Prostatepedia[1]

[1]expert insight + advice

Diet + Lifestyle

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In this issue....

Well-designed randomized controlled clinical trials are the best tool we have for determining these optimal treatment for diseases. Unfortunately, we don't yet have trials like for the impact of diet and exercise on prostate cancer, but we do have them for exercise and diet's impact on general health and cardiovascular disease.

In the famous PREDIMED trial, 7,447 subjects who were at high risk for cardiovascular disease but who did not have it were randomized into three groups. One group went on a low fat diet. The other two groups went on a Mediterranean diet: one with olive oil and one with with nuts. The trial was supposed to run for 6 years, but stopped at 4.8 years because the two Mediterranean diet groups already showed such a significant reduction in myocardial infarction, stroke, and cardiovascular death. The Mediterranean diet also reduced the risk of peripheral artery disease, atrial fibrillation, and invasive breast cancer. There was no information about prostate cancer incidence in any of the three groups.

This month, Rob Newton discusses his Movember-funded GAP4 trial testing exercise's impact on progression-free survival in advanced prostate cancer patients. This randomized controlled trial looks at 890 patients. This trial is exciting: it breaks important new ground in adequately testing lifestyle changes' impact on key endpoints in prostate cancer treatment.

Randomized controlled trial design requires an assessment of the likely impact of the experimental treatment on the outcome of the trial. If the likely benefit is 10%, many more subjects are required than if the benefit is 50%. This month, Drs. David Levy and Stephen Freedland outline trials that are so designed that they might allow for subsequent randomized trials.

Note that the nonprofit Movember financially supports the GAP4 trial. Currently, government funding for such trials is painfully inadequate.

The United States was for many years a major source of funding for cancer clinical trials through the National Institute of Health (NIH). But the current political climate in the United States has become definitely anti-science.

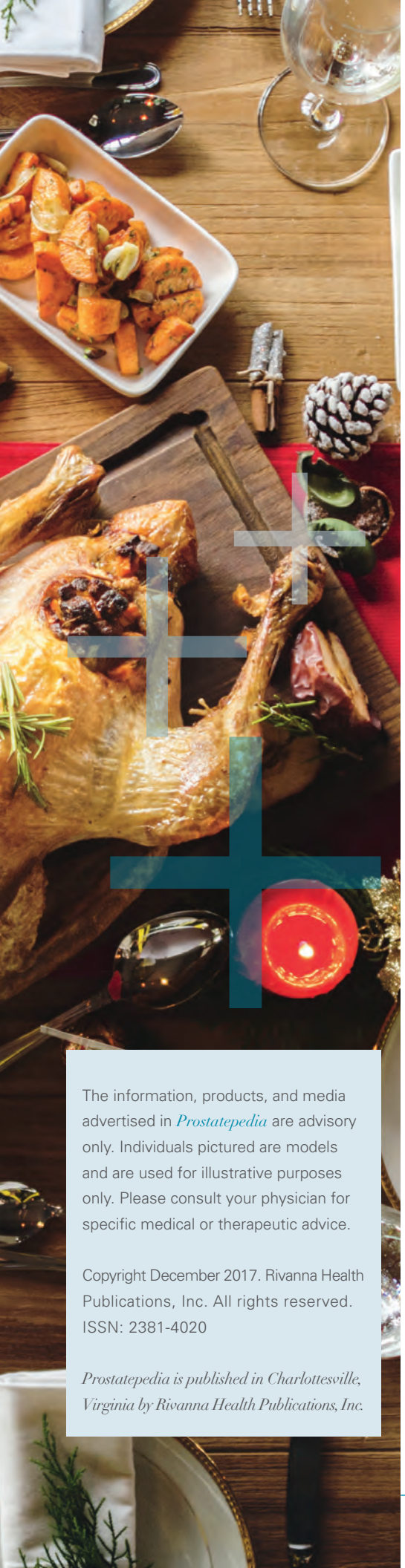
As a result, an increasing proportion of clinical trials are funded by the pharmaceutical industry as a path to FDA-approval. This has had a positive impact in that we now have a growing list of drugs approved for prostate cancer.

However, pharmaceutical companies have a responsibility to their shareholders to maximize profit. There is no reason for these firms to spend the large sums needed to test the impact of something like diet and exercise. This leaves philanthropy as the only source of support for these large randomized trials. We all need to keep this in mind.

We do now know that your general health and survival benefit from exercise, a prudent diet, maintaining a healthy weight, not smoking, and stress reduction. Existing data support the importance of diet and lifestyle changes in prostate cancer management, but we lack proof provided by high quality randomized trials.

The bottom line is that altering your diet and lifestyle can definitely improve your general health, but may or may not help control your prostate cancer.

Charles E. Myers, Jr., MD



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Guest Commentary
Mark A. Moyad, MD

Dr. Mark A. Moyad, the Jenkins/ Pokempner Director of Complementary and Alternative Medicine in the Department of Urology at the University of Michigan Medical Center, has published over 150 medical journal articles and 12 books, including *The Supplement Handbook: A Trusted Expert's Guide to What Works & What's Worthless For More Than 100 Conditions.*

Dr. Moyad frames this month's conversations on diet and lifestyle for prostate cancer.

First, I'd like to say that I find it incredibly wonderful that we're now talking about diet and exercise for prostate cancer. In the old days, it was unusual to even talk about it, but now you stick out if your institution doesn't cover diet and exercise. What a wonderful and diverse collection of experts in this issue—such a pleasure to read and learn from some of the best in this field now and in the future.

I always say that heart-healthy is prostate-healthy. Heart-healthy is all healthy. Reducing your cardiac risk as close to zero as possible is the smartest thing you can do as a prostate patient. That's the top of the pyramid when it comes to diet and exercise for prostate cancer. Maintaining a health weight is the first step in becoming heart-healthy.

Every few years, we realize that more and more cancers are associated with obesity. Now we know that obesity is associated with up to at least 13 types of cancer, not to mention the ongoing, ravaging obesity epidemic.

"Heart-healthy is prostate-healthy."

That said, I don't believe that we have neither the power nor the right to tell people what diet to follow. It doesn't matter if you want to go vegan, high fat, or low carb: there's nothing more important than maintaining a healthy weight and having the heart-healthy numbers to support that healthy weight loss.

The new elephant in the room is alcohol. Alcohol often becomes self-medication in elderly people, but it is one of the largest sabotages to a heart-healthy and prostate-healthy lifestyle.

