Prostatepedia[1]

[1] expert insight + advice

Erectile Dysfunction After Treatment

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In this issue....

There is really very little controversy about both the causes of and treatments for erectile dysfunction as outlined in the conversations that follow. But there are two themes that emerged this month that warrant additional discussion.

First, cardiovascular disease, hypertension, and diabetes are the most common causes of erectile dysfunction. In fact, erectile dysfunction should trigger an evaluation for all three diseases. Diet and exercise are effective in managing all three, though many men will also need drug therapy to obtain optimal results. Fortunately, aggressively treating these diseases can improve erectile dysfunction.

For example, blood pressure medications of the ACE inhibitor class often improve erectile dysfunction. Cozaar (Losartan) is a widely used ACE inhibitor that appears to improve erectile dysfunction. One clinical trial showed that adding Cozaar (losartan) to Viagra (sildenafil) resulted in better sexual function than Viagra (sildenafil) alone.

Most prostate cancer experts are too busy to manage these three diseases in a comprehensive fashion. It's in your best interest to have a specialist in cardiovascular disease, hypertension, and diabetes on your medical team.

Second, in Dr. John Mulhall's interview, he makes strongly negative comments about the use of testosterone withdrawal in the treatment of prostate cancer. He notes, correctly, that testosterone withdrawal markedly reduces libido and can cause atrophy of the penis. He points out that with radiation therapy, testosterone withdrawal can last 2-3 years and that this can result in permanent loss of sexual function. He argues that it is reasonable for men to decline such treatment and instead favor quality of life over maximum survival. He points out that most medical oncologists, including those in his own institution, disagree with his views.

I am a medical oncologist and agree that some of his opinions go against standard approaches to treating advanced or aggressive prostate cancer. His views reflect an overly simplistic view of the treatment issues medical oncologists face in treating aggressive, metastatic prostate cancer.

There is no question that removing testosterone is an effective treatment for metastatic prostate cancer. Furthermore, the greater the suppression of testosterone, the greater the duration of cancer control and survival benefit.

Many argue that it is reasonable to avoid hormonal therapy because some wish to focus on quality of life rather than life's duration. It can be perfectly rational to place a greater value on quality of life, but you should understand the consequences of that decision. If you take a treatment path that increases your odds of dying of prostate cancer, you should find out what it is like to actually die of prostate cancer.

For many men with prostate cancer, the suffering associated with end-stage prostate cancer is often much worse than the side effects of treatments like Lupron (leuprolide) and Zytiga (abiraterone). For these men, the decision to not take aggressive treatment results in both shorter survival and lower quality of life.
For the most part, medical oncologists are the ones who care for men during terminal illness. I think that experience is why Dr. Mulhall finds that medical oncologists so often disagree with his views: they are painfully aware of the adverse impact terminal prostate cancer has on a man's quality of life. Men who forego effective treatment usually come to regret that decision when they finally confront the reality of dying from prostate cancer.

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Guest Commentary

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Dr. Abraham Morgentaler is the Founder of Men's Health Boston (www.menshealthboston.com) and an Associate Clinical Professor of Urology at Harvard Medical School, Beth Israel Deaconess Medical Center. He is a regular contributor to television and radio shows addressing male issues and has appeared on *NBC Nightly News, CBS Evening News,* CNN with Anderson Cooper, and *The Connection* on NPR.

Dr. Morgentaler frames this month's conversations on erectile dysfunction and testosterone after prostate cancer.

Erectile dysfunction (ED) affects a very high percentage of men who get any form of treatment for prostate cancer. And yet, ED is an issue that has not received enough attention. I've certainly seen many men who didn't want to have any treatment for their prostate cancer because they were afraid they were going to lose their ability to have sex. Some men say it's not worth it: "If I can't have sex, I'm not a man. I feel like I can't provide sexually for my partner."

In my last book *The Truth About Men and Sex*, I discuss a number of cases from my practice. I think that people have misunderstood what sexuality is for men. The stereotype is that men are stuck back in their spring break years regardless of how old they are or how much they've evolved and matured and that they're only into sex for themselves and their own satisfaction.

The truth is that many of the men I see who are in established relationships feel terrible about their erectile dysfunction not only for themselves but also because they feel like they're letting down their partner.

> *"People have misunderstood what sexuality is for men."*

Sex, as I like to say, is the special sauce of relationships. It's the thing we don't talk about much, but most happy couples are having sex and most unhappy couples are not. That doesn't mean that happiness comes directly from the sex, but it's part of it certainly.

Now, the good news for men is, thanks to advances in modern medicine, we can help pretty much any man be able to have sex, even if he's got erectile dysfunction from treatment of his prostate cancer. It may not be quite as easy and simple as sex was beforehand, but losing one's erections after treatments of prostate cancer doesn't mean that it's the end of a man's sex life.

The reasons why men develop ED after prostate cancer depend on the form of treatment he's had.

For surgery—one of the most common prostate cancer treatments—the issue is likely related to the nerves that control erections, which run to the penis but are plastered along the sides of the prostate itself.

In 1982, Dr. Patrick Walsh of Johns Hopkins figured out how to save the nerves in what's called a nerve-sparing procedure. Before that, 100% of men who had the surgery had ED afterward. But even this nerve-sparing technique, which has been used for 30 years, is imperfect.

Almost all men will lose their erections for a period of time after surgery. A good number will get them back, but it's much less than 100%. Some estimates say 20% will be able to recover erections fully, and others say 50%. Based on my experience and the literature, I'd say probably about 25% of men are able to regain full erections without the need for aids like Viagra (sildenafil) and Cialis (tadalafil).

Radiation and brachytherapy, in which radioactive pellets, or seeds, are placed within the prostate, can cause trouble in two ways. One is by damaging the tissues of the penis through the radiation, as the deep structures of the penis are not that far from the prostate. The second is that they may hurt the nerves that control the erections just like with surgery.

> *"We can help pretty much any man be able to have sex."*

The difference with radiation is that ED is delayed so that right afterward, men who were fine before treatment are still fine. Two years following treatment, the number of men with good erections is pretty much the same for both radiation treatments and surgery.

For men about to go into treatment, I think it's important to consider that ED becomes more prominent as you get older. The number of men in their 60s and 70s who have erectile dysfunction is very high. The Massachusetts Male Aging Study published in the 1990s showed that men between the ages of 40 and 70 had a 52% self-report rate of some degree of ED.

For those men who already have ED, the decision to have surgery or radiation for their prostate cancer is a little bit easier. Regardless of the cause of ED, there are doctors who care and offer services to help men to have sex again, whether they've had prostate cancer treatment or not.

It's a difficult question about how to balance treatments that may save one's life 10 years down the road with the unpleasant and unwanted side effects that may begin right after treatment. That decision is complicated further by confusion about which prostate cancers need to be treated. We've been treating too many men, leaving them with little in the way of upside for benefits and with all the complications that come from treatment.

If you have been diagnosed with prostate cancer, the first step is to determine if yours is the type of cancer that's going to affect you in your lifetime. The second step is to have an honest, open conversation with your physician about what it means in terms of sexual function.

I see a lot of men *before* they decide on a treatment: they want an opinion about how likely it is that the radiation or surgery will affect them sexually before deciding on a path.

> *"I see a lot of men before they decide on a treatment."*

At that point, we go over the options available to them *after* treatment. If you have that conversation, you may then have a clearer mind about getting treatment. One of the relatively nice things about prostate cancer, as compared to many other cancers, is that it does tend to grow slowly, giving you the luxury of being able to make decisions and gather all the information over a period of time without really affecting your outcome.

Martin Miner, MD

Erectile Dysfunction After Prostate Cancer

Dr. Martin Miner is the Co-Director of the Men's Health Center at The Miriam Hospital in Providence, Rhode Island.

Prostatepedia spoke with him about how his center helps men who have erectile dysfunction after prostate cancer treatment.

Why did you become a doctor?

Dr. Martin Miner: I wanted to become a doctor at a very young age due to two primary influences. First, my father, who just passed away recently at age 100, was born in Poland and never went to college. In his mind, success meant you became a physician or a lawyer. I have two younger sisters who are attorneys, and I'm a physician.

The second influence was my own discovery. When my pediatrician would examine me, she was very silent listening to my heart and lungs. When she would pronounce me healthy, I felt a tremendous affirmation and sense of relief. That was a tremendous gift that she gave to me when I feared something was wrong.

I'm 62 and have been practicing medicine for 34 years. I was trained as a family physician, and I did full-time family medicine with my same six partners for 26 years. Then I went back and did another fellowship training in what's called medical andrology, which is the study of male sexual function and hormonal therapy. I've been doing that in an academic setting at Brown University for the last 15 years.

> *"I was seeing between 34 and 36 patients a day."*

Why did you go back to school to study medical andrology?

Dr. Miner: I loved family medicine, and what I enjoyed most of all was sitting down with patients and listening to their stories. If you're compassionate and caring, you're more in demand, and the more you're in demand, the more your schedule is no longer under your control. I was seeing between 34 and 36 patients a day, many of whom had multiple problems. That's fairly standard for primary care doctors.

I wanted to do something that was more intimate. I was always interested in research and cardiovascular research in particular. When Viagra came out in 1998, men I'd never seen before came to see me. In 2000, the Commonwealth Fund published a study of how American men utilize healthcare.

The Commonwealth Fund study showed that men are very hesitant to go to the doctor—they wait until they become quite ill. Thirty-three percent of men studied didn't have primary care doctors and 41% hadn't been screened for prostate cancer in the year before the study. (There has never been a subsequent study.) I thought perhaps sexual function was a means to get them to come in for more preventative checkups, so I started doing research at Harvard Medical School.

I know for many women, their obstetrician becomes sort of a primary care physician.

Dr. Miner: Right. Women are very active in caring for their children and can be very active in caring for their partners or spouses. Men, by themselves, are not as comfortable.

The Miriam Hospital opened up the first men's health center in the US in 2008. It is a multidisciplinary center of urology, medicine, preventative cardiology, psychology, and physical therapy. We deal specifically with survivorship after prostate cancer. We also use preventative measures to detect early heart disease following the onset of vasculogenic erectile dysfunction, which is erectile dysunction (ED) primarily related to a disorder of the blood vessels.

How common is ED in the general population? What causes it?

Dr. Miner: Most studies show that ED occurs in 50% or more of men. The public thinks it's related to aging, but in truth, it's more prevalent with aging because there are more comorbidities (meaning coexisting medical problems) that occur in men as they age. As men age, they tend to develop high blood pressure, elevated lipids, and type 2 diabetes. Many become obese, and specifically get visceral adiposity, or belly fat. Erectile dysfunction is related to all of these conditions.

Once present, ED is not only related to the issue of vascular filling but also to psychological issues. Men are devastated when their sexual function is impaired. They become anxious and performance-focused. That only makes attaining an erection more difficult.

What kind of an impact can ED have on a man?

Dr. Miner: For most men, ED affects every phase of their lives. We're pretty simple creatures. From youth, we are used to waking with morning erections, and whether we used them or not, they can be validating, making us feel virile and healthy.

When that no longer happens or when we have difficulty achieving erections, it impairs our self-esteem. We can become depressed and frustrated, which can cause us to seek to blame and distance ourselves from those we love, especially our sexual partners. We no longer initiate lovemaking and are unreceptive to lovemaking because we don't want to do something at which we consistently fail.

Most cases of ED begin with difficulty keeping erections and then progress to difficulty getting and keeping an erection. It's a gradual process, almost insidious in nature. You know that your erections are no longer rigid or hard. Your partner is aware of it as well, so you can become ashamed.

Does that shame prevent men from seeking help?

Dr. Miner: At some point, most men will seek treatment. Medications like sildenafil have revolutionized the way we look at sexual functioning. They've allowed men who previously might have been quiet and accepted this as a normal part of aging to address an impairment that they no longer feel they need to accept.

They'll bring it up to their clinician. It may be difficult for them to raise that issue with their clinicians, though, since they might feel embarrassed. Often it's an end-of-the-visit discussion or what we call a backdoor complaint: "By the way, Doc, do you have any samples of Viagra?"

Studies show that patients appreciate when providers initiate discussions about their sexual functioning. Even if they have no problems, they feel validated because they know they can raise the issue of sexual functioning if necessary.

Women now outnumber men as primary care clinicians. While many women have no difficulties asking men about sexual function, some do. We need to retrain those female providers to help them feel comfortable.

How common is ED after prostate cancer?

Dr. Miner: We know that erections occur normally due to an increase in blood flow, or vasodilation, of the very small blood vessels that fill the penis. It's also related to neurologic excitation, or release of a gas called nitric oxide, which is why meds like Viagra (sildenafil), Levitra (vardenafil), and Cialis (tadalafil) work; they prevent the breakdown of that gas. A neurologic, vascular, endocrinologic (hormonal) insult, or compromise, can cause ED.

In prostate cancer, there are insults in all three of those spheres, the most significant being the complete loss of erections following surgical treatment, which has an incidence of 98%. It is also associated with complete incontinence.

The nerve bundles around the prostate gland are like tendrils of a spiderweb, and it's very difficult not to harm those bundles. When those bundles are even exposed to the atmosphere, opened, or touched, they go to sleep. Not even the best surgeons can spare them. After surgery, they have to return to function over time.

The first thing that happens after prostate cancer is men have an overwhelming fear about their incontinence. They wear pads, which can be very humiliating. Their first desire is to get dry and we recognize that. Then we work on a program to reawaken these nerve bundles to the penis while we continue to keep their penile tissue healthy until recovery.

