dihydrotestosterone (DHT) in prostate cells.

**biochemical recurrence:** A post-treatment increase in PSA, indicating that prostate cancer has recurred or spread following the original treatment for prostate cancer.

**biomarker:** A distinctive biological indicator of an event, process, or condition.

**biopsy:** A procedure in which small samples of tissue are removed for analysis under a microscope.

**circulating tumor cell (CTC):** Cells that are shed by tumors into the bloodstream that may seed new tumors elsewhere in the body.

**core:** A piece of tissue obtained in a biopsy of the prostate.

**cryotherapy:** A focal therapy technique used to eliminate cancerous areas in the prostate by freezing them.

***de novo* metastatic cancer:** Newly diagnosed metastatic cancer in someone who has not yet been treated for the disease.

**digital rectal examination (DRE):** A screening test in which the physician inserts a gloved finger into the rectum to examine the prostate for abnormalities.

**endorectal coil MRI:** Magnetic resonance imaging done with a coil (consisting of a probe and an inflatable balloon) inserted into the rectum. The test helps doctors assess cancer spread and local invasion.

**epigenetic changes:** Changes that alter the functioning of a gene without altering its DNA sequence.

**exosomes:** Tiny capsules that develop inside a cell and contain some of its RNA, DNA, and proteins. Exosomes are released into blood by many cell types, including tumor cells.

**focal therapy:** Treatment intended to remove or destroy only the cancerous portion of the prostate and to spare healthy prostate tissue.

**free PSA:** PSA circulating in the blood that is not bound to other proteins.

**germline mutations:** Inherited genetic changes found in all cells in the body.

**Gleason score:** A number assigned to prostate cancer cells based on their likeliness to spread. The scores of the two main cell types in a tumor predict its aggressiveness.

**GnRH antagonists:** Gonadotropin-releasing hormone antagonists, used in hormonal therapy. Like LHRH agonists, these drugs treat prostate cancer by blocking the release of luteinizing hormone, but without a temporary surge in testosterone.

**high-intensity focused ultrasound (HIFU):** A treatment that ablates, or destroys, tumors with heat generated by ultrasound energy.

**indolent:** A term that describes slow-growing tumors that will ordinarily not cause symptoms or be life-threatening.

**intensity-modulated radiation therapy (IMRT):** High-precision delivery of radiation in multiple beams adjusted to conform to the three-dimensional shape of a tumor.

**laparoscopy:** A surgical approach in which a procedure is carried out with tiny instruments inserted through small incisions in the skin.

**LHRH agonists:** Luteinizing hormone–releasing hormone agonists, used in hormonal therapy. Like GnRH antagonists, they treat prostate cancer by blocking chemical messages that signal the body's cells to make testosterone.

**lymph nodes:** Small, specialized clusters of tissue that help fight infections and capture cancer cells that have moved out of a given tissue or organ.

**medical oncologist:** A physician who specializes in chemotherapy, hormonal therapy, biological therapy, and targeted therapy for cancer; usually the main health care provider for someone with cancer.

**metastasis:** The spread of cancer to areas of the body beyond the organ or tissue in which it originated.

**metastasis-directed therapy:** The use of radiation, surgery, and other treatments targeted specifically at metastatic tumors.

**metastatic castration-resistant prostate cancer (mCRPC):** Metastatic cancer that doesn't respond to hormonal therapy.

# Glossary *continued*

**metastatic castration-sensitive prostate cancer (mCSPC):** Metastatic cancer that responds to hormonal therapy.

**multiparametric MRI (mpMRI):** A hybrid imaging technique that combines several different MRI strategies to improve diagnostic accuracy.

**nanograms per milliliter (ng/mL):** A small quantity of a substance equivalent to one-billionth of a gram in one-thousandth of a liter.

**nerve-sparing prostatectomy:** A surgical procedure for prostate removal designed to avoid damaging the nerves that are necessary for potency.

**nonmetastatic castration-resistant prostate cancer (nmCRPC):** A condition marked by rising PSA levels after initial prostate cancer treatment, without visible metastases, that persists despite the use of hormonal therapy.

**nonmetastatic castration-sensitive prostate cancer (nmCSPC):** A condition marked by rising PSA levels after initial prostate cancer treatment, without visible metastases, that responds to hormonal therapy.

**oligometastatic prostate cancer:** Cancer with five or fewer detectable metastases detected on imaging scans.

**open prostatectomy:** A surgical procedure in which prostate tissue is removed through an incision in the abdomen.

**perineum:** The area between the anus and the scrotum (in males) or the anus and vulva (in females).

**positron emission tomography (PET):** An imaging technique that visualizes the locations of injectable tracers in the body.

**primary cancer:** The original location of a cancer, from which metastatic disease originates.

**prostate-specific antigen (PSA):** A protein released by normal prostate cells and in higher amounts by prostate cancer cells.

**prostate-specific membrane antigen (PSMA):** A protein found at high levels on the surface of prostate cancer cells.

**radiation oncologist:** A physician who specializes in the use of radiation to treat cancer.

**radiation therapy:** Treatment with high-energy rays (from x-rays or other sources) designed to destroy cancer cells.

**radical prostatectomy:** A surgical procedure used to remove the prostate, seminal vesicles, and pelvic lymph nodes.

**radiofrequency ablation:** A type of therapy that uses electrical energy and heat to destroy cancerous tissues.

**radioligand:** A type of therapy that kills cancer cells using radiation particles.

**retrograde ejaculation:** A side effect of prostate surgery and some medications, in which semen flows back into the bladder rather than out through the penis.

**salvage radiation:** Radiation given to treat suspected recurrent cancer; in the case of prostate cancer, it is given in response to rising PSA levels after initial surgery.

**seminal vesicles:** Structures next to the prostate gland that produce seminal fluid.

**stereotactic body radiation therapy (SBRT):** A procedure that delivers high doses of radiation to tumor sites throughout the body, usually in soft tissues, with guidance from imaging.

**surgical margin**: An edge of normal-looking tissue surrounding an excised tumor. The margins can be checked for cancer under a microscope after the tumor is removed.

**systemic therapy:** Hormonal therapies, chemotherapy, or targeted therapies for cancer that circulate throughout the body.

**targeted therapy:** Drugs or other agents that attack cancer cells containing specific genetic mutations.

**transperineal biopsy:** A method of taking samples from the prostate in which doctors access the prostate through the perineum.

**transrectal ultrasound–guided biopsy (TRUS biopsy):** A method of taking samples from the prostate through the rectum under ultrasound guidance. Also called a standard biopsy.

**transurethral resection of the prostate (TURP):** The most common procedure to treat benign prostatic hyperplasia, in which excess prostate tissue is cut away.

**triplet therapy:** A treatment approach that combines chemotherapy with conventional ADT plus an androgen-receptor inhibitor such as abiraterone.

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www.health.harvard.edu/mens

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### Better Bladder and Bowel Control

www.health.harvard.edu/bbbc

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Mobility & Independence
Neck Pain
Nutrition
Osteoarthritis
Osteoporosis
Pain Relief
Positive Psychology
Prostate Diseases
Rheumatoid Arthritis
Self-Care
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