First, the caloric content of alcohol is high: seven calories per gram. Second, the data clearly show a relationship between excessive insulin production and excessive alcohol exposure. This makes it so easy to gain weight when you drink alcohol. Some of the greatest weight loss I've seen in the past 12-months has come when a patient eliminates alcohol. There is also a correlation between alcohol and potentially aggressive prostate cancer. So alcohol makes you gain weight, encourages prostate tumor growth, encourages cardiac risk, and encourages risk of other cancers.

Exercise is important, but we have to be careful as we age. We become very delicate machines. That's why I agree with Dr. Rob Newton that finding an exercise physiologist is a great idea. We have to be smart about exercise: if you don't preserve yourself, you won't be able

"There's nothing more important than maintaining a healthy weight."

"The new elephant in the room is alcohol."

to stay active and get the benefits of exercise for your prostate cancer.

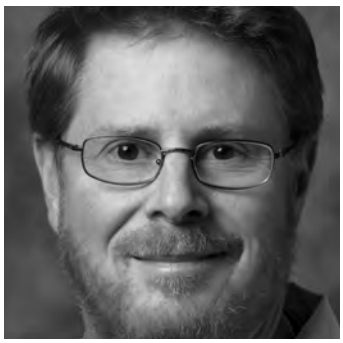
I'll also add that the biggest benefit to exercise is a mental health benefit. I love the cardio/metabolic effects of exercise in men on hormonal therapy, but I don't give a damn if exercise ends up being physically beneficial to cancer patients. What excites me is the impact on the quality of life of a man. Patients are completely different on hormonal therapy when they are regular exercisers. Mentally, they're still in the game. They're beautiful to be around.

"We have to be smart about exercise."

Socialized exercise also gives you a boost. When you work out in your basement, you're not getting all the benefits of exercise. When you have a trainer, go to a gym, or work out with support group members, you get an added mental health boost. You can become isolated in exercise.

Finally, I'd like to add that we lose credibility if we don't follow probability with supplements. The results from the VITAL trial, which looks at vitamin D and cancer in about 26,000 people, will be published next year. I'm going to wait for those results before I recommend higher vitamin D intakes to patients. Pp

Stephen Freedland, MD
Carbohydrates + Prostate Cancer



Dr. Stephen Freedland is a urologist at Cedars-Sinai in Los Angeles, California, and the Director of the Center for Integrated Research in Cancer and Lifestyle, Co-Director of the Cancer Genetics and Prevention Program and Associate Director for Faculty Development at the Samuel Oschin Comprehensive Cancer Institute.

Dr. Freedland treats the whole patient and not just a man's prostate cancer.

Prostatepedia spoke with him about diet and prostate cancer.

Why did you become a doctor?

Dr. Stephen Freedland: Like any good Jewish boy growing up, you do what your mother tells you to. She assigned me to become a doctor and my brother a lawyer. That's the way life turned out.

I was interested in science. My dad was a science researcher. He was very passionate about medical research, but he did nutrition research. I wanted to get as far away from nutrition as I possibly could, so I chose to study cancer. And see how that turned out!

Full circle.

Dr. Freedland: Exactly. I was one of those people who went to medical school to become a better researcher. I very much enjoy interacting with patients, and I still have a passion for that, but I think in my core, my passion is for research, for making a difference on a large scale and answering big questions. I love answering questions because every good question leads to five new ones. It's a never-ending cycle. I like that.

Well, one could argue that, at its essence, scientific research is a dialog.

Dr. Freedland: Yes. For me, it's about the process. We all want to make life better for our patients, but you have to enjoy the process of trial and error, discovery and failure. That brass ring we all seek, the thing that could make a difference: it's important to have that as your overriding search. But that can't motivate you on a day-to-day basis. You need to enjoy the process itself.

I love doing research, asking questions, having a dialog with science, with nature, and with my colleagues. Trying to understand what is the truth, what is the way the body actually works, and how we can make it better. It's fun.

What do we know about the role that diet plays in developing prostate cancer?

Dr. Freedland: The challenge in answering that question lies in another question. How strong must proof be before we accept that we know something? Do we have level-one randomized control trial data showing that if you eat this way and I eat another way, that your risk of prostate cancer is different than mine? No. We don't have data to show that.

Everything we know about prostate cancer and diet is really what we *think* we know. We don't have level-one evidence that eating differently will do anything in regard to prostate cancer.

We can think we know something and then later be proved wrong.

Dr. Freedland: Correct. I think a lot of what we *think* we know is wrong. In terms of nutrition, getting prostate cancer is a little less interesting because the number one risk factor for getting prostate cancer is just living a long time. If men live long enough, almost every one will get prostate cancer. In a way, eating a healthy diet and *not* dying of heart disease puts you at higher risk of getting prostate cancer in your lifetime because you've lived a long time.

What is relatively unequivocal is: if you are obese, you are more likely to get an aggressive form of prostate cancer and you're more likely to die from that cancer. This has been shown in study after study. Can you take an obese 60-year-old with prostate cancer, get him to lose weight, and ensure that the adverse health effects of those 60 years of obesity are going to go away? Probably not. But we might be able to mitigate his risk of cancer if he loses weight. In animal models, most tumors grow more slowly when the animal eats less and loses weight.

Isn't obesity linked to a variety of different cancers?

Dr. Freedland: Yes, obesity is linked to many different cancers. The link with prostate cancer is probably weaker than with other cancers. There is stronger data linking obesity with post-menopausal breast, colon, endometrial, kidney, and many other cancers.

What do you tell your patients about prostate cancer and diet?

Dr. Freedland: Given the link between obesity and prostate cancer, I focus on getting my patients to lose weight. The easiest way to lose weight is to cut out all the extra sugar in your diet: cookies, cake, candy, all of that. A meta-analysis published in the *Journal of the American Medical Association* of all the popular diets found that the best diet for weight loss was a low-carb diet. That was *the* best diet. They're all decent, but low carb is the best.

Is that true primarily for American patients or for everyone?

Dr. Freedland: I think it's true for everyone. A recent study published in the *Lancet* followed over 135,000 people in 18 different countries on over five continents. They found that the more carbs you eat, the more likely you are to die earlier. Eat fewer carbs, live longer. Fewer carbs and more fat make you live longer.

This is a landmark study that supports what an increasingly loud minority of us has been saying. Fat is not the problem. Carbs are the problem.

I focus my patients on their carb intake. Let's focus on the carbohydrates in the diet and see which of those we can get rid of. If you're having whole-grain oatmeal for breakfast, maybe that can stay. But most people are having pancakes with butter and syrup. We can get rid of that.