There are some emerging treatments for less aggressive prostate cancer, like proton beam therapy, which may have less of an impact on sexual function. But most, if not all, therapies for prostate cancer have a significant and direct impact on sexual function. Male survivorship treatments, including the return of sexual function, are not covered by insurance because they're termed experimental.

What does your penile rehabilitation program (PRP) entail?

Dr. Miner: In the mid-2000s, doctors became interested in penile rehabilitation to improve the percentage of men who return to sexual functioning with or without the aid of medication. That program has evolved although it's inconsistent among centers.

There are various methods of PRP. Studies show that one doesn't particularly work better than another, yet most men desire to have some facilitation or guidance in the return of their sexual functions as well as initially working to become dry. We have two skilled, sensitive, and compassionate pelvic floor therapists who work with men to help get them dry.

Then penile rehabilitation might simply mean taking a low dose (5 mg) of Cialis (tadalafil) every other day for six months.

In 2007, the Cleveland Clinic published some interesting data about a medication called intraurethral alprostadil. Men inserted a suppository into their penises a few days a week that increased blood flow to the tissue. The tissue didn't become scarred but remained healthy and had an adequate blood supply.

Many can't afford these suppositories because they're about $40 apiece, so we've had them compounded into a gel. We have men apply that gel in various strengths to allow them to obtain an erection. In conjunction with that, they use a vacuum device that stretches or fills the penis at least three to four times a week. We monitor their psychological well-being closely and coach them in the return of their sexual function.

It's very hard to study these treatments with randomized placebo-controlled trials in men undergoing radical prostatectomy. Very few men, when offered treatment for their sexual dysfunctions after prostate cancer, will choose the placebo. Most of these studies are observational.

How successful are treatments for ED after prostate cancer treatments?

Dr. Miner: I think that regardless of how aggressive a man's treatment, we can help him restore erections.

As I said, all prostate cancer treatments usually result in ED. If someone had ED prior to surgery and needed oral medication, he's not going to get better erections than he had before surgery. The hope is to restore him to his baseline.

Men who are younger and healthier or older men who are healthier without other diseases—such as high blood pressure or type 2 diabetes—have a better chance at restoration of sexual function. Many will no longer have spontaneous erections but will be able to develop erections with medical therapies.

Many men don't worry about their sexual function until they're six months down the line after surgery because they're still leaking and going through up to three pads a day.

Should a man who is about to have surgery or radiation go see someone like you first?

Dr. Miner: We don't routinely see men first; I believe this is a missed opportunity. If men see the pelvic floor therapist before the surgery, they can start exercises that could lessen future incontinence.

If we have a discussion about their sexual function before, we can start giving them advice about how a healthy lifestyle improves sexual function.

"Prostate cancer can be a lonely path."

We can allay a lot of fears and establish a timetable for when to be more aggressive in treating sexual dysfunction.

Is there any benefit to going on medications like Viagra (sildenafil) before surgery or radiation?

Dr. Miner: There is no data to show any difference. Most men who develop prostate cancer—especially aggressive prostate cancer—tend to be 45 to 70 years old. They have already noticed changes in their erections. Some men have no issues at all before prostate cancer, and I would not recommend that those men use medications prior. The medications are very safe, however, and may be very helpful for all vasculature in the heart and body. They're very expensive, though. Not everyone can afford them.

Are there any resources available for patients who need help with the cost of the pills?

Dr. Miner: Pfizer has a program to help based on income. Most of these meds should be generic by the end of 2017. Each pill costs between $50 and $60. Most insurances do not cover them. If you take Cialis (tadalafil) daily, that is $325 a month.

That's a lot of money.

Dr. Miner: Many men get the pills from Canada where they're re-sold from some other country where they've been manufactured. We can't trust what's in them, so I don't encourage this. I try to go with the resources at hand. The typical dose for erectile dysfunction is 100, 50, or 25 mg. There is a generic form of Viagra called sildenafil in a 20-mg dose approved for pulmonary hypertension. Some pharmacies sell doses of sildenafil for less than a dollar per tablet while others sell them for $20. Since this requires men to be smart drug shoppers, we try to facilitate those skills for our men.

Are there some treatments that don't necessarily work with prostate cancer patients?

Dr. Miner: I think it's all individualized. We don't rule out any one treatment for prostate cancer patients. If you look at the effectiveness of oral therapies after prostate cancer, it is based on a man's overall health. Is he obese? Does he have diabetes? High blood pressure? Does he eat properly? Sleep properly? Is his testosterone normal? Does he have obstructive sleep apnea? All of these conditions can impact sexual functions, whether or not he has prostate cancer, and all determine his response to oral medication.

I tell every man a variation of the following when I see him: "We can help you get an erection. Whether it feels mechanical depends on what method you use and how you relate to your partner. It may be different than what you're used to, but it's up to you to refocus your love life to include greater touch." Men tend to be genital-focused—we tend not to use a lot of touch. We urge men to incorporate sensate therapy, or touch therapy. Couples who remain close physically are much more likely to have positive outcomes.

What role does psychosocial counseling play in the program?

Dr. Miner: Prostate cancer can be a lonely path. Many men go through this alone. I think that we're much more advanced in survivorship for women's issues like breast cancer, for example. Discussion is important. I often see patients as a couple, and a partner's presence is most significant and additive. It's not just about sex, but also about intimacy. That's probably true for breast cancer, as well.

Both change how you view yourself as a sexual person, right?

Dr. Miner: Right. It's just that men tend to be less verbal and they disclose less. At our center, I'm fortunate to have between 40 minutes and an hour with new patients and their partners. I take a full history and ask for a lot of personal information. If I establish that I'm comfortable asking intimate questions, most men and their partners are then comfortable answering them. I try to create a therapeutic and comfortable environment.

I think that when men have not only the support of partners but also of friends, acquaintances, or other people with whom they can talk, it is enormously helpful. Support groups, though not as common, are also effective.

What about online support groups?

Dr. Miner: Those are helpful. However, I fear they tend to be dominated by individuals who are angry, hopeless, or despairing. I've seen people say things like: "I should have never done this," or "This is the worst thing I've done." It can be very discouraging to one entering such a group, so you've got to understand that a lot of people online can be very angry. And they're not angry because of the circumstance necessarily, but because life isn't predictable and neither are outcomes. We tend to look for someone to blame when things go wrong, but that's not helpful for us as we heal. We must remain positive. Pp¹

Nelson Bennett, MD
Erectile Dysfunction After Prostate Cancer

Dr. Nelson Bennett, an Associate Professor in the Department of Urology at the Feinberg School of Medicine at Northwestern University, specializes in erectile dysfunction.

Prostatepedia spoke with him about erectile dysfunction after prostate cancer treatment.

Why did you become a doctor?

Dr. Nelson Bennett: I originally went to college to be a mechanical engineer. I quickly changed over to biomedical because I thought it was much cooler. I went through the curriculum, and in my junior year, I did a summer internship at Baylor College of Medicine in Houston, Texas. That's when I decided to completely switch careers and become a physician.

Engineering was fun, hands on, and creative, but it didn't give me the human contact that I wanted on a day-to-day basis. As a doctor, I see patients and spend 90% of my day interacting with people and helping them.

How did you come to focus on erectile dysfunction (ED)?

Dr. Bennett: I settled on urology as a specialty, and during my training, we'd see all types of patients, including cancer patients and female urology patients. The male erectile dysfunction patients seemed to be the happiest. Once you help them out and help them put their lives back together—this a very intimate part of their lives—they're truly happy.

How common is ED in the general population, and how common is it in men after prostate cancer?

Dr. Bennett: The incidence of ED increases after age 30 or so. By 40, about 40% of men have some evidence of erectile dysfunction, and it just increases from there.We tend to collect other medical issues like high blood pressure and diabetes, so the incidence of ED gets worse as we get older. In men with prostate cancer, the prostate cancer itself doesn't necessarily cause ED: it's the treatment afterward.

Is there a higher incidence of ED in men on active surveillance?

Dr. Bennett: If it's slightly higher than the general population, it's because people are stressed or frustrated with their prostate health and worried about the spread of cancer. It is more of a psychological issue in active surveillance patients.

Is ED more common after certain types of prostate cancer treatment, say hormonal therapy versus surgery versus radiation?

Dr. Bennett: After prostate cancer surgery, 100% of people have ED. It gets better with time, but initially, 100% experience softening of the erection. And it can take up to two years to recover.

> *"After prostate cancer surgery, 100% of people have ED."*

When radiation therapy starts, men don't experience any erectile issues. As the years go by, up to about five years, they settle down to the level of those who've had prostate cancer surgery. There's a slow decline in erectile dysfunction after radiation.

What about hormonal therapy? If you block testosterone, you're going to block out erections too, right?

Dr. Bennett: Yes, you're going to have immediate decreases in erectile rigidity, libido, sexual thoughts, and so on. Usually, hormonal therapy is used in conjunction with radiation, so they end up getting lumped together. The penile muscle has testosterone receptors, and if they're not filled, the muscle doesn't function as efficiently as it could or should.

You said 100% of men have erectile dysfunction after surgery, and they slowly recover over the course of two years. Why is that?

Dr. Bennett: The prostatectomist has to get the whole prostate out with the cancer inside of it. The nerves that go down to the penis run right along the side of the prostate. Simply exposing or touching those nerves damages them. It causes a concussion, or stunning, of those nerves, and they just don't function as efficiently immediately after surgery.

It takes a good two years for those nerves to become as functional as they're going to be. All else being equal, 60% of men will get back to where they were prior to surgery if they have had good nerve sparing and if they had excellent erections prior to their surgery.

What can be done about this? Are there treatments that work?

Dr. Bennett: The treatment for post-prostate cancer ED is logical, methodical, and hasn't changed too much in the past 20 years. The first thing we try is oral medications like Viagra (sildenafil), Levitra (vardenafil), and Cialis (tadalafil). If those are ineffective or unaffordable, the next steps are penile injections, vacuum erection devices, or intraurethral therapy like with MUSE (alprostadil pellets). If those are either ineffective or intolerable, then the final step would be surgery for a penile prosthesis.

If Viagra (sildenafil) is successful, then we have them take that on a regular basis to generate erections in the bedroom. If it's ineffective, then I recommend that we switch directly to penile injections because that's the most effective way of getting an erection every single time you use it.

Penile rehabilitation is also important. We want a patient to get the best quality erection he can after prostate surgery. The penis is a muscle that needs to be exercised on a regular basis. If you're not getting regular erections, that muscle begins to atrophy or shrink, and that doesn't leave a good muscular bed for those nerves to work on two years later. You've got to keep that muscle healthy.

What we recommend here at Northwestern is using 5 mg of Cialis (tadalafil) daily or 25 mg of Viagra (sildenafil) every night to keep the penile muscle healthy.

Are there any side effects to these medications?

Dr. Bennett: These are medications that enhance blood flow not only to the penis but also to the brain. That's where most of the side effects are: headaches, stuffy nose, red face. Some men get heartburn. Particularly with Cialis (tadalafil), blood can pool in the large muscles of the lower back and buttocks, so men get a charley horse sort of a feeling if the blood pools there for a significant period of time. This all goes away once the medication is stopped. For the headache or the muscular pain, Kapanol (morphine sulfate) works wonders.

Does exercise have any impact on the side effects?

Dr. Bennett: Not really, no. But the longer you take this medication, the less severe the side effects may be.

Are there any side effects for the penile injections?

Dr. Bennett: Penile injections are extraordinarily safe. It's a small amount of a highly concentrated compound called either Bimix or Trimix, which are vasogenic substances. They basically open up the blood vessels where injected and let more blood flow. They also relax the penile smooth muscle. The medication stays in the penis, so there are no systemic side effects.

There are two physical side effects. The injection site can get irritated or bleed, which is easily controlled with direct pressure. Also, men can get priapism, an erection that doesn't go away. That's probably the biggest side effect.

To adequately do a penile injection, you should be trained. Someone should monitor the progress and coach the patient on what to do if the dosage isn't quite what the patient expected.

Do people have any difficulty injecting their own penis?

Dr. Bennett: Certainly the words "needle" and "penis" should never be said together. Once you get over the mental image of that, it's actually very easy. The needle that's used is an insulin-type needle that's inserted into the shaft of the penis, a little bit less than halfway down. The sensation is less painful than getting a PSA blood draw, and certainly less painful than wearing a Foley catheter after prostate surgery. Many men become accustomed to this concept. It's a half-inch needle with 29 or 30 gauge, so you feel it, but it does not hurt.

In my clinic, we require two visits in the office. First visit, we inject the patient because I know that they're going to be nervous. After that, many say it isn't that bad and feel they can do it at home. On the second visit, we do a little bit more teaching and training. Men adjust very well, especially when they see what's involved.

What are the side effects and considerations of the penile prosthesis?

Dr. Bennett: The penile prosthesis is a plastic device that goes inside the penis; it's inserted during surgery, which takes under two hours. Infection from the device is a chief concern as it is inserted through a groin incision. We do everything we can to prevent infection, including preoperative antibiotics and surgical scrubs.

Approximately six weeks after the surgery, the patient is cleared to use the device in the bedroom. All it does is make the penis erect. Other aspects of the sexual response, the libido, desire, orgasm, and ejaculation remain as they were prior to surgery. Yet it has the highest satisfaction rate of any erectile dysfunction therapy in both the patient and the partner.

Why do you think that is?

Dr. Bennett: Because it takes about 10 seconds to get an erection that stays erect for as long as desired. It's very spontaneous. The caveat is that the penile prosthesis is a last resort because, once you have one, you cannot go back and do penile injections or take the pills.

Putting in the prosthesis destroys the smooth muscle of the penis. We have to make space for the cylinders, so injections don't work after. The pills don't work because the muscle isn't there anymore. If a man no longer wants his prosthesis, he can't go back to other treatments. If he wants an erection, he always has to use the prosthesis. It's best to try all the other treatments first.