While you're giving up the sugars, cakes, and candies, we focus on what we can put in their place: fruits and vegetables. Yes, fruits have sugar, but it's a natural source. As long as patients aren't juicing, natural fruits contain a lot of fiber that will slow the absorption of sugar in the intestine. Nuts, beans, and those types of things are also good replacements.

I worry that because we've been advocating that people cut out fat and tell them to eat lots of fruits and vegetables, people are going to go to the store, buy fat-free ice cream and say, "I had a salad with my dinner so I can eat all the ice cream I want now. I'm being healthy!"

Remember the old food pyramid from the 1980s? Carbs were at the bottom of the pyramid, the largest food group.

Dr. Freedland: Right. Lots of bread. Our entire way of thinking has been very carb-centric. Let's eat carbs and avoid fat. And the result has been that the obesity rates have almost tripled in the United States in the last 30 years.

What do you say to people who argue that you should have carbs in balance with fat and protein?

Dr. Freedland: Your body doesn't need carbs. There are animals and people raised without eating a single carb. You can't survive without eating fat. You can't survive without eating protein. You *can* survive without eating carbs.

What protein sources do you recommend?

Dr. Freedland: People get in this mindset that red meat is bad and fish is good. Fish (*we think*) is good because it contains fish oil, an omega-3 fatty acid. But I found an article that looked at tilapia. It turns out that tilapia doesn't have much fish oil. If you want fish oil, you know what are better sources than tilapia? Doughnuts and bacon.

Bacon?!

Dr. Freedland: Doughnuts and bacon have more fish oil than tilapia per gram.

I guess not all fish are created equal.

Dr. Freedland: Correct. And not all meat is created equal. A nice grass-fed steak probably has as much omega-3 fatty acid as many kinds of fish.

The worst protein for prostate cancer is charred meat. Those black lines you get on your steak in charring form heterocyclic amines that can cause cancer. This is true mostly for meat because that's what you tend to char, but it's also true for chicken and potentially fish.

What about cholesterol?

Dr. Freedland: With prostate cancer, it's important to watch cholesterol. Even though people on low-carb diets eat cholesterol, their levels tend not to go through the roof. Not eating sugar actually controls cholesterol.

This does not mean that you can consume cholesterol unbridled if you don't eat sugar. Plant- and fish-based diets are healthier for reducing cholesterol. But the best way to control cholesterol is to lose weight.

There has been all this talk about statins. Statins lower serum cholesterol by about 25%. But if you had a hormonal therapy drug for prostate cancer that lowered testosterone by 25%, would it do a lot for the tumor?

Probably not much.

Dr. Freedland: Right. The hormonal therapy that we use lowers testosterone by 95% to be effective.

Still, statins are good in terms of targeting cholesterol. Some tumors will be sensitive to statins and some will not. And there are risks, such as diabetes.

I don't automatically tell men to go on statins simply for their prostate cancer because the data aren't there yet. But I do encourage men to look into using statins with their primary care doctor.

Are there any supplements that prevent or delay prostate cancer progression? Or supplements prostate cancer patients should avoid?

Dr. Freedland: All of them. There are no data to show that your general multivitamin supplement does anything beneficial in terms of prostate cancer. No data. Period.

If you look at general multivitamins, the data suggest that they have no effect on prostate cancer risk.

In fact, some studies show that, particularly if you take more than one multivitamin per day, this will increase the risk of aggressive prostate cancer.

Why would it increase the risk?

Dr. Freedland: Your tumor cells grow faster than normal cells. They need the same vitamins to survive that your regular cells do. Once you provide for your body's needs, anything else is just going to help the tumor. If you take too high of a dose of some of these vitamins, say antioxidants, they become pro-oxidant.

The vitamins we take are either water-soluble, which means they come out in urine—some say Americans have the most expensive pee in the world!—or they're fat-soluble, which means you don't absorb them unless you eat fat.

Vitamins D and E are fat-soluble. Vitamin D is quite beneficial, but you need to consume fat to absorb it. Skimmed milk that's fortified with Vitamin D won't help you absorb any of it.

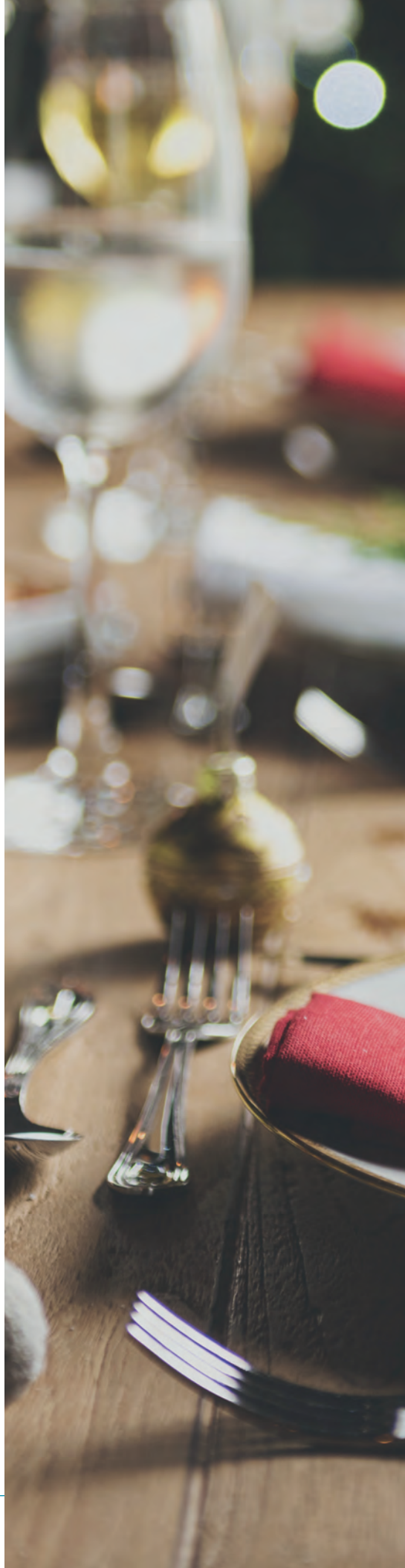
Would you be better off drinking whole milk?

Dr. Freedland: If you drink whole milk with Vitamin D, then you are actually going to absorb the Vitamin D.

Why do so many cancer patients flock to supplements if they're not beneficial?