Are any of these treatments covered by insurance? Are they expensive?

Dr. Bennett: Over the past few years, insurance companies have been dropping coverage for ED pills. In typical pharmacies, ED medications can cost upwards of $50 per tablet, which is extraordinarily expensive. Some third-party insurance companies will cover four to six pills per month with a high copay. We're talking $75 to $100. Most of my patients who are over 65 have Medicare, which does not cover these medications at all. Seniors need to pay out of pocket for them. Many turn to offshore pharmacies to get cheaper generic medications. The good news is Viagra (sildenafil) and Cialis (tadalafil) will be generic by the end of 2017, so we're hoping the price will come down to a reasonable level.

Penile injections are a compounded medication provided from a specialty compounding pharmacy and there are several of them. A four- to six-month supply of this medication runs about $100 to $150. That works out to be about 75 cents to $1 per injection.

Vacuum erection devices run $200 to $300. They're no longer covered by insurance.

The penile prosthesis is covered by nearly all insurance companies including Medicaid and Medicare. The hospital stay, the surgery, and the device itself are all covered, which would cost about $30,000.

You said most of the treatments have been in play for a number of years. Are there any new developments or treatments?

Dr. Bennett: There are some topical agents being researched. Topiglan is a prostaglandin that, when put on the head of the penis and absorbed, allows the man to get an erection. It acts a lot like penile injection without the needle. It has been approved in Canada but not yet in the US.

In Europe, there's been a lot of buzz about a therapy called low-intensity shock wave lithotripsy. This is a technology that was previously used to treat kidney stones, but they've dialed down the intensity and it's applied to the penis with a smaller probe. It's supposed to cause microtrauma, which then causes some angiogenic factors to encourage smooth muscle blood flow, resulting in a better erection once that's healed. It's not yet covered by the FDA, but we know that it's safe, so stay tuned for that.

The other big thing is stem cell transplants. In men who have had long-term erectile issues, the penile muscle is not as functional as it should be, so an injection of a specialized stem cell can help repopulate and repair some of that old tissue. Stem cell treatments are five to 10 years off, at the earliest.

Do you have any advice for a man with ED after prostate cancer?

Dr. Bennett: The best thing you can do is talk to an ED specialist before you have your treatment so that you have realistic expectations of what will happen after the surgery. As soon as the treatment starts, whether radiation or surgery, get back to that doctor and discuss penile rehabilitation options that will keep that muscle healthy.

The exact wrong thing to do is wait for your body to heal, wait for the incontinence to get taken care of, wait until you feel completely normal and back to your life, and then try to work on erections. At that point, it might be too late. Early treatment, alongside conversations with your urologist, is essential. Pp+

John Mulhall, MD

Testosterone + Prostate Cancer

Dr. John Mulhall is the Director of the Male Sexual & Reproductive Medicine Program at Memorial Sloan Kettering Cancer Center in New York City.

Prostatepedia spoke with him about erectile dysfunction and testosterone replacement therapy after prostate cancer.

Why did you become a doctor?

Dr. John Mulhall: I've been in the States for 28 years. I grew up in Ireland, went to medical school there, and did four years of surgery there. Then I came over here. I went to medical school because I loved science. I was the only kid in my high school who took biology, chemistry, and physics for six years. I was also an athlete. I played rugby. So I'm very fascinated by anatomy. My mom said I wanted to be a doctor since I was 12. It was one of the best outlets for exercising my scientific instincts, more than anything else. I continue to think of myself as a scientist. Science is the foundation of medicine and an important part of my life.

What is it about patient care that you like the most?

Dr. Mulhall: I like talking to patients, sitting down and connecting with people. You remember great physicians. They are good at talking to people. On the very first day I was in medical school, the professor of surgery came in and said: "You'll make 80% of your diagnoses by talking to patients." I don't know how accurate that is, but if you talk to a patient long enough, you get a sense of what's going on. Human interactivity is the most satisfying part of my job.

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> *"I like talking to patients."*

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Insurance companies are trying to do away with that. We're in such a crisis. Now we joke: when in doubt, examine the patients. It's just ridiculous. It's all volume now, shuffling people in and out.

This month, Prostatepedia is talking about erectile dysfunction after prostate cancer. Many men assume that this erectile dysfunction is caused by lack of testosterone, but what is testosterone's role in normal erectile function?

Dr. Mulhall: Testosterone is not really a general erectogenic hormone, which is a common misconception. Even some urologists put patients on testosterone to help erections. You do not need a lot of testosterone for erections, so unless somebody's testosterone level is incredibly low, it's unusual for testosterone to help with erections.

Testosterone is involved in many other nonsexual processes, though. It's a motivation hormone. It's a mood-stabilizing hormone. The normal testosterone range is between about 300 and 800. Testosterone levels below 200 put you at risk for osteoporosis, diabetes, and premature cardiovascular events. The problem in the United States is that a lot of men on testosterone shouldn't be on it because their levels are normal. Twenty percent of men will go on testosterone and they have never had their testosterone levels checked. This is staggering.

Are testosterone level checks part of a normal checkup?

Dr. Mulhall: It's not part of a normal checkup. The signs or symptoms that a patient has a testosterone level that should be checked include diabetes and testicular atrophy. If you've been exposed to chemotherapy, had testicular radiation, stem cell transplants, or bone marrow treatment, you should have your testosterone level checked.

Then there are a bunch of people who need testosterone and don't get it because family doctors think testosterone supplementation causes prostate cancer. It does not. The literature is black and white. Testosterone therapy does not cause prostate cancer. And low testosterone is a bad thing.

What is the role of testosterone in prostate cancer?

Dr. Mulhall: Prostate cancer has difficulty growing without testosterone present. On the surface of a malignant prostate cell, there is an androgen receptor that is maximally stimulated at testosterone levels at or above 150 ng/ml. It doesn't grow more beyond that. That's called the saturation model. There's good scientific evidence to support this concept.

If your level's 250, and we put you on testosterone, we know that prostate volume and PSA barely change for most men. If five years after radiation you have hormone therapy with a testosterone level that's still castrate, say around 50, and then go on testosterone, your PSA will change because your androgen receptor is not yet maximally stimulated. That's the clinical evidence.

There is no link between your testosterone level, whether it's 290 or 1400, and the development of prostate cancer. Testosterone is necessary to make PSA. You need testosterone to bind to the androgen receptor on the cell to generate PSA. If your testosterone is below 200, you probably don't have an optimal testosterone level to make PSA.

A man with low testosterone may have higher-grade, higher-stage prostate cancer because there is a delay in diagnosis. His PSA is fine, but his testosterone level is really low. There is good evidence that if you give testosterone to men in randomized, controlled trials, there is no higher instance of prostate cancer in the group who get testosterone than in those who get placebo. Again, this supports the saturation model concept.

Does this then mean that PSA may not be the best marker for prostate cancer?

Dr. Mulhall: It means you shouldn't look at PSA in isolation without looking at testosterone levels. Some men have Gleason 7 (high-volume) cancer, but their PSA is 1.2 and their testosterone level is low. The biopsy confirms prostate cancer. PSA should not be looked at in isolation. If it's elevated, that's one thing.

The question really is: Is it safe to give men who *already* have prostate cancer testosterone supplementation? Some physicians have been giving testosterone to these men for 12 years. There is no consensus.

We always write in the medical record that the patient has been made aware of the absence of long-term safety for testosterone therapy in the prostate cancer population. But there is no long-term data. It's been estimated that we need to follow 75,000 men for 15 years to answer that question.

Six to 12 weeks after radical prostatectomy, we give testosterone to men with an undetectable PSA, favorable pathology, and Gleason 6 or 7 organ-confined cancer. We have data on 360 men and haven't seen a single PSA elevation—not one. But that's 360 men, not 75,000.

And that had no impact on erectile function?

Dr. Mulhall: It has very little impact upon erectile function. Most of my patients go on testosterone because we're worried about their bone density. We have a huge amount of bone density loss in our prostate cancer patients. They've got an elevated hemoglobin A1c and don't know it. They're prediabetic and at risk for premature cardiovascular events. That literature is crystal clear. When your testosterone level is below 200, premature death is increased.

> *"Testosterone is involved in many other nonsexual processes."*

In Dr. Molly Shores's Veterans Health Administration study, she showed that premature death is likely in patients with testosterone levels below 200. Low testosterone is a bad thing. Low testosterone likely impairs nerve recovery in prostatectomy patients. When patients have a radical prostatectomy with excellent surgeons who have done perfect nerve-sparing procedures and are not doing as well as expected 18 months after surgery, this is sometimes a signal of low testosterone.

We know that testosterone is a neuromodulator. If you don't have enough testosterone you may not recover your nerves the way you would if your testosterone were normal.

But what do you do with the testosterone in a prostatectomy patient who has a Gleason 9 or 10 cancer, positive margins, positive nodes, and positive cardiovascular disease? There is even less data on those patients. We give testosterone to those patients; it's a negotiated decision. We tell them we have no idea what is going on. It all depends on how symptomatic they are.

I've had two men in the last few years brought in by their partners asking us to do something. He was on testosterone for years, the partner says. Now, his doctor won't allow him to get testosterone because he's got Gleason 8 cancer and the patient is suicidal. What are you going to do then? Most of the time, we'll have a negotiated decision with the patient. If he is aware of the issues and agrees, we'll put him on testosterone.

> *"People have completely unrealistic expectations."*

I'll tell you that there is absolutely no signal that the PSA recurrence rate in those patients is any higher when they're on testosterone than it is when they're not on testosterone.

There is a suggestion from investigations done at Harvard University and Baylor University that such men have PSA recurrence rates that might be lower than in patients who don't get testosterone. That is called the bipolar testosterone concept. That's still not a widely accepted practice.

If a patient sees a medical oncologist, they will rarely get testosterone supplementation because one of the main things medical oncologists do for a living is androgen deprivation therapy (ADT). You're not going to get testosterone from them. Even at Memorial Sloan Kettering Cancer Center, where we do it all the time, the medical oncologists are the most concerned.

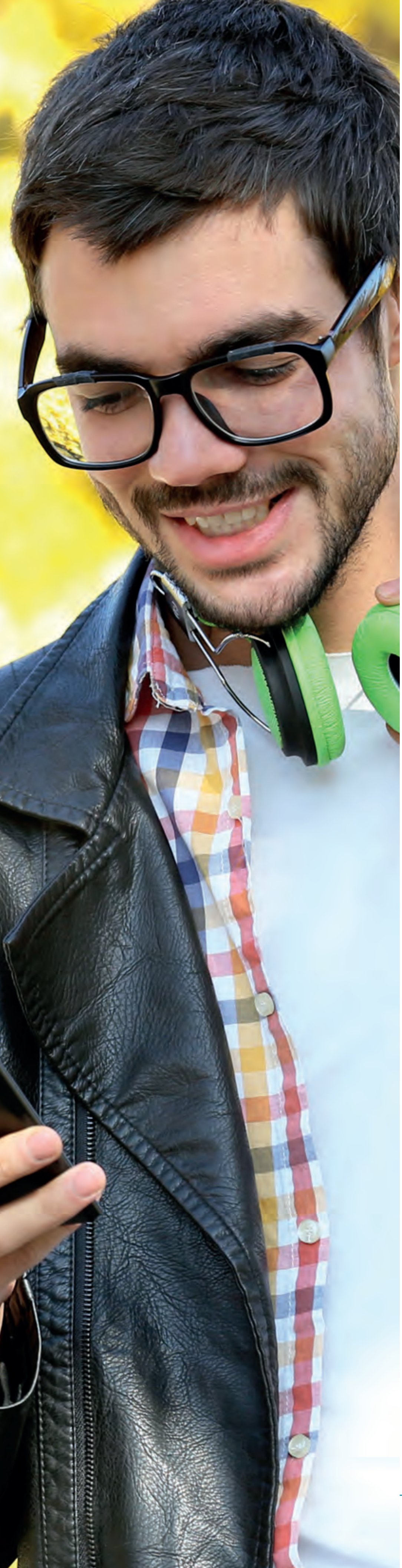
If you take a man's testosterone away, you don't know what his PSA really is. In the background, you're getting these castrate-resistant clones of cells growing. If the PSA is undetectable and the testosterone is 20, you don't even know what his PSA truly is because he doesn't have enough testosterone to make PSA. The PSA is not hurting him. The PSA is a marker.

Now, radiation patients still have a prostate. How do you know if the prostate cancer is dead? Often, they have a detectable PSA. In radiation and hormone therapy patients, we see problems two years after their treatment when they're still at castrate testosterone levels. They've got osteoporosis and they're walking around like zombies because their testosterone level is 40. They never bounce back. Those guys are definitely going to get osteoporosis with time, and they're at higher risk for cardiovascular events.

There is a select group of radiation and hormone therapy patients here at Memorial Sloan Kettering for whom we'll wait three years to give testosterone. This is not national consensus, but if you're going to have a PSA recurrence after radiation, it's nearly always in the first three years. Then we'll put those men on testosterone. There are a handful of very small papers in the literature that suggest there is no concern. They've documented 30 or 40 patients. We now have over 100 patients on testosterone who have had radiation, and we have not had a single concerning PSA elevation.

So you wait three years to see if the cancer is going to come back before putting them on testosterone?

Dr. Mulhall: Yes. But then we've got men who come in 12 months after radiation who had been on testosterone for 10 years beforehand and are miserable. This is another negotiated decision. We wait three years if we can.



We also have about 60 men on active surveillance on testosterone. Not a single PSA elevation that we're concerned about. One-fifth of them have a PSA level that went down significantly. This group challenges the whole dogma of testosterone in prostate cancer.

Then we have those who have had a prostatectomy and then their PSA goes up. They get radiation and two years later their PSA is undetectable. What do you do with them? They're high risk. This becomes a very complicated and negotiated decision.

How does testosterone therapy impact ADT patients?

Dr. Mulhall: We presented a paper at the American Urological Association conference this year that has not yet been published that looks at testosterone recovery in our ADT patients. Twenty-five percent of the patients never got back out of castrate range and 30% never got back to normal. Fifty percent of men never get back to normal. That depends on the patient's age at the time of ADT and duration of the ADT.

Does that mean that they never regain erectile function because their testosterone levels never go back to normal?

Dr. Mulhall: If someone's on ADT long enough, their erectile tissue will degenerate, which is the reason they don't get erectile function back. If you're on ADT for six months or longer, your erection tissue undergoes collagenization: it turns to collagen. If you think of the penis like a bicycle tire, the valve is broken. The blood flows in and flows right back out. They can't get a good erection.

When you're on ADT and your testosterone is near zero, you have no sex drive, which is hormone-dependent. It's rare that a man on ADT experiences an orgasm. They have bad erections. They don't respond to pills. Even if they haven't had their prostate removed they won't make semen. The ADT patient is not the same as the man who comes in with low testosterone. ADT patients have no testosterone.

What can be done for those men?

Dr. Mulhall: That's a permanent thing. Those men tend not to do well with pills. Most of them need penile injection therapy. Extensive collagenization means that often they fail even injections, and the only thing that will allow them to have intercourse is a penile implant.

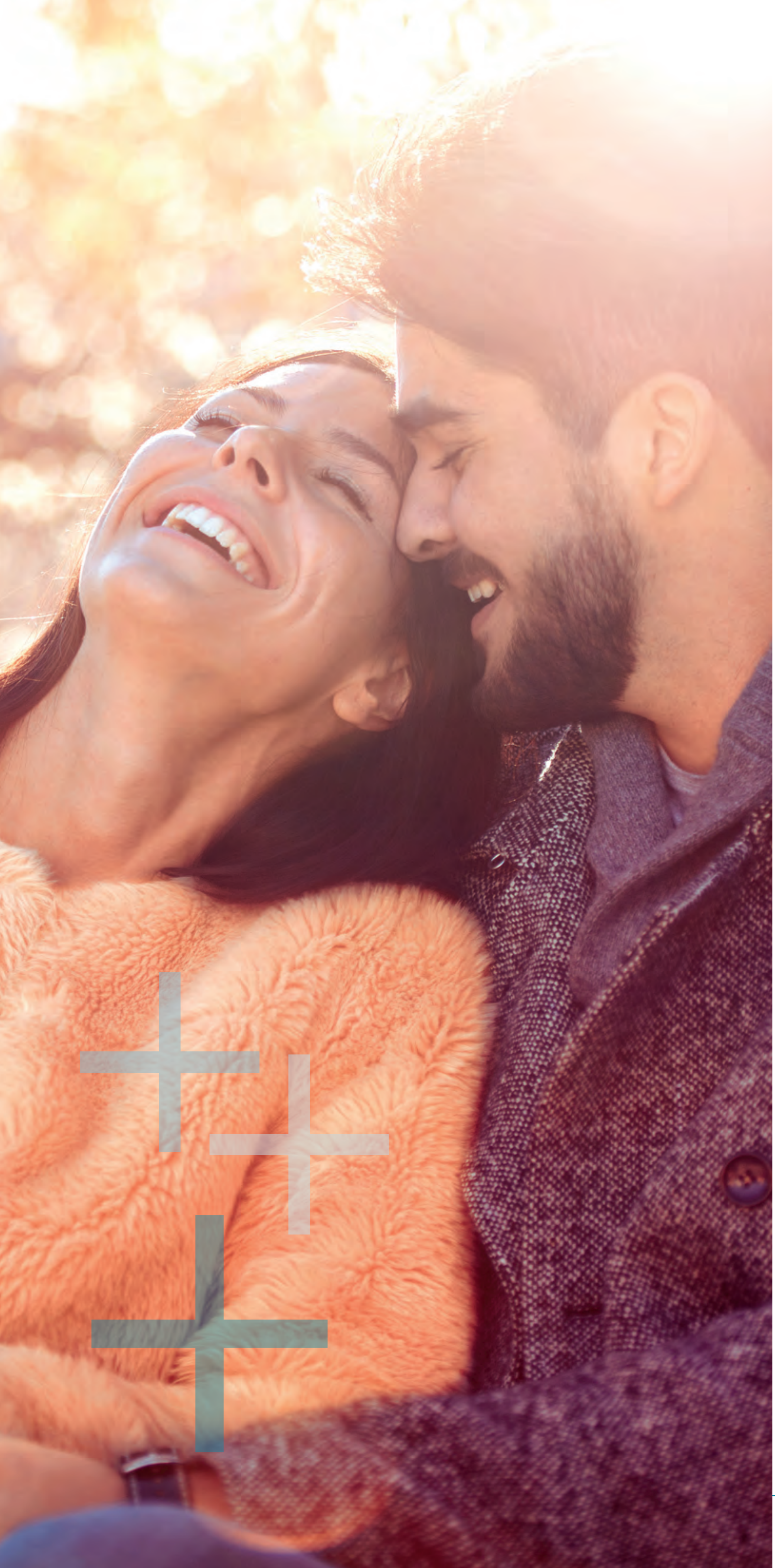
Whether it's prostatectomy, radiation, hormone therapy, or any combination thereof, people have completely unrealistic expectations.

Why is that? Are the doctors not up front?

Dr. Mulhall: No, the doctors have often explained it, but the patients weren't in receiving mode. They were worried about their PSA and weren't thinking about sex. Doctors intrinsically don't like to talk about complications. We like to give good news. Honestly, there is a fear among surgeons and radiation therapists that if you start talking too negatively, the man is just going to go see another doctor.

Isn't erectile dysfunction also more common as men age?

Dr. Mulhall: It's age-dependent, but there are plenty of patients who come to us with perfect erections to start off with. The average age of prostatectomy at Memorial Sloan Kettering is about 60 years. The diagnosis of prostate cancer can cause ED: you've got cancer and you're stressed. When you're



stressed, you don't do well in the bedroom. If you have one bad erection, it then becomes a spiral.

We published a paper showing that when men have baseline ED they're five times less likely to get nerve-sparing surgery. This is at Memorial Sloan Kettering. If that's the case here, what do you think it is in a small community hospital?

Patients think that their surgeon or radiation therapist will tell them everything *they* need to hear, when in fact, the treating physician will tell you everything that *the physician* thinks you need to hear.

Have your eyes wide open as a patient. Know what questions you need answered. How important is quality of life? How important are your erections?

> *"Most people rush because cancer scares them."*

Are some patients hesitant to talk about this subject?

Dr. Mulhall: Patients do not bring up their sexual health because two thirds of them are worried they will embarrass the physician. We physicians give off vibes to our patients that we're uncomfortable talking about this. There are many barriers to getting a good sexual health history. If you're a 40-year-old female physician and a 68-year-old smoker comes in with diabetes who might have prostate cancer, what are the chances that you're going to bring up sexual health with him?

The bottom line is that if your testosterone level is low and you've been diagnosed with prostate cancer, you should go speak with someone who is facile with testosterone therapy in prostate cancer.

Isn't that difficult to find?

Dr. Mulhall: The Sexual Medicine Society of North America (www.smsna.org) has a physician finder tool on their website. Nearly all of those physicians will be facile at having that conversation. In *Urology Times* a few years ago, a survey showed that 85% of urologists said they give testosterone to prostate cancer patients under certain conditions.

Fifteen years ago, if you were on a panel at a medical meeting and said that you give testosterone to prostate cancer patients, they would have looked at you like you're a heretic. There has been a dramatic change.

We have enough patients now to start talking about this with some degree of comfort. A few years ago there was concern that testosterone therapy causes heart attacks. There were three papers over the course of three years that suggested that was the case. All of them were incredibly flawed. All of them fly in the face of 20 years of data showing that low testosterone causes heart attacks and that testosterone is protective. The most recent net analysis concludes that there is no evidence to show that testosterone therapy causes major cardiovascular events. There is no data to show that it's protective, but there is no data to show that it's harmful.

Remember, I said earlier that hypogonadism, which is *low* testosterone, is not the same as agonadism, which means you have no testosterone. We now have an ultrasensitive tool that measures testosterone levels as low as 4. The average man with low testosterone has a level of around 250.

The lower your testosterone goes, the greater your cardiovascular risk, the greater your bone density risk, and the greater your diabetes risk. If your testosterone level is low and you've got prostate cancer, you should have an active discussion with a knowledgeable urologist, not with your cardiologist, primary care physician, or medical oncologist.

Should patients speak to an erectile dysfunction specialist?

Dr. Mulhall: If I say that, it sounds a little self-promotional. We see about 15% of the Memorial Sloan Kettering Cancer Center patients before their radical prostatectomy surgery. I've never had one of them say that seeing me pre-op was a waste of time. They have realistic expectations. We get them on rehab early and they understand what they need to do.

Not every facility has somebody in place with the expertise, support, and infrastructure to look after these patients. Penile rehabilitation after prostate cancer is energy-, space-, and personnel-intensive. I have four nurse practitioners while most of my colleagues don't have a single nurse practitioner of their own.

What about someone who can't travel to see someone like you? Are there other ways for them to get help?

Dr. Mulhall: Some communities have physicians with expertise or interest in this area. The average patient spends more time deciding how to pick a plumber than a physician. It's amazing to me there are people with complicated cancers who are within striking distance of one of the world's top cancer centers and they end up going to some community practice. It doesn't make any sense.

If your health and sexual health are that important to you, whether you have your surgery today, in three months, or six months makes no difference. The doubling time for a Gleason 6 cancer is years. Most people rush because cancer scares them. The physician's job should be to help them relax, take their time, and get all of their questions answered. It's important to go see a sex specialist and an incontinence specialist.

Because we work in a fee-for-service world, there is a bias among many physicians for their own specialty. I'm a surgeon so you should have your prostate out. I'm a radiation therapist so you should have radiation. It's terrible to sound so cynical, but this is the reality.

I've got patients in my office every week: a 50-something guy with tears in his eyes saying: "If I had known it was going to be like this, I would have never done it. I would have lived with my prostate cancer. My life is ruined. I'm leaking like a faucet. My penis is shorter. I've got to use penis injections for the rest of my life."

Cancer doctors stand behind the statement: "I'm sorry that you're leaking like a faucet and you need an artificial urinary sphincter, but we cured your cancer."

I don't know if that flies anymore. We should not focus solely on adding years to life. We should focus on adding life to years. Quality versus quantity. We physicians should not be the ones making that decision. The patient is the decision-maker, not the physician. Pp¹

Clinical Trial:
Christian Nelson, PhD
Sexual Rehabilitation After Surgery

Dr. Christian Nelson is a Clinical Psychologist at Memorial Sloan Kettering Cancer Center and liaison to the genitourinary and sexual medicine services.

Prostatepedia spoke with him about his clinical trial on helping men adhere to a sexual rehabilitation program after prostate cancer surgery.

Why did you become a psychologist?

Dr. Christian Nelson: I became a psychologist because I was interested in helping patients. I was also interested in the research or academic aspect of psychology.

I started working as a research assistant at Memorial Sloan Kettering Cancer Center (MSKCC) over 15 years ago while getting my PhD. When I started working with cancer patients, it was just a good fit for me personally. I got to work with patients while researching at MSKCC. It all fit and I was able to stay.

When I was a fellow, I worked with a physician named Dr. John Mulhall who is a specialist and world leader in sexual medicine. (See page 14 for a conversation with Dr. Mulhall.) With him, I got more involved in the impact that cancer treatments have on sexual function, and I developed this specialty.

The path found you?

Dr. Nelson: The path found me. That's right. It wasn't planned. It was a bit serendipitous.

How common is erectile dysfunction (ED) after prostate cancer? What are some of the issues ED presents that are specific to prostate cancer patients?

Dr. Nelson: Some of it depends on what treatment you have had, but no treatment is *free* from a sexual function perspective. Unfortunately, all men take a hit to some extent.

About 85% of men treated for prostate cancer are going to have difficulty with erections. Those 15% of men who *don't* have difficulty with erections or who get their erections back after treatment, still report a drop in sexual satisfaction after treatment.

Do you think that the loss of sexual satisfaction among people who don't have ED is related to anxiety or a psychosocial issue?

Dr. Nelson: It could be a few things, but absolutely there is anxiety associated with the process, which is not there before prostate cancer treatment. That anxiety has an impact on sexual functioning. Even though at some point some patients get their erections back, they've been through this process where they've lost erections or had some dissipation in erectile functioning. That causes anxiety, shame, and fear when going into a sexual situation. The anxiety can trigger more anxiety about entering a sexual situation for the couple. All that can add up to a loss of sexual satisfaction.

Can you walk us through the thinking behind the trial that you're running?

Dr. Nelson: The trial is attempting to help men utilize penile rehabilitation following prostate cancer surgery. Just about every man is going to lose his erections right after surgery. There is hope of recovery. Ultimately, what helps that recovery is penile rehabilitation, which is based on the notion that all men will have difficulties with erections after surgery. Men do not get nocturnal or morning erections, nor do they get erections in a sexual situation after surgery. If that's the case, the penile tissue can atrophy. When penile tissue atrophies, it's a little different than other muscles that can be built back up.