Dr. Freedland: Patients want an easy answer and supplements seem to provide one. When the question is how to beat cancer, simple answers are typically not the right answers.

Treating cancer needs a wholesale lifestyle change: lose weight and exercise. While it's underexplored, stress management is likely very important for cancer too. Low stress helps boost the immune system because you're in the right state of mind. Social support is also beneficial. There are actually data showing that,



for cancer patients, being married is as effective in fighting cancer as getting chemotherapy.

Are you saying social isolation can be dangerous?

Dr. Freedland: Yes. People who are married have a survival benefit on a par with chemotherapy. You can't just go to McDonald's, avoid exercise, eat low-fat ice cream, and then take a little pill and expect your cancer to go away. Life doesn't work that way.

What do you tell your patients about exercise?

Dr. Freedland: There are more data to support high-intensity interval training. You need to get your heart rate up. A gentle walk in the evening for 30 minutes probably won't do much.

If you can hold a conversation during exercise, it's not vigorous. You've got to get your heart rate up. You've got to be a little short of breath, push yourself.

What about stress relief?

Dr. Freedland: I don't talk to my patients as much as I should about stress relief. They're all going through stressful times. But that's where exercise can help. Meditation and yoga-type activities help with stress management too.

Your medical team will fight your cancer a few times a year with hormones, radiation, surgery, chemo, or whichever treatment they prescribe.

But *you* can fight your cancer several times a day. *You* can choose to have the salad, fruit, and water or the hamburger, fries, and a coke. It's your choice. You know the consequences. By making the right choices, you can fight your cancer at least three times a day.

You have some ownership over your disease. There is something you can do that we know will have an impact.

Dr. Freedland: Correct. At Cedars-Sinai, we're running a low-carb clinical trial. A patient lost 25 pounds in six months. He was very happy, and he said that while he knew he was helping our research, he wanted to thank us for making a huge difference in his life.

Is this a low-carb prostate cancer clinical trial?

Dr. Freedland: This is a randomized low-carb versus control trial for men with recurrent prostate cancer. We hope that we can slow down the rate of rising PSA by getting people to lose weight.

Are you still recruiting patients for this?

Dr. Freedland: Yes. We still have another 20 or so to go.

If someone reading this is interested, should he contact you directly?

Dr. Freedland: Yes, he can contact me directly.

To join this trial, does someone need to be in the Los Angeles area or can they participate remotely?

Dr. Freedland: The dietician parts can all be done by phone, but we would need them to come out for a few diet visits. We have two sites for diet visits: one in North Carolina and one in Los Angeles.

Is there anything else patients should know about diet?

Dr. Freedland: I always go back to the root of the word *diet*. It's from the Greek for way of life. To change diet, you must change your way of life. You can't go on a short-term crash diet hoping for miracles. It's truly a wholesale lifestyle change. Pp'

Lorelei Mucci, ScD
Diet + Aggressive Prostate Cancer

Dr. Lorelei Mucci specializes in prostate cancer epidemiology and her research focuses on cancer risk and mortality in populations across the globe.

Prostatepedia spoke with her about epidemiology's take on the link between diet, lifestyle, and prostate cancer.

How did you become involved in prostate cancer research?

Dr. Lorelei Mucci: My background is in public health, specifically an area of public health known as epidemiology in which we study the causes of a disease and think about its prevention.

I have always been interested in cancer epidemiology and came about my research in prostate cancer a little bit serendipitously. I had an opportunity to work in prostate cancer. At the time, it wasn't a disease that I was familiar with. I didn't have any family members who had had prostate cancer.

But now I have a 13-year-old son. I want him to grow up in a world where we know the causes of prostate cancer and how to prevent it. It was a little bit of a serendipitous route to get here, but now I couldn't imagine studying anything else.

What do we know about diet's impact on prostate cancer?

Dr. Mucci: Epidemiology studies of diet, lifestyle, and prostate cancer have really evolved a lot over time because of PSA screening and our understanding of the disease's biologic heterogeneity. With PSA screening, we are both diagnosing more men with prostate cancer and diagnosing more men with a more slow-growing form of prostate cancer.

What we've learned is that the relationship between the majority of dietary and lifestyle factors seems to be more associated with the risk of *aggressive* prostate cancer. We're starting to see that certain factors are associated with either worse or better survival. It has taken us a while as a field to realize that the relationship of risk factors varies for aggressive versus nonaggressive cancer.

It has also taken us a while to understand the role that PSA screening has played in our studies.

The other consideration with prostate cancer is that it could be many years, if not decades, after diagnosis before a man experiences metastatic disease. Thus, we need long-term follow-up studies to understand the impact of lifestyle factors.

In terms of diet, I don't think there is yet strong evidence for any particular lifestyle factor to say it is causal. There are some probable factors and some new factors we're starting to think about.

There is good data on the role of an antioxidant known as lycopene. Lycopene is commonly found in high levels in cooked tomato products such as tomato sauce, but also in things like salsa. What is interesting about lycopene is that it accumulates at high levels in the prostate. A number of epidemiology studies have shown lycopene to be associated with a much lower risk of aggressive prostate cancer. There was a small, randomized study in which men were given capsules of cooked tomato products. The study showed lycopene could make changes in the prostate tumor tissue. So there is probable evidence for cooked tomato products and lycopene in prostate cancer prevention.

We are also starting to see evidence emerge around regular consumption of coffee, either decaffeinated or caffeinated. Coffee is one of the strongest antioxidants available, even stronger than berries. Coffee is interesting for a number of cancers. It seems to be associated with a lower risk of liver cancer, potentially colorectal cancer, and diabetes. In randomized

studies, we also see that coffee helps regulate insulin levels after a meal. Insulin may be very important for advanced prostate cancer.

Again, I wouldn't say this evidence is convincing yet, but we're starting to see many studies suggesting the benefit of regular coffee consumption.

There is also emerging evidence about fish consumption. In particular, fatty fish like tuna or salmon are associated with a lower risk of aggressive prostate cancer.

On the other side, there is now data suggesting high calcium intake at the levels you'd get more from many supplements may be associated with an increased risk of a more aggressive form of prostate cancer.

Finally, the association between obesity and aggressive prostate cancer is strong. Any dietary factors, or dietary patterns, that contribute to obesity may be associated with more aggressive prostate cancer and with worse outcomes for patients.

Isn't obesity associated with a variety of different types of cancers?