Hopefully, the surgeon has done nerve-sparing surgery—sparing the two nerves that run bilaterally along the prostate to the penis, the nerves responsible for erections. If the prostate cancer is not close to those nerves, the surgeon can pry away from the prostate. The surgeon must then stretch, clamp, and pull the nerves out of the way. Then they remove the prostate, and the nerves adhere to the prostate bed. Even though the nerves have been saved, those nerves are injured intraoperatively. It's that injury that causes the erectile dysfunction or the difficulty with erections.

It can take about 18 to 24 months for the nerves to heal. That's a two-year recovery period. In that time, if men are not getting either nocturnal or morning erections nor erections in a sexual situation, then that penile tissue can atrophy. The idea is to help men get medication-assisted erections consistently in this period where the nerves are healing.

Which medications do they usually use?

Dr. Nelson: The first choice is pills: the PDE5 inhibitors like Viagra (sildenafil), Levitra (vardenafil), or Cialis (tadalafil). Those work off of the nitric oxide secreted from the nerves, so if the nerves aren't healthy and aren't secreting nitric oxide, then the mechanism of action for those pills isn't there. For many men after surgery—especially right after surgery—those pills aren't effective.

For most sexual medicine professionals who do this kind of rehab, the next step is to use penile injections to restore erections. The injections are used every time a man wants an erection. The injection is in the shaft of the penis, toward the base. It's a very thin needle, so it doesn't really hurt. For example, after the first injection, we've asked men how painful it was on a zero to 10 scale, where 10 is pain as bad as you could imagine. Men generally rate the pain between a zero and two on the pain scale. There's anxiety associated with it, but after you do it a few times, the anxiety tends to dissipate.

The notion of penile rehabilitation then for most men is to use these penile injections about two or three times a week. The idea is that the injection will pull oxygen-rich blood into the penis, give the man an erection, and keep the penile tissue healthy. In terms of rehabilitation, what men do with the erection is up to them. It can be used in sexual situation or not. The idea is just to have an erection to keep the penile tissue healthy.

> *"Unfortunately, all men take a hit to some extent."*

With injections, the goal is to get an erection two to three times a week through the recovery period, which is up to two years. The hope is this will give men a better chance to recover erections. We don't know exactly what will happen. But the data suggests that this gives men a better chance of recovering erections on their own without medications.

Then if they don't recover erections, they have a better chance of responding to pills, like Viagra (sildenafil), Levitra (vardenafil), or Cialis (tadalafil). That's the rehab program.

Now, you can imagine that it's hard for men to stay on that type of penile program.

How do you help men adhere to the rehabilitation program?

Dr. Nelson: Compliance is difficult with any type of medication, and now we're asking men to self-inject their penis two to three times a week. Men say that difficulty with erections is a shameful experience. There is fear of entering into sexual situations with ED, and on top of this, the notion of injections causes fear.

Some men say injections are great—I can get an erection! A lot of men say that it's nice to get an erection, but the whole process is humiliating. Even just using a pill and having to plan for sex feels much different, and so there's a sense of dread. Something that was an enjoyable, spontaneous experience now is something that needs to be planned and provokes anxiety. If there's anxiety and dread, the quickest way to get rid of that is to avoid the cause of the anxiety.

If the anxiety and stress builds, then it becomes easier to put it off. Whatever the excuse, avoiding the anxiety is an instant mechanism to reduce that anxiety. In the short-term, it works really well. But in the long-term, men go a week or two without an injection. Then you start to feel bad that you're not keeping up with the rehabilitation. In the long-term, it's not helping you get to the goal. That's the psychological loop that can happen.

Our intervention explains this process of avoidance, and then uses concepts such as why it's important to recover erections in terms of his or the couple's values. Maybe he wants to feel like a man again. Maybe he wants to just feel healthy again or whole. If a man is single and dating, maybe he wants to feel that he can still date. The idea is to start with the values and build from there.

Then the next step is acceptance: accepting that he is going to be anxious and nervous when he does the injection. There are going to be times when he's

How To Get Involved…

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not going to want to do it and will need to accept that this is an important process. Instead of avoiding that anxiety by avoiding the situation, a willingness to engage in the situation when he might be anxious is essential.

When we talk to men in our focus groups who have used the injections successfully, they really emphasized this notion of short-term pain for a long-term gain.

Does doing injections without the expectation that sex will happen remove the anxiety for these men?

Dr. Nelson: It can. You're absolutely right. One strategy is for men to practice injections on their own five, six, seven times without any partner, just so they become comfortable with the injections. Once he knows how it works, gets the dose right, and he knows it's going to be effective, he becomes comfortable and confident. Then he can integrate it into a sexual relationship with a partner.

Just as a partner adds a layer of anxiety because the man wants to perform, the partner doesn't want the man to feel bad, anxious, or upset, and so often times the partner takes on some anxiety too.

Each person's anxiety can feed the other?

Dr. Nelson: Yes. That leads to avoidance. Partners stop initiating because they don't want to put him in a situation where he feels anxious or bad. Partners in a couple can collude to avoid a sexual relationship.

In your program, you take men who've just had a prostatectomy, put them in focus groups, and talk to them through therapy. What happens then?

Dr. Nelson: Actually, our study staff meets with them individually

"Anxiety has an impact on sexual functioning."

twice while they come in for their injection training. Then the rest is by phone. We follow-up with a 10-15 minute phone call about once a month to check in with them, reinforce acceptance that it's going to be an anxiety-provoking situation, and discuss their willingness to experience that anxiety while doing injections anyway.

Do you only accept patients who've had a radical prostatectomy at your center, or are you open to seeing people who've had surgery elsewhere?

Dr. Nelson: In general, we're open to men who have surgery elsewhere. To be part of the trial, they would need to come here to our sexual medicine program. In terms of rehabilitation, everything needs to be standardized for a study like this, so we target men who are going through our rehabilitation program, which we know is standardized. We haven't really branched out to other places. Somebody visiting New York could come to our center. They come to see Dr. Mulhall, they're signed up for rehab, and then they're here for two visits. The rest is long-term. There are six-month follow-ups with the sexual medicine program.

Is there anything else patients should know if they're interested or may be a good fit?

Dr. Nelson: Whether they come here to a sexual medicine program, or whether they seek out a sexual medicine program where they had their surgery or in their area, this notion of erectile activity is important during the recovery period. There are sexual medicine professionals throughout the United States who do this rehabilitation.

It's not just penile rehabilitation but sex therapy, whether individual or for a couple, right?

Dr. Nelson: That's right, absolutely. That's what our study does. Our study tests a specific type of intervention: combined therapy for erectile dysfunction, which is medical therapy, and psychological, whether support or sex therapy. It's not just the medicine because there are many other emotional and relationship issues along with it. The data indicates that combined therapy is more effective. Patients are more likely to use the medications, be happy using them, and have better relationship communication and integration.

Would you recommend that men who can't participate in the trial seek some kind of support for their prostate cancer?

Dr. Nelson: Absolutely. The trial is just testing a specific type of intervention that we've shown worked in pilot data. Hopefully, we can show it works in a larger study. Once we do that, we'll disseminate this concept and the specific intervention. If a man is in a rehab program, reaching out to support groups or to a psychologist who specializes in sexual issues can be really helpful.

Is there anything else that you think patients should know about erectile dysfunction after prostate cancer?

Dr. Nelson: Most men are surprised at how distressed and upset they are about their difficulty with erections after prostate cancer treatment. There is not really good communication about the impact of surgery or of any prostate cancer treatment. Most patients aren't aware of the prevalence and the length of ED after these treatments. A lot of men are surprised at how much it impacts them. Even men who anticipate ED don't realize how upset they'll get. It really goes to the core of what it is to be a man.

I'm in New York City where people don't drive around, they walk. A lot of my patients say that when they walk down the sidewalk and see other guys, they think: those guys are normal, but I'm not. Think about that construct, how often they're thinking about it just walking down the street. Others are normal *and they're not*.

It's not just about sex, or the ability to have sex. It's about how you see yourself as a person?

Dr. Nelson: It's how they view themselves as a man. Again, this is where a lot of people are surprised. They didn't realize that it was so crucial to how they viewed themselves as a man.

Would you suggest that men go see someone like yourself or Dr. Mulhall before treatment so that they're prepared?

Dr. Nelson: Yes. The earlier, the better. Before treatment, they get better information and they can adjust their expectations. Advice before treatment helps with the follow-up after treatment.

They'll have a plan for how they're going to deal with it.

Dr. Nelson: That's absolutely right. To have good expectations, a good understanding of what's coming, and to have a plan all help with fear of the unknown. Pp1

Erica Marchand, Ph.D.

Couples + Sex Therapy

Dr. Erica Marchand is a licensed psychologist specializing in couples therapy and sex therapy in Los Angeles.

Prostatepedia spoke with her about the impact erectile dysfunction after prostate cancer can have on couples.

Why did you become a psychologist?

Dr. Erica Marchand:: I've seen plenty of ups and downs in my own life and in the lives of family and friends. I started to be curious about how some people seem to weather life's ups and downs and always land on their feet, and how other people seem to get worn down and diminished by the hard times. So I became a psychologist in part because I wanted to know how to help people become more resilient to life's problems.

What is it about working with patients in couples and sex therapy that you find most rewarding?

Dr. Marchand: Intimate relationships are so integral to human life. We're wired for connection with other people, and in romantic partnerships, part of that connection involves sex. When relationships are going well, they're a source of happiness, care, and nurturing; when they're going badly, they can be miserable for everyone involved. People who have satisfying, loving relationships tend to have better long-term physical and mental health outcomes. So I find it incredibly rewarding to help people get back to happiness in their relationships.

> *"I wanted to know how to help people become more resilient."*

I find it particularly rewarding to provide space to talk openly about sex since it's so often taboo but is such an important part of life, pleasure, and connection for so many people.

What are some of the psychosexual issues that can come up for men with prostate cancer and their partners? How do these issues impact their sex lives and their marriages?

Dr. Marchand: There are several issues that tend to come up. First, the experience of cancer can be pretty scary and life-changing. Even though prostate cancer is usually curable these days, many men and their partners feel fear, worry, sadness, and stress going through the process of diagnosis and treatment. Partners can become caregivers and/or temporarily take on additional roles, which can strain both partners but can also lead to greater closeness, understanding, and strength in the relationship.

Second, some of the most common side effects of prostate cancer treatment involve changes in sexual function. Prostate surgery and radiation can lead to erectile dysfunction and, less commonly, retrograde ejaculation. Androgen-blocking drugs can decrease sexual interest and desire. Those effects can interrupt or change a couple's sexual relationship, and it can take some communication and effort to re-create a sex life together.

How does therapy for prostate cancer patients work? Just talking about what is going on?

Dr. Marchand: To some extent, yes. There's plenty of talking in therapy about what is going on. I also tend to work with my clients to come up with strategies to improve things and try them out. For example, if someone is struggling with high stress and anxiety, we might integrate some stress-reducing activities into that person's life in addition to talking about the problems. If someone is trying to re-create a sex life with their partner, we might identify some activities that feel good and fit into their current sexual functioning.

> *"Many men and their partners feel fear, worry, sadness, and stress."*

Does your approach to prostate cancer patients differ from your approach with men without cancer?

Dr. Marchand: There is definitely some overlap in therapy for sexual concerns for men with and without prostate cancer. But with prostate cancer, we're also talking about all the other concerns that come along with having cancer.

Do you have any advice for men who are about to start prostate cancer treatment and are worried about potential erectile dysfunction? Or for men who are already dealing with erectile dysfunction and related sexual issues post-treatment?

Dr. Marchand: Yes! Talk to your urologist about your concerns and about anything you can do to help restore erectile function after treatment. Ask about the pros and cons of different treatment options for maintaining sexual function. Also, try to have an open, honest discussion with your partner about sex before and after treatment. Try to keep your partner in the loop about your current sexual functioning and interest and any concerns or questions you might have. If you find yourself really struggling to adjust, or have difficulty communicating with your partner about sex, consider scheduling an appointment with a therapist who specializes in sexual concerns to help get you back on track. Pp!

Angela Gaffney

Your Number One Fan Is Looking for Love

Picture your number one fan, the one who supports you most in life. The one who shows up no matter your mood, how tired you may be feeling, or how much pain you may be experiencing. Whatever the situation, your number one fan is there for you. I'm sure many of you pictured your spouse, partner, or maybe a parent or best friend. While these people are all great supporters in your life, your number one fan is much, much more! Your number one fan is your body.

We hurry through life at such a fast pace that we often forget to support the one that supports us most! Sometimes it takes a diagnosis or health crisis before we realize that our body may need more from us than what we've been willing to give. It was true for me, and it was true for many of you. Caring for your body goes far beyond just eating well and exercising. It takes commitment and conscious effort to ensure you're giving your body all it needs to heal and achieve optimal health.

We all need to practice these four principles to care for our bodies through diagnosis, treatment, and in lifelong health.

Build Awareness

Daily habits are so second nature that it's easy to underestimate the impact they have on our health. Start tapping into your daily habits and assess whether they're offering you the supportive environment your body needs to heal and be well. If change is needed, take it one step at a time.

Consciously Choose

We often make decisions, big and small, out of convenience, haste, or emotions we're feeling. It's time to pause and choose differently. Before every decision you make, stop and ask yourself: "What will this provide me?" Just answering this one question will help you make a conscious choice and to move forward in a healthy direction.

Create a Supportive Environment

It's hard to avoid sugar if there are cookies and cake in the kitchen. Building a supportive environment is of greatest importance if your goal is lifelong health. Replace processed foods with whole, fresh foods that nourish the body. Say no to unnecessary obligations to give yourself space and time to heal. Share your needs with your friends and family so they too can support you in this journey. Everything in our environment—the food we eat, the toxins we're exposed to, and the stress we feel from everyday life—impacts our health. Do your best to create a healthy, supportive environment for you and your family.

Above All Else, Be Kind

You are on a health journey, which means some days will be easier than others. Use positive affirmations and encouraging words to support yourself in healing and lifelong health. If you veer off track, assess what you'd like to do differently next time and move forward. You have a choice in every matter, and you get to decide how you'd like to participate. Above all else, be kind to yourself in the process.

You are your best advocate! Take care of your number one fan by assessing your current habits, making conscious choices that serve you well, creating a supportive environment, and above all else, being kind to yourself through the process. Pp1

Want to know more?

Wellness speaker Angela Gaffney teaches simple and effective strategies to help people achieve health, increase productivity, and live stress-free while reaching their personal and professional goals.

To hire Angela to speak at your next event, discuss a wellness program for your corporation, or take advantage of complimentary health tools, please visit www.AngelaGaffney.com.

Patient Access Network Foundation: Finances + Cancer

PAN Foundation

The Patient Access Network (PAN) Foundation offers cancer patients help with copay assistance, out-of-pocket costs, insurance premiums, and travel expenses.

Prostatepedia spoke with two members of their team, Mr. Dan Klein and Ms. Amy Niles, about their services for prostate cancer patients.

How did you become involved in cancer advocacy?

Mr. Dan Klein: I'm the president and CEO of the PAN Foundation. I've been with the foundation for about three years now. Before coming here, I was with the Cystic Fibrosis Foundation for nearly 10 years, and I ran their specialty pharmacy and patient access program.

I've been involved in this type of work for quite some time, and since coming to the PAN Foundation, I have tried to make sure that we're able to continue helping as many people as possible get access to their critical medications.

Ms. Amy Niles: I'm vice president of external affairs, and I have been with the PAN Foundation for about four years. I've been involved with nonprofit work, patient advocacy, and access issues for my entire career. Prior to this position, I was involved with an organization focused on the uninsured. Prior to that, I was CEO of an organization that addressed women's health issues.

What does PAN do?

Mr. Klein: PAN's mission is to help people with life-threatening, chronic, and rare diseases get access to their critical medications and also to advocate on their behalf.

Primarily we provide copay assistance to patients and help them cover the out-of-pocket costs of their prescription medications. We also help with insurance premiums and travel expenses.

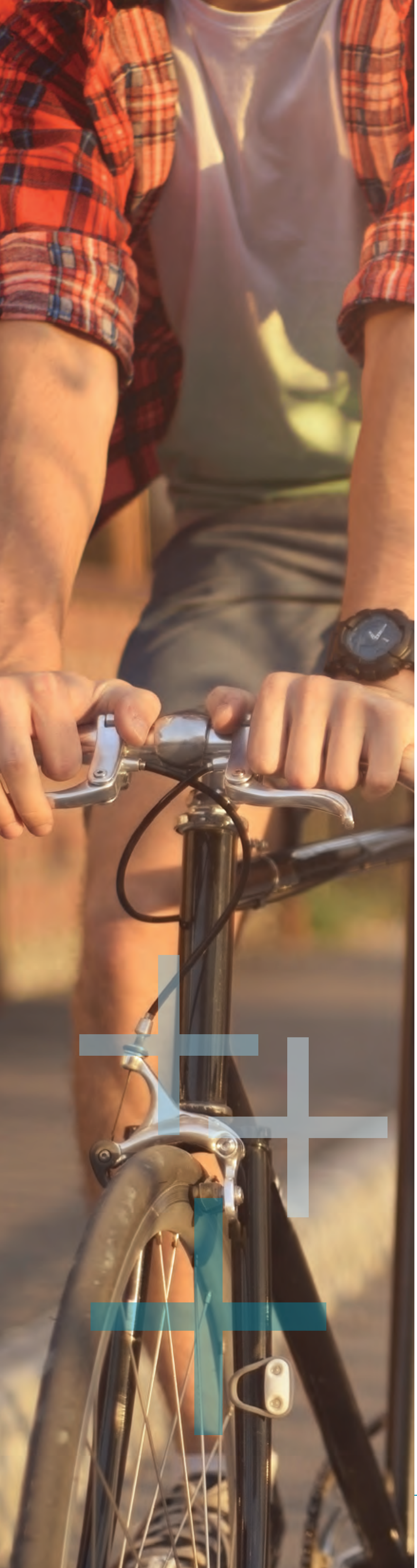
We have about 60 different disease areas where we provide assistance to patients. In most of those, we only provide copay assistance, but in a small number of those areas—including prostate cancer—we also provide travel assistance. In some instances, we provide assistance with premiums.

We are a fairly large-scale organization. We help several hundred thousand people a year, and we provide many hundreds of millions of dollars in financial assistance a year. There are many people who need help, the need is growing, and we expect it to continue to grow. By that, I mean more and more people struggle with covering the out-of-pocket costs of their care.

We focus on people with income between 200% and 400% of the federal poverty level. That's sort of our sweet spot if you will. We focus largely on people on Medicare because, under the regulatory rules, people on Medicare can only get assistance of this kind from independent charities like the PAN Foundation. They're not able to get help directly from drug manufacturers.

You're making a distinction between the uninsured versus the underinsured. Does "underinsured" refer to patients who have health insurance that does not cover all of their expenses?

Mr. Klein: Right. We really are organized around helping the underinsured. Within Medicare programs, and Medicare Part D particularly, many people are underinsured because of the high out-of-pocket costs. In Medicare, there's an infamous donut hole, or coverage gap, that people have to get through. Once they're through, they still have to pay 5% of the cost of their medication with no out-of-pocket limit. If they take an expensive specialty medication—and many people with prostate cancer take expensive medications—it can easily cost $10,000 a year out-of-pocket just for a single drug.



And you also help with travel?

Mr. Klein: We do. We have a travel fund for people with metastatic prostate cancer. In particular, people who may live far from a treatment center sometimes struggle to afford to get to the specialized care that they need. The travel fund will pick up those expenses related to travel. It could be livery services. It could be the hotel expenses, and we'll help with those.

What other kinds of out-of-pocket expenses do prostate cancer patients face?

Mr. Klein: There are all sorts of out-of-pocket expenses, and people tend to forget about the fact that it's not just the copays and deductibles related to the medications. There can also be out-of-pocket expenses related to their medical care or to hospitalization.

How can patients apply to benefit from your programs? What's the process like?

Mr. Klein: It's a very streamlined process. Patients can enroll in multiple ways. They can come to our website and enroll through the patient portal, or they can call our 800 number and enroll. Many patients are enrolled by their physicians or by their pharmacists. A pharmacist or physician can enroll a patient through the portal or the call center.

It takes around 10 minutes to complete the enrollment. Within that 10 minutes, they'll learn whether or not they've been approved, and if so, they can use the grant immediately to fill a prescription.

Are they one-time grants or recurring?

Mr. Klein: The grants are for a maximum amount. In the case of prostate cancer, that amount would be $7,500 a year. That's meant to cover out-of-pocket costs for one year. We use a lot of data to help us try to set that number. Patients who need more than that can ask for a second grant in that same 12-month period. Then at the end of the 12 months, they can renew the grant, provided funding is available.

The eligibility criteria for prostate cancer are that the patient has to be at or below 500% of the federal poverty level, and they need to live in the US. It's a Medicare-only fund, so they need to have Medicare coverage, not commercial coverage. Patients who have commercial insurance coverage can get help directly from drug manufacturers.

Are there any nonprofits who do something similar for private health insurance companies?

Mr. Klein: Charities like PAN generally provide a similar kind of assistance to patients on Medicare. The reason is that under the Anti-Kickback Statute, drug manufacturers are able to serve people who have commercial insurance, but they're not able to serve people who have coverage through Medicare.

As an independent charity, we're highly regulated in what we can do, and we have to keep an arm's-length relationship from the drug manufacturers.
For example, we're required to cover all of the different medications that might be needed by a patient with prostate cancer. We cover about 35 different medications for prostate cancer.

What about people who are completely uninsured? Is anyone offering help to them?

Mr. Klein: Yes. There are several ways that those patients can get assistance. Drug manufacturers operate Patient Assistance Programs (PAPs), or free drug programs. These are designed to help people who do not have insurance and who are below a certain income threshold. It varies from manufacturer to manufacturer.

> *“Primarily we provide copay assistance to patients.”*

The other option is to talk to one of the patient advocacy groups that help navigate the system to find insurance coverage available through the Affordable Care Act (ACA) health exchanges or possibly through Medicaid.

Are financial issues more prevalent in patients who are newly diagnosed and starting on medications, in patients who have been through a couple rounds, or is it all over the map?

Mr. Klein: All of the above. Our particular prostate cancer funds are for people with metastatic prostate cancer. That could either be newly diagnosed patients who were diagnosed at a later stage, or it could be patients who had been diagnosed with local disease that has progressed.

With the types of treatments available today, many patients live longer and manage their disease almost like a chronic disease, and so they may need assistance with out-of-pocket costs for a number of years.

Anything else patients should know?

Ms. Niles: We are very pleased to be working with Us TOO so that patients who contact PAN for assistance can benefit from the range of services that the organization provides. Financial assistance is obviously very important, and it removes barriers to care. But patients, especially when first diagnosed, have many questions about their illness. Addressing those concerns is beyond PAN’s mission, but it’s not beyond what we want to do for patients.

We have aligned with Us TOO which helps patients have a conversation about their illness, medication adherence, and provides a range of support services.

We have close to 20 alliances with various leading patient advocacy organizations to provide this level of support for patients.

Does Medicare refer patients to you?

Mr. Klein: Medicare does. If you go to www.cms.gov, they have a whole page that refers people to PAN and programs like PAN.

Do you have any advice for patients who face these issues?

Mr. Klein: There is help available. Patients should not get frustrated or despondent. If a patient calls PAN and we can’t help them, we’ll try to refer them to someone who can.

Ms. Niles: I think it’s really important for patients to have conversations around cost. It’s a difficult conversation to have with their physician or the staff in his or her office. We don’t want patients to refuse treatment because of costs or do things like cut pills in half, delay treatment, or go into medical debt and bankruptcy because of the cost. They should have these conversations and know that resources exist to help them.

Why are patients hesitant to have these conversations?

Mr. Klein: Someone who’s provided for himself for most of his adult life who then gets diagnosed may feel isolated and stigmatized in terms of asking for help. For people who are older, it can feel uncomfortable. Patient advocacy groups like Us TOO and charities like PAN can help them navigate these issues as well.

I imagine there must be a lot of fear involved. Not only are you struggling to pay for your medication, but what is it going to mean for your financial future?

Mr. Klein: Healthcare cost is still one of the leading causes of personal bankruptcy in the US.

Is that more problematic among, for example, older patients who are perhaps on a fixed income?

Mr. Klein: Yes. It’s more problematic for older patients who have serious illnesses because they aren’t able to recover financially. They may not have the ability to go back to work. They may not have a lot of assets. It’s a challenge across the board.

From a public policy perspective, we’re concerned that an increasing number of people have difficulty meeting the deductibles, copays, and coinsurance. And yet, the direction that the insurance industry and the government have taken is not going to make that problem go away anytime soon. We’re worried about the current situation and even more worried about what may come in the next year or two.

What about people who would like to donate?

Mr. Klein: Like any not-for-profit, we are happy to get donations from all sources. [Visit https://panfoundation.org/ to donate.] Because of the amount of money that’s needed to support the large number of patients who need help, the drug manufacturers are our main source of support. Without their help, we wouldn’t be able to provide the number of grants that we do.

Patients Speak: Tim M.
Dealing With ED After Surgery

Tim M. had a Gleason 9 prostate cancer removed by his urologist. He spoke with *Prostatepedia* about his struggles with ED posttreatment.

How did you find out you had prostate cancer?

Tim M: I had the typical issues that people talk about: urination and a PSA that was increasing a little bit. I had a phenomenal general practitioner, a doctor who really cared. He wanted me to do a biopsy. I was resistant. I said, “Oh, come on, Doc. This must be an infection or something.” Unfortunately, I resisted for about six or seven months, maybe even longer.

> *“I had aggressive cancer.”*

Finally, he said, “No, you’ve got to go for the biopsy.” So I went to a top doctor in my area. He did a check and said, “I don’t really think there’s going to be a problem, but let’s do the biopsy.” So I did it. He called and said he was surprised to say that I had aggressive cancer.

What kinds of treatment did you have?

Tim M: I really didn’t have much of a choice. My doctor said I needed surgery right away. He was a leading surgeon with a phenomenal reputation. I had the surgery two years ago.

Did the urologist talk to you before surgery about the potential for erectile dysfunction (ED) after treatment?

Tim M: Not really. He did not really touch on it. We asked him about it at one of the interviews. If we hadn’t asked him, I don’t think he would have really talked about it. I’ll never forget his answer. He said it was 50/50 whether or not I’d get ED.

What happened after the surgery?

Tim M: The surgeon completely removed the prostate. The cancer had gotten out of the capsule, but he thought he got it all because my margins were clean. I was very lucky. He was comfortable that we had it all. I didn’t have any problems with urination. The catheter clogged up one time, which was actually one of my biggest fears, believe it or not.

The catheter?

Tim M: When I was about 17, I went to see a friend who was in the hospital. He had a catheter and he explained to me what they had done to him. It left a burning impression in my mind. There’s a tube where? That kind of stuck with me. That was one of my concerns. I did have some issues with the catheter, but after that, everything was fine except for the erectile dysfunction.

Can you talk a bit about that?

Tim M: Nothing seems to really work anymore.

Have you been able to talk to your urologist about it?