Dr. Mucci: Yes, several cancers: post-menopausal breast cancer, colorectal cancer, pancreatic cancer, and kidney cancer. There is really good evidence that obesity increases the risk for a number of cancers.

What about high-fat versus low-fat diets?

Dr. Mucci: The data around fat is complicated. We need to think about the type of dietary fat: there is good fat versus the fats that you get from red meat, for example.

I would say that the evidence about fat that is specific to prostate cancer is weak. We know that red meat or specific types of animal protein can lead to obesity. Cardiovascular disease is one of the leading causes of death for men with prostate cancer. Avoiding animal fat and making sure you consume a lot of vegetable fat is the way to think about it.

Let's talk a little bit more about red meat, specifically grilled or charred red meat. Is eating grilled red meat associated with a higher risk of aggressive prostate cancer?

Dr. Mucci: The data specific for prostate cancer is pretty weak. There have been some animal studies that have looked at this association, but the data for human studies is weak. But because eating red meat is associated with an increased risk of obesity, limiting the amount of grilled or cooked meat you eat is probably a good thing in general.

There are a number of dietary factors that don't seem to be independently associated with aggressive prostate cancer. The ones that I've mentioned are. It has been challenging to study in humans what is happening with grilled meats, so I would label the evidence for aggressive prostate cancer as weak. But again, it's a good thing to avoid regularly eating any sort of grilled or cooked meat for a number of other reasons.

What about the role of cholesterol? And statins?

Dr. Mucci: This is a very interesting and important area of research. There have been a number of well-conducted epidemiological studies showing that high cholesterol levels are associated with a higher risk of more aggressive prostate cancer.

Cholesterol synthesis and biosynthesis pathways seem to be altered in men with more aggressive forms of prostate cancer. Cholesterol can be used to synthesize androgens; they're the backbone for androgen synthesis.

The epidemiological evidence for the association between statins and the decreased risk of advanced prostate cancer is quite good. The question is: Is this a true association? Is the mechanism specifically through cholesterol-lowering? There seems to be some evidence that the lowered risk of aggressive prostate cancer may act through regulating cholesterol levels, but some of statins' effects on aggressive prostate cancer may be independent of cholesterol.

I do think the data are fairly strong around statins. Again, whether that is totally through cholesterol-lowering or other specific pathways is not clear.

(See http://ascopubs.org/doi/pdf/10.1200/JCO.2017.74.7915 to read more of Dr. Mucci's thoughts on statins and prostate cancer.)

Do statins impact the effectiveness of drugs like Zytiga (abiraterone)?

Dr. Mucci: I am a co-author on a study looking at the effect of statins on androgen deprivation therapy. One of the pathways that statins use to get into prostate cells is the same set of pathways that androgens use.

One thought is that statins may help these other antiandrogen medications by blocking the cellular pathways androgens use. There is both interesting human and experimental data suggesting that statins may benefit these antiandrogen therapies.

This is a very interesting area of research. It might be early on in terms of evidence, but I do think it will be really important to look at how things like statins—and potentially other things like aspirin—are associated with a lower risk of aggressive prostate

cancer. It may be really important to think about the possible impact on treatment that other medications that men may be taking at the same time as medications for prostate cancer could have. We may be able to repurpose drugs we hadn't really thought about before for prostate cancer either on their own or in combination with other therapies.

Should we prescribe statins for all men with prostate cancer? I don't know that the evidence is good enough for us to recommend that, but we do feel that statins are probably very safe for men who have prostate cancer. If a man with prostate cancer has high cholesterol levels and a high heart disease risk, I think going on a statin is safe. I think it's premature to suggest that we put all men on statins, though.

Do we have long-term data on statin use from the cardiovascular community?

Dr. Mucci: Looking at secondary outcomes like prostate cancer?

Yes.

Dr. Mucci: That's a great question. A lot of the cardiovascular studies have been small, but if there's enough follow-up, and if you pool all the studies together, that may be enough. I would be surprised if someone hasn't started looking at that.

We've been talking about diet's link with the development of aggressive prostate cancer, but what about diet for men who already have prostate cancer?

Dr. Mucci: Our recommendations are similar. In general, things like lycopene and coffee, antioxidant dietary factors, and fish have been shown in patients to improve outcomes after a prostate cancer diagnosis.

Those factors may just be healthy for cardiovascular health. Again, because most men are at a greater risk for cardiovascular events than prostate cancer, dietary patterns thought to benefit cardiovascular health would help in overall survival.

There are many dietary patterns that have been suggested to be beneficial. There is a lot of interesting data around the Mediterranean diet pattern, which includes eating a lot of fruits, vegetables, fish, and legumes and minimizing red meat intake.

Olive oil is at the core of the Mediterranean diet. Olive oil has been shown to be one of the good fats.

There was a large Spanish trial called PREDIMED in which they randomized individuals to the Mediterranean diet and found not only a benefit for cardiovascular health, but also a much lower risk of breast cancer. I'll be really interested to see when they publish what the outcomes are for prostate cancer.

Again, obesity is associated with increased mortality in men with prostate cancer. So eating a Mediterranean diet and generally not consuming too much food are good ideas. Keeping a healthy diet after a cancer diagnosis is really important.

What about supplements?

Dr. Mucci: Supplements are a really interesting issue. Some concerns are starting to emerge. One study looked at high levels of selenium supplementation and prostate cancer death. In general, there is probably not much of a benefit for taking a multivitamin. Most nutritional experts believe that it's much better to get a healthy diet through eating rather than through supplements.

The only supplement to take would be vitamin D. The evidence for vitamin D and prostate cancer is intriguing.

Vitamin D levels seem to be really important for a number of health factors, including bone health, which we know is an issue for men with prostate cancer because of the therapies they take and because they are getting older. Vitamin D also seems to be important for immune status.

There are some hints that high vitamin D levels may benefit men with prostate cancer. I think the evidence specific to prostate cancer mortality is still too early but because of all the other benefits of vitamin D, supplementation seems reasonable. It's hard to get vitamin D in your diet: we only get vitamin D from the sun in the summer, so most people in the United States are vitamin D deficient. Something like 75% of men are vitamin D deficient.

That high?

Dr. Mucci: Yes. And women are deficient as well. We just don't get enough vitamin D from our diets. Vitamin D is made through the sun, but that only lasts a month or two and then your blood levels start to go down.

What about lycopene supplements versus lycopene from cooked tomatoes? Or omega-3 fatty acid supplements versus fish? Is it better to get all those nutrients through food because there's something inherently unhealthy about the process of creating the supplement? Or because the supplement industry is unregulated and we really don't know what's in a given pill?