Tim M: He gave me some pills—Cialis (tadalafil) and the other pills. It didn’t help.

Then he said to try the injections, which seemed to help a little bit, but not really. He wanted me to increase the dose, but I really didn’t want to do that because of all the warnings: *if something goes wrong, get to a hospital right away*. The whole deal with the needle and the possibilities of side effects put a damper on things.

Did you talk to him about any other options?

Tim M: He went through all the options with me, including the vacuum and an implant and none of them seemed too attractive to me.

How do you feel about all that?

Tim M: Pretty bad. But you know, as you get older, you begin to accept things a little bit more. I guess you have to. I wasn't happy about the cancer to begin with. All I can do is do what I can do.

I just turned 70 this month. I also have some cardiovascular issues. I go to the gym. I try to do what I have to do to keep conditions under control as best I can.

My doctor called me at 8:30 the night of my diagnosis and said, "I have to tell you you've got an aggressive cancer. It has to come out right away." There was no light discussion. It's not like I had a choice. If I had let it go, I would have died.

> *"From age 15 to 68, it was all just a natural happening."*

He was so focused on your cancer that he wasn't really even thinking about potential ED?

Tim M: Yes, I believe so. That was the priority.

Did you have any problems with incontinence after the surgery?

Tim M: A little bit. I still wear pads, but I barely need them. I just got used to them.

He had suggested that I do Kegel exercises. But it's weird. Because of my cardio situation, I wind up going to the gym and working like a fool for hours a week, but I just couldn't get into those exercises. The pads were just too convenient, but that's pretty much dried up at this point. The only time I have a problem is with stress if I'm exercising or something like that.

Do you have any advice for other men about to have prostate cancer treatment?

Tim M: You have to do what you have to do and deal with what you have to deal with. What you have to deal with might not be too good. There is nothing good about it in my view. My advice is to consider that ED is going to be an issue.

Do you think that more men are suffering from ED than surgeons think?

Tim M: Yes. I do absolutely think that. I'll tell you something else. It's a little bit sensitive to talk about, but I'll just come out and say it. How do you define erectile dysfunction? You know what I'm saying? There are different levels of an erection. Obviously, when you are younger, it's one way. My question is, where is the threshold? What if you end up with a three-quarter situation? My doctor told me 50% of men have ED, but of the other 50% what in the hell was the quality of what they had left?

Was the erection like what they had before or was it just enough so that they could use it?

Tim M: Yeah, just enough to use. I mean if you're not going to be able to perform to some degree of quality, why bother?

Also, there's a secondary problem, which is a psychological issue. When you ejaculate, there's nothing there.

That must be a bit demoralizing.

Tim M: That was very demoralizing. Some people say, "What's the difference?" There is a difference. It's a mental thing. To tell you the truth, my first thought was: "Have I become like a woman? Is this an orgasm that a woman would have?" The physical aspect is not the big thing. It's how you're interpreting it and what's going on inside your mind that's the major thing.

> *"This is not a binary A or B thing."*

It changes the whole experience.

Tim M: Thank God this didn't happen when I was in my forties.

It might be worth going to see an expert in ED.

Tim M: Well, I know all the possibilities. It's the shots. It's the vacuum. It's the operations.

From age 15 to 68, it was all just a natural happening. And now, you're talking about mechanisms and devices and shots and operations and you have to push a button?

It sort of takes you out of the moment.

Tim M: It puts a whole different perspective on the deal. Men should definitely be prepared for what's going to happen. I do think more information needs to be out there.

The more men know about what may happen the better they can prepare themselves?

Tim M: Yes. I think where doctors make a mistake, at least in everything I've seen and read and everything that the doctor has said to me, is that this is not a binary A or B thing. Do you have ED or don't you? It's not like that. It's more like: do you have *no* dysfunction or do you have *some*? Is it the same as before or not? That's important. My guess is that the vast majority of guys are going to say no.

Patients Speak: Steve A. Erectile Dysfunction After Surgery

Steve A. talked with *Prostatepedia* about his experience with erectile dysfunction (ED) after surgery and radiation for his Gleason 9 prostate cancer.

What was your life like before you had prostate cancer?

Steve A: A hell of a lot better than it is now. I think about and read about prostate cancer daily. I have no symptoms. Never have had any. But I work hard to combat the side effects of treatment and forestall recurrence. Eat right, exercise daily, and try to help others with prostate cancer.

> *"I work hard to combat the side effects of treatment and forestall recurrence."*

I'm retired. I was a senior executive at a Fortune 10 company. I retired early back in 1998 and moved part-time to a resort community. I played a lot of golf and worked in community projects, including community government, and started a real estate development business.

I moved here full-time in 2001 and noticed that I had a problem with urination frequency. I saw a urologist who determined that I had benign prostatic hyperplasia (BPH) and put me on Avodart (dutasteride).

Then my prescription drug plan dropped Avodart (dutasteride), so I switched to Proscar (finasteride). Later my urologist added Flomax (tamsulosin) to shrink my prostate. I was on Proscar (finasteride) and Flomax (tamsulosin) continuously until 2013. They controlled my BPH pretty well but impacted my sexual performance. My sex life was not as good as it was before that as a result. I had mild ED.

Did you go on any medication for the ED at that point—like Viagra (sildenafil) or Cialis (tadalafil)?

Steve A: I tried them. They worked.

When and how did you find out you had prostate cancer?

Steve A: I had been getting annual PSA tests since age 40 as part of annual company physical exams.

The PSA was around 0.4 for years, then increased gradually as I aged. But it was never considered a problem since it was well below the magic 4.0 considered "normal."

Then, in 2013, my PSA suddenly doubled to 5.4 from 2.7 in 2012. I had it checked again and this time it went up to 6.6 in only a few months. So my GP, who recognized that PSA velocity (doubling time) was an indicator of a potential problem, recommended a biopsy. I found out that finasteride cuts PSA roughly in half, so my PSA was actually 13.2. This shocked me. Should I have had a biopsy years earlier? Could I have cured my cancer if I'd found it earlier?

So you had a biopsy?

Steve A: I got a biopsy from my local urologist. The Proscar (finasteride) had reduced my prostate size quite a bit, so I only needed to have six cores taken. It was painless. Pathology found 40% prostate cancer in one core and 10% in another core. The others were clean. My Gleason score was 4+4=8. I had a second opinion done by prostate cancer doctor Jonathan Epstein at Johns Hopkins; he upgraded my Gleason score to 4+5=9.

My urologist talked about what I should do. Was I a candidate for active surveillance? He didn't think so. Turns out that was a huge understatement!

He said I was a candidate for either radiation or surgery due to my age (69 then) and otherwise good health.

So I saw a couple of radiation oncologists and a couple of surgeons. In addition to seeking a cure, I was concerned about three things: ED, hormone therapy, and dragging out the treatment process. I'm the kind of person who likes to get stuff done quickly, which is probably stupid on my part. I now question my decision to have surgery since the cancer had already escaped the prostate. Should the urologists or I have known that?

When you met with these different surgeons and radiation oncologists, did any of them speak to you about ED after treatment?

Steve A: I asked both surgeons if they could do nerve-sparing surgery because I was concerned about my sex life after treatment. The local surgeon said, "No, I wouldn't try it. With Gleason 9, I've got to go pretty wide on the margins to ensure I get it all. I can't promise that at all." He was totally unconcerned about ED. I didn't like his bedside manner!

When I spoke to Dr. Epstein he said he would do nerve-sparing surgery and gave me printed handouts which addressed all facets of what I could expect post-op, including incontinence, ED, etc. I liked his can-do attitude and was impressed with his credentials and Johns Hopkins's reputation in the field of urology.

What about the radiation oncologists?

Steve A: I don't remember them saying anything about ED. But they both agreed that hormonal therapy would be necessary before and after radiation therapy. That turned me off completely. I had read about the side effects of hormonal therapy and wanted no part of it. However, in addition to talking to people, I do a lot of reading. I read that you're going to have ED with surgery, but that it'll go away after a year or maybe two. ED with radiation comes later on.

I decided I'd rather have ED up front and get it over with than have it come two or three years later. So I went with surgery.

What happened after the surgery?

Steve A: The day before surgery, the doctor changed his mind and suggested that I have open surgery rather than robotic. He wanted to be able to feel the tumor, margins, and lymph nodes to determine which to resect. I was a bit concerned about recovery from open surgery, but he convinced me it would be no worse than robotic.

He resected about 10 lymph nodes and found nothing there. Pathology ended up very poor: positive margin at the base, seminal vesicle invasion, and extracapsular extension. It was serious because it had already escaped the prostate. I was downgraded from stage pT1c to stage pT3b.

When the surgeon came in to talk to me about my prognosis, he was not happy and said, "You're going to be fighting this for the rest of your life." Turns out I was one of the 10% with a high-risk case. I asked him how long I had to live. He said I'd still be alive in 10 years and sent me a nomogram that scored each of my risk factors in terms of life expectancy. I hope he was right!

So obviously, I had ED after surgery. I had incontinence for a while too, but it was mild. I wore one pad a day for 13 weeks, but haven't had much of a problem since. I had no complications from surgery. My wife and I flew to Baltimore. She stayed in my recovery room. We flew back home three days later. The catheter and stitches were removed by my local urologist 10 days later. I was playing golf three weeks after the surgery. I've been unable to have any sex ever since. But subsequent radiation treatments are probably the main cause of my ED now. I've been fried!

Were you able to talk to your doctor about it?

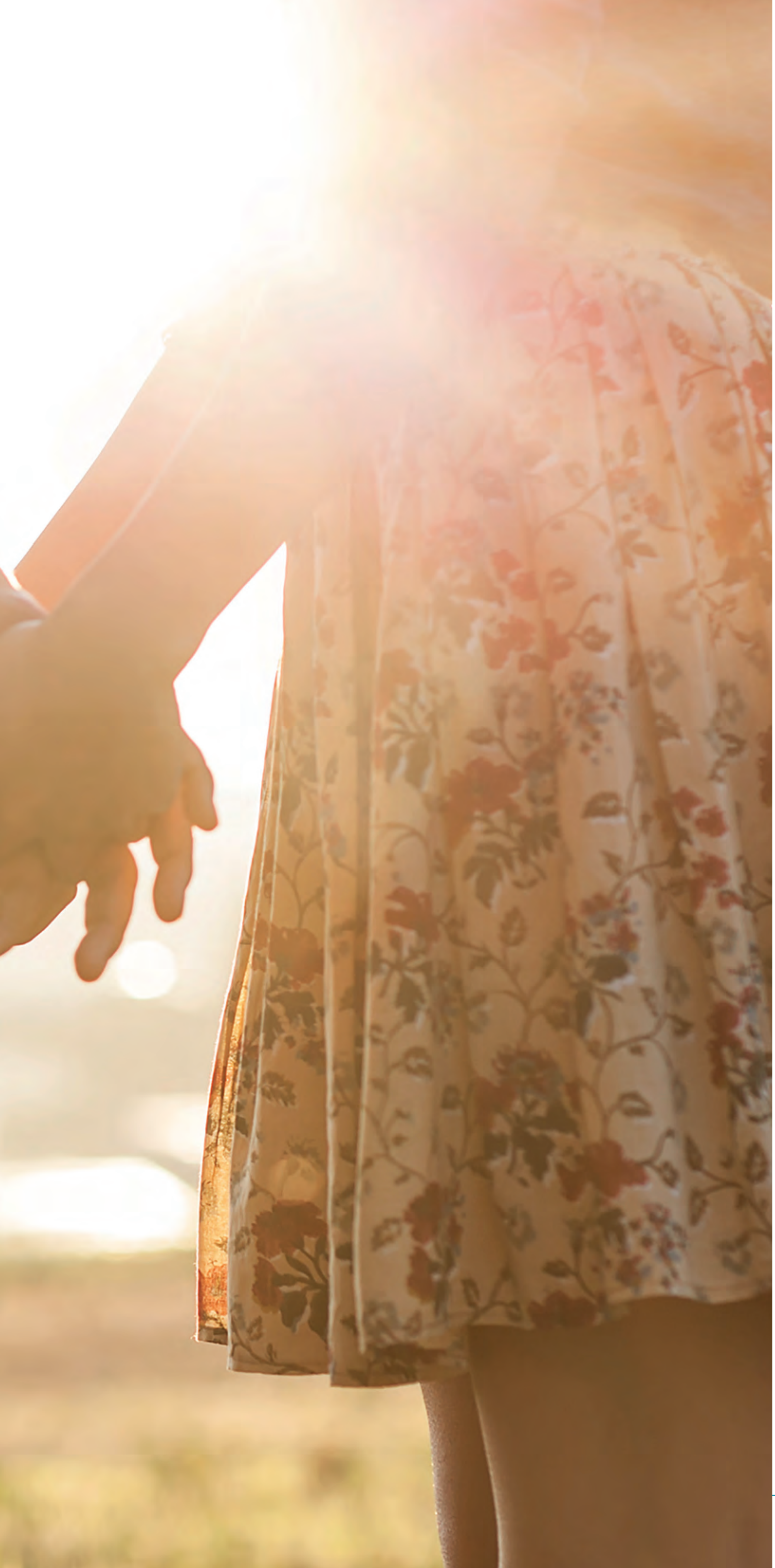
Steve A: Yes. He said you have to use it or lose it. Then I had recurrence (rising PSA) so I no longer conferred with my surgeon. Only six months after surgery, my PSA started going back up again. I needed hormone therapy and radiation after all! In mid-2014, I had 38 fractions of salvage radiation therapy (SRT). I was also on Lupron (leuprolide) for six months. That completely destroys your libido anyway. I didn't even have any desire for sex.