Dr. Mucci: I'm not sure. Different researchers would argue different things. I wonder whether it's not just the omega-3 fatty acids, but also other things, in fish that work in concert to be helpful. When you isolate a specific compound like omega-3 fatty acid, you lose the benefit of all the other things in the fish. Some scientists will say it's this and some will say it's that. But we probably just don't know. Pp'

Rob Newton
Exercise Prescriptions + Prostate Cancer

Professor Rob Newton is the Associate Dean of Medical and Exercise Sciences and the Co-Director of the Exercise Medicine Research Institute, School of Medical and Health Sciences at Edith Cowan University in Perth, Australia.

Prostatepedia spoke to Dr. Newton about his exercise recommendations for men with prostate cancer.

What do you find most rewarding about working with cancer patients?

Dr. Rob Newton: I've worked with a lot of different patient populations and people with cancer are probably the most motivated to make lifestyle changes or any change they think would help them survive. It's very rewarding in that way because they're really willing to put in the work to improve their quality and quantity of life. It's very real for them: they have their mortality staring them in the face.

I've done a lot of work in the past with people who are overweight, obese, and have type 2 diabetes. They don't feel that unwell, and because they don't feel that they're at risk of dying, there's just not the same motivation to make changes. Someone with cancer is very different. If their oncologist presents evidence that exercise will definitely improve their quality of life, will definitely reduce treatment side effects, and will likely increase their chances of surviving this thing, they're highly motivated to change. By the time they come to us, it's quite a joy because it's like working with an enthusiastic young athlete who wants to get into the NBA. They're there to work. They've got a goal in mind and they're going for it.

Can you tell us about your current research projects?

Dr. Newton: We've got about 12 trials currently running in a range of cancers. There are two large projects.

The first is the Movember Gap4 Project. This is an advanced, randomized controlled international trial with 25 clinical sites around the world. We are recruiting 890 men with advanced metastatic, castrate-resistant prostate cancer. These men are palliative; there is no cure for them now. Their cancers are managed by a range of drugs—in particular, newer super antiandrogens Xtandi (enzalutamide) and Zytiga (abiraterone).

The most exciting aspect of this study is that the primary outcome is progression-free survival. This will be the first exercise trial in prostate cancer where the primary outcome is to see if a targeted exercise program will extend life. There is only one other study in the world that has ever been conducted along these lines, and it was in colon cancer. That is an ongoing study; the primary outcome was survival.

The Gap4 Project is quite exciting because if we can demonstrate that exercise helps these patients to live longer, then that will drive a shift in prostate cancer management. The management of all cancers, really. Exercise will most likely become a required part of patient care. A high-quality exercise prescription will be as much a part of patient care as hormone therapy or chemotherapy.

The other major study we are running at the moment is at the exact opposite end of the spectrum. These are men with early-stage prostate cancer. They've been recommended for active surveillance.

Many men and their partners want us to just take their cancer out. We know from a few decades of data that this does not often result in a very good outcome. The man has a prostatectomy; he then has a range of continence problems and sexual dysfunction. His quality of life is really impacted. Many men and their partners have serious treatment regrets.

Good evidence now suggests that in many of these men, it's better just to wait and see if the disease progresses and then determine whether they need active treatment.

In this particular five-year study, we are looking at whether exercise medicine can help men be more comfortable with their decision. We say to them that at this stage, surgery or hormone therapy are not advised and that there is a whole range of side effects associated with testosterone suppression. We recommend that they undertake an exercise prescription instead.

From a very nice study done by Dr. Dean Ornish's group out of the University of California, San Francisco, we know that appropriate exercise will slow the progression of your prostate cancer. It may never become a problem for you.

So, in this study, we're looking at two things: first, will exercise delay men seeking radical treatment; and second, will it delay the actual progress of the disease?

Most men with prostate cancer die of cardiovascular disease or metabolic syndrome, particularly if they're going on androgen deprivation therapy (ADT). Because exercise will reduce their risk of all chronic diseases and extend their lives if they make that change, then chances are the prostate cancer won't progress to a stage where they need more active therapy.

What specific exercise plans do you recommend for prostate cancer patients?

Dr. Newton: At the moment, we have a very generic recommendation from the American Cancer Society: complete 75 to 150 minutes per week of moderate to vigorous aerobic exercise and two or more resistance training sessions per week. That's the same recommendation that the American College of Sports Medicine gives for any healthy adult, whether he or she has cancer or not. That recommendation needs to be more tailored to the stage of prostate cancer and the treatments the patient is undergoing.

"Exercise will most likely become a required part of patient care."

I'm writing a letter to the *Journal of Clinical Oncology* in response to a paper by a group in Perth that they published in the last edition. The paper recommends that the way forward with the management of cancer will be home-based exercise programs prescribed by physicians, and most likely, walking programs. This is a tragic step backward in terms of the management of cancer with exercise medicine. It's ineffective.

Compliance in home-based programs is woeful. It's the wrong medicine. Depending on the problem the patient is experiencing, walking may be the wrong medicine. It's like giving antibiotics as contraception. This is not the direction in which oncology should go.

For men on active surveillance, we have two principal targets. First, we try to reduce the risk of other chronic diseases. At this stage, the prostate cancer is not progressing that fast, so chances are the patients are going to die of something else.

If they're overweight, obese, or their blood glucose is out of control, for example, metabolic syndrome will kill them long before their prostate cancer will. You've got to say, "Why are you worried about your prostate cancer? You won't live long enough to get it." If a man is overweight, physically inactive, or has a poor diet, then the focus should be on controlling that, not on the prostate cancer.

The other target for patients on active surveillance is to stimulate the mechanisms that might inhibit the tumor from developing further. We're starting to get a good understanding of this. The key is to maintain or increase the amount of muscle in the patient's body.

Muscle produces strong antitumor drugs. It's natural, internal medicine, but it produces a range of substances that have an antitumor effect. We need to increase the size of the muscle and then activate that muscle regularly to get it to dispense these chemicals.

We're unsure at the moment of what specific types of exercise drive the greatest quantity and which specific endogenous medicine will suppress tumor growth. At this stage, that's why we recommend a combination of resistance exercise and aerobic exercise. That should help to slow the tumor progression.

Do you have similar recommendations for men before and after therapy?

Dr. Newton: Yes. For preprostatectomy, our group and others have had a lot of success with a prehabilitation program, if you like. We published a paper on this concept earlier this year.

There is no great rush for a man to get a prostatectomy. We generally have about six to 12 weeks to intervene prior to prostatectomy.

We know that patients with high cardiorespiratory fitness have fewer complications under anesthetic and recover faster. Depending on the patient's

physical condition, we work to get their aerobic fitness up. We're trying to maintain muscle mass.

Once the man undergoes surgery, he will have considerable deconditioning. He'll lose muscle and most likely bone mass. We try and build these men up so they've got more of a muscle mass reserve before surgery.

We also focus on strengthening the pelvic floor muscles to reduce their risk of incontinence.

After surgery, we get them up and moving as quickly as possible. We try to get them back to a healthier body composition. Along with whole-body exercises, we have them do pelvic floor exercises again.

In terms of radiation therapy, some recent work shows that exercise increases blood perfusion through tumors. This is very important in radiation therapy because it appears that if the patient exercises immediately before (preferably) or immediately after their radiation dose, the exercise will probably enhance the treatment's effectiveness.

Our current recommendation is that patients perform aerobic or resistance training, but we're promoting aerobic exercise immediately before they go into the linear accelerator. Exercise increases oxygenation within the tissue, which results in greater cancer cell deaths. There is growing evidence that this results in greater effectiveness of radiation therapy.

We also know that exercise enhances chemotherapy and reduces side effects. Exercise forces more chemotherapy into the tumor because it increases blood flow. We weren't aware of the mechanism in radiation therapy until earlier this year.

It relates to the oxygen enhancement theory of radiation therapy, whereby the radiation directly damages the DNA of the cells. In many cases, this will cause cells to become dysfunctional and they will die. You get a greater death rate among cancer cells, particularly because they divide more rapidly. You're more likely to strike them with radiation at a vulnerable point. That is a direct mechanism.

What do you recommend for men about to start radiation therapy?

Dr. Newton: At this stage, they should be doing strength training and cardio. Cardio is probably a better bet immediately before treatment.

But it really depends on their issue. Low muscle mass means we have to do resistance training. Low cardiorespiratory fitness means they're going to die of something else, so we have to get them fitter. Because our recommendation depends on the main issues they face, a thorough health and fitness assessment is best.

We call this 20-minute aerobic exercise workout immediately before receiving a radiation dose *priming the radiation therapy*. Priming the radiation therapy with aerobic exercise causes an overall increase in blood pressure, an increase in body temperature, and an increase in blood perfusion through all the tissues of the body.

That's fascinating. And exercising before treatment is something patients can do themselves.

Dr. Newton: Absolutely. Radiation therapy causes overwhelming fatigue. The only way to reduce that is to get as fit as you can and increase your muscle mass leading up to the course of radiation therapy. That will help reduce side effects and reduce fatigue.

After the radiation therapy, try to get back to physical activity as quickly as possible.

What about with metastatic disease? What exercises do you recommend?

Dr. Newton: Traditionally, the recommendation for patients with metastatic disease was to rest. The patient should avoid physical activity, and weight/resistance training in particular, due to concerns that bones might fracture at a point of weakness.

> *"We recommend a combination of resistance exercise and aerobic exercise."*

We've run two studies that challenge this idea. One has been published; the other is ongoing. We've been exercising men with metastatic prostate cancer and women with metastatic breast cancer and we've seen no adverse events—no increase in pain medication. We've seen good physiological responses and improved fitness, strength, and muscle size.

It appears that in a well-controlled environment, with appropriately qualified personnel, the risk of a fracture at the site of metastasis is very low.

We use accredited exercise physiologists, but in the United States, men should find a clinical exercise physiologist in a good, monitored facility. Patients respond very well.

It's counterproductive to recommend to patients with metastatic disease that they rest because they'll only decline faster and die quicker. Physical inactivity is not an option; they have to exercise. The challenge is to implement this safely and effectively.

Clearly, a home-based program is inadvisable. These patients most likely will have cardiovascular issues, so they're at risk of having a heart attack or stroke. Their program needs to be monitored by the right personnel using the correct equipment with sound emergency procedures. Our recommendation—and what we have implemented—is a clinic-based program, supervised by exercise physiologists.

In those particular clinical trials, we designed a program so that the exercises avoided the side of the metastasis. For example, if they had a lesion in their left femur, then we wouldn't exercise that limb to avoid overloading it and causing a fracture. Some preclinical work in an animal model showed that controlled exercising on the metastatic site compressed tumor progression.

When you load bone, bone cells send chemical and electrical signals to other cells that they should respond, generally by laying down more bone to make the bone stronger. Those same electrical and chemical signals also suppress tumor cells.

We have two trials running currently —one in breast cancer and one in prostate cancer—looking at exercise for patients with metastatic spinal lesions. We're doing controlled isometric contractions to produce compressive load on the side of the lesion. Then we're using sophisticated MRI techniques to monitor the volume of the metastatic tumors.

Those two studies are ongoing but, again, we've had no adverse effects.

We have no exacerbation of bone pain. We're just waiting now for the complete studies to see if, relative to usual care, we've observed a slower rate of growth of the bony metastases.

What would you suggest to a man with metastatic disease reading this? Contact his doctor to develop an exercise program?

Dr. Newton: If he has metastatic disease within the skeleton, then he has to avoid any risk of falling. Obviously, contact sports are out, as well as waterskiing, skiing, and snowboarding. It's critical he exercises. It's critical he does both aerobic and resistance exercise. Currently, we recommend he avoid loading the specific site of the metastases, but in the near future, we may see a prescribed exercise program that targets and controls loading.

"Try to get back to physical activity as quickly as possible."

An oncologist or physician would not be able to prescribe an exercise program because they have no background or training in exercise physiology. You have to have the right medical professional give the right exercise prescription.

In Australia, we're strongly encouraging people to seek the consultation of an accredited exercise physiologist. In the United States, you would look for a clinical exercise physiologist.

The American College of Sports Medicine (http://www.acsm.org/) now has specific certifications for exercise oncology, but as this is a relatively new field, there are not many of these health professionals out there at the moment. But the field is growing and specialists can be found.

What if a prostate cancer patient can't find the right exercise doctor?