> *"At night, when you dream, you sometimes think about it and really miss it."*

Were you more worried about the recurrence than any ED?

Steve A: Absolutely. When you have Gleason 9 with my poor post-op pathology, survival—not sex—is all that matters.

I've had recurrence twice since SRT: in two pelvic lymph nodes in 2015 and in my right femur in 2017. In 2015, I went down to Florida to have 50 fractions of intensity-modulated radiation therapy (IMRT) to all my pelvic lymph nodes and was on Lupron (leuprolide), Casodex (bicalutamide), and Avodart (dutasteride) for 13 months. Just a month ago, after stopping hormonal therapy, they found a lesion on my upper right femur. I'm now back on hormonal therapy and had stereotactic body radiation therapy (SBRT) in three fractions locally to my femur. I'm also on Xgeva (denosumab) for bone mets.



So far, no cancer has been found in my prostate bed, lymph nodes, or other soft tissue or organs. In that sense, I guess I'm lucky.

I've completely forgotten about the whole issue of sex. At night, when you dream, you sometimes think about it and really miss it, but the reality is that my primary goal is to be healthy, happy, and live as long as I can. I don't need sex for that.

Did you ever seek treatment?

Steve A: I talked to my urologist. After surgery, I used the pump.

Did it work?

Steve A: It was marginally successful. I just wasn't too keen on it. I thought it was more of a pain than anything else.

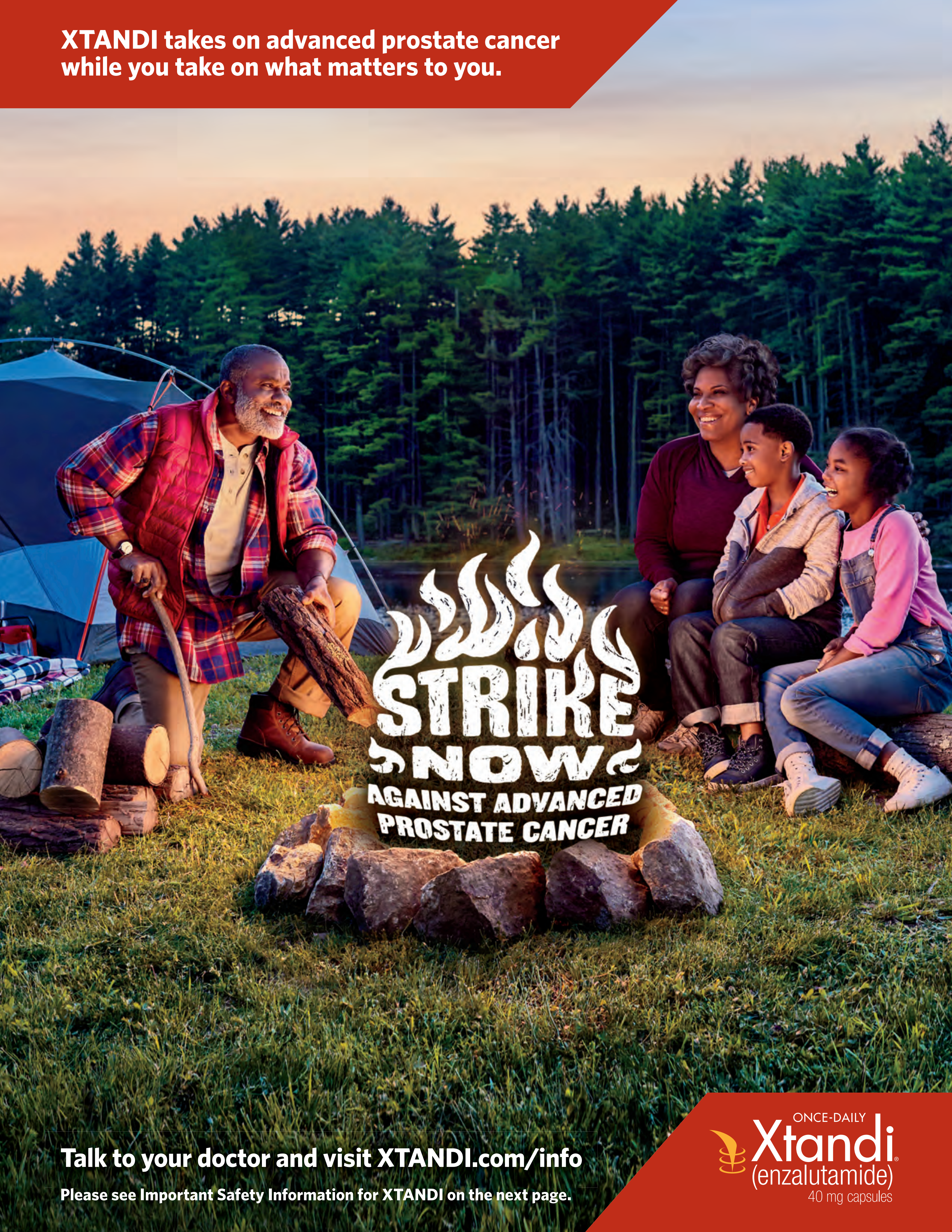
I didn't try injections. I tried daily Cialis (tadalafil). That didn't do anything. The urologist talked to me about having an implant.

I haven't really given that any thought. Now that I'm back on Lupron (leuprolide), I don't have the desire for anybody. I'm just totally oriented to quality of life and length of life at this point. Quality of life doesn't necessarily mean sex anymore.

Has it impacted your marriage at all?

Steve A: No. She couldn't care less about it. That's why I say, if you're young and your wife cares a lot about it, that's a big issue. I'm 73; she's 71. It's not a part of our life anymore. Pp¹

XTANDI takes on advanced prostate cancer while you take on what matters to you.



Talk to your doctor and visit XTANDI.com/info

Please see Important Safety Information for XTANDI on the next page.

ONCE-DAILY
Xtandi®
(enzalutamide)
40 mg capsules

ONCE-DAILY
Xtandi®
(enzalutamide)
40 mg capsules

Talk to your doctor and visit XTANDI.com/info

Who is XTANDI for? XTANDI is a prescription medicine used to treat men with prostate cancer that no longer responds to a medical or surgical treatment that lowers testosterone and that has spread to other parts of the body. (This is a type of advanced prostate cancer.)

Important Safety Information

Who should not take XTANDI?

XTANDI is not for use in women. Do not take XTANDI if you are pregnant or may become pregnant. XTANDI can harm your unborn baby. It is not known if XTANDI is safe and effective in children.

Before you take XTANDI, tell your healthcare provider if you:

- Have a history of seizures, brain injury, stroke or brain tumors.
- Have any other medical conditions.
- Have a partner who is pregnant or may become pregnant. Men who are sexually active with a pregnant woman must use a condom during and for 3 months after treatment with XTANDI. If your sexual partner may become pregnant, a condom and another form of birth control must be used during and for 3 months after treatment. Talk with your healthcare provider if you have questions about birth control. See "Who should not take XTANDI?"
- Take any other medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements. XTANDI may affect the way other medicines work, and other medicines may affect how XTANDI works. You should not start or stop any medicine before you talk with the healthcare provider that prescribed XTANDI.

How should I take XTANDI?

- XTANDI is four 40 mg capsules taken once daily.
- Take XTANDI exactly as your healthcare provider tells you.
- Take your prescribed dose of XTANDI one time a day, at the same time each day.
- Your healthcare provider may change your dose if needed.
- Do not change or stop taking your prescribed dose of XTANDI without talking with your healthcare provider first.
- XTANDI can be taken with or without food.
- Swallow XTANDI capsules whole. Do not chew, dissolve, or open the capsules.
- If you miss a dose of XTANDI, take your prescribed dose as soon as you remember that day. If you miss your daily dose, take your prescribed dose at your regular time the next day. Do not take more than your prescribed dose of XTANDI in one day.
- If you take too much XTANDI, call your healthcare provider or go to the nearest emergency room right away. You may have an increased risk of seizure if you take too much XTANDI.

What are the possible side effects of XTANDI?

XTANDI may cause serious side effects including:

- **Seizure.** If you take XTANDI you may be at risk of having a seizure. You should avoid activities where a sudden loss of consciousness could cause serious harm to yourself or others. Tell your healthcare provider right away if you have loss of consciousness or seizure. Your healthcare provider will stop XTANDI if you have a seizure during treatment.
- **Posterior Reversible Encephalopathy Syndrome (PRES).** If you take XTANDI you may be at risk of developing a condition involving the brain called PRES. Tell your healthcare provider right away if you have a seizure or quickly worsening symptoms such as headache, decreased alertness, confusion, reduced eyesight, blurred vision or other visual problems. Your healthcare provider will do a test to check for PRES. Your healthcare provider will stop XTANDI if you develop PRES.

The most common side effects of XTANDI include weakness or feeling more tired than usual, back pain, decreased appetite, constipation, joint pain, diarrhea, hot flashes, upper respiratory tract infection, swelling in your hands, arms, legs, or feet, shortness of breath, muscle and bone pain, weight loss, headache, high blood pressure, dizziness, and a feeling that you or things around you are moving or spinning (vertigo).

XTANDI may cause infections, falls and injuries from falls. Tell your healthcare provider if you have signs or symptoms of an infection or if you fall.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of XTANDI. For more information, ask your healthcare provider or pharmacist.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see the Brief Summary on the following page and the Full Prescribing Information on XTANDI.com.

QUESTIONS ABOUT XTANDI?

Call 1-855-8XTANDI (1-855-898-2634)

astellas MEDIVATION

PATIENT INFORMATION
XTANDI® (ex TAN dee)
(enzalutamide)
capsules

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Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. XTANDI may affect the way other medicines work, and other medicines may affect how XTANDI works.

You should not start or stop any medicine before you talk with the healthcare provider that prescribed XTANDI.

Know the medicines you take. Keep a list of them with you to show your healthcare provider and pharmacist when you get a new medicine.

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These are not all the possible side effects of XTANDI. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store XTANDI?

- Store XTANDI between 68°F to 77°F (20°C to 25°C).
- Keep XTANDI capsules dry and in a tightly closed container.

Keep XTANDI and all medicines out of the reach of children.

General information about XTANDI.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use XTANDI for a condition for which it was not prescribed. Do not give XTANDI to other people, even if they have the same symptoms that you have. It may harm them.

This Patient Information leaflet summarizes the most important information about XTANDI. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about XTANDI that is written for health professionals.

For more information go to www.Xtandi.com or call 1-800-727-7003.

What are the ingredients in XTANDI?

Active ingredient: enzalutamide

Inactive ingredients: caprylocaproyl polyoxylglycerides, butylated hydroxyanisole, butylated hydroxytoluene, gelatin, sorbitol sorbitan solution, glycerin, purified water, titanium dioxide, black iron oxide

Marketed by:

Astellas Pharma US, Inc., Northbrook, IL 60062
Medivation Inc., San Francisco, CA 94105
15I074-XTA-BRFS

076-1977-PM

This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: October 2016

Count Me In to Get Tested

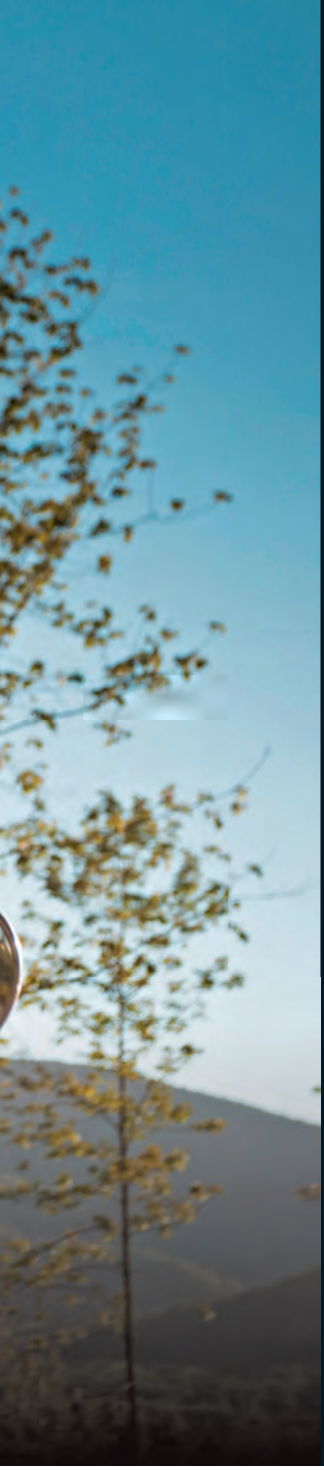
1 in 6 African-American men will get prostate cancer in his lifetime.

ZERO
THE END OF PROSTATE CANCER

Know Your Risk:

zerocancer.org/psatest

MAP YOUR PATH FORWARD WITH ADVANCED PROSTATE CANCER



MyProstateCancerRoadmap.com is an online resource that can help patients and caregivers navigate through advanced prostate cancer topics such as:

UNDERSTANDING YOUR ROAD

You already know about prostate cancer. What is advanced prostate cancer?

CHOOSING YOUR ROAD

Explore your treatment options so you can partner with your doctor to decide what is best for you.

FINDING YOUR WAY

Learn how to adapt to changing relationships and begin to navigate other changes in your life.

VIEWPOINTS FROM THE ROAD

Educate and empower yourself with educational articles and real stories about people facing prostate cancer.

Visit www.MyProstateCancerRoadmap.com/start to stay in the know and subscribe to our newsletter.

janssen Oncology

274 Redwood Shores, #739
Redwood City, CA 94065
(800) 975 6238
info@prostatepedia.net
www.prostatepedia.net

Coming Up!

October:
Imaging

November:
Focal Therapy

December:
Diet and Exercise