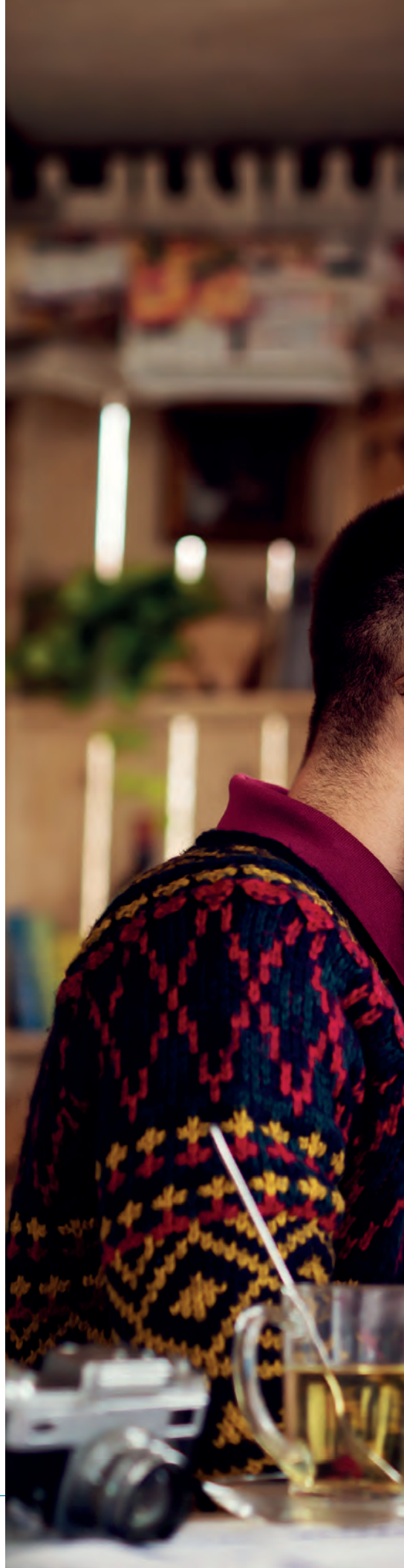
Dr. Newton: Visit the Movember website (https://us.movember.com/), which has some support programs in the United States. In Australia, which is as big a country geographically as the United States, we now manage around 2,000 men with prostate cancer entirely via telephone and online.

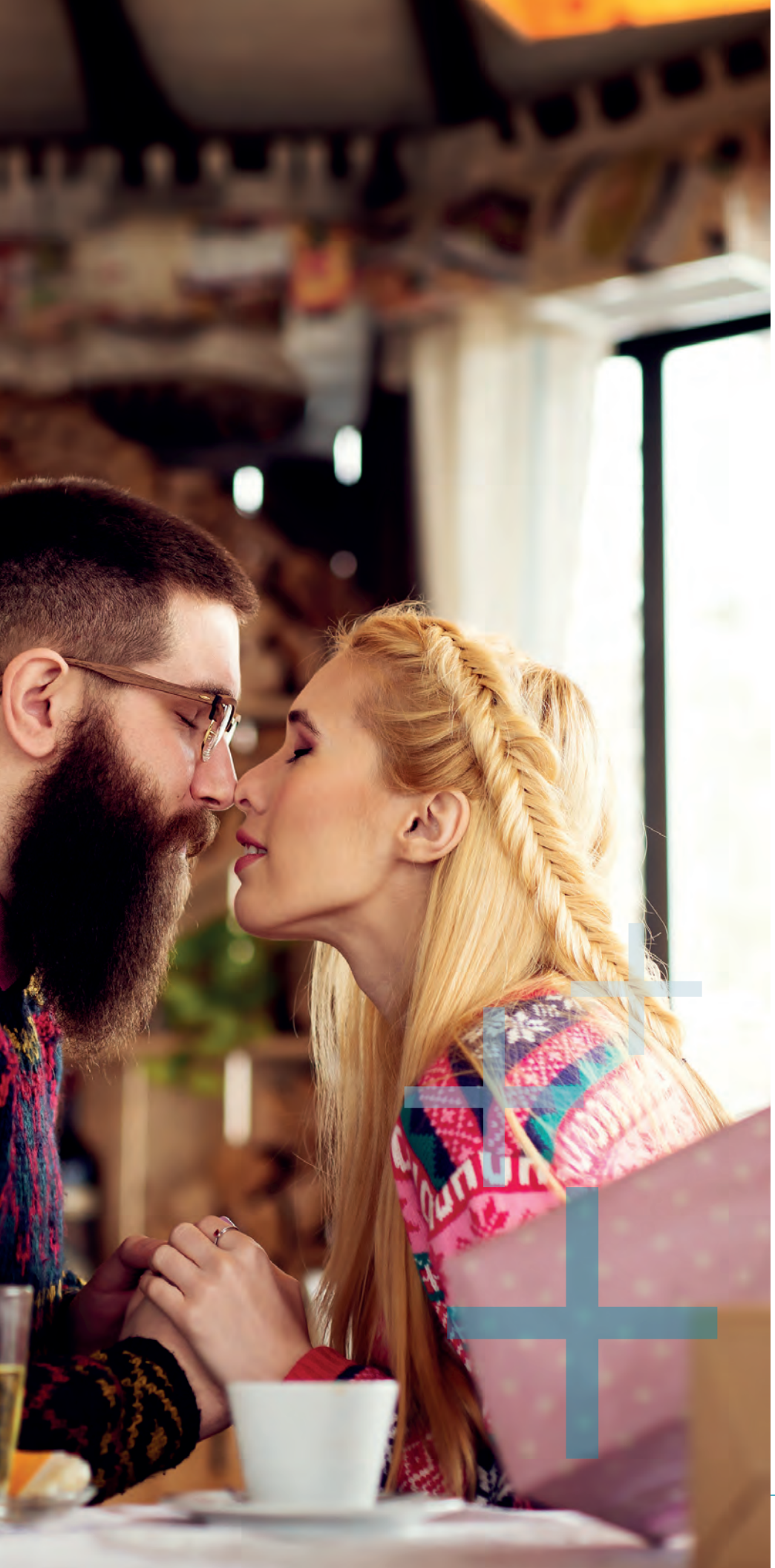
You mentioned the American Cancer Society's recommendations for exercise as 75 to 150 minutes a week. Do you think that's adequate?

Dr. Newton: Absolutely. Seventy-five to 150 minutes per week of moderate to vigorous aerobic exercise and two or more resistance training sessions per week is sufficient to maintain normal health. That means that if you do vigorous exercise, 75 minutes is sufficient. That is for healthy people.

If you've got cancer, you're going to have to be more specific about the exercise you do. You're going to have to do exercise medicine that will give you the best cancer survival.

It's highly problematic to recommend to patients that they be more physically active. For example, if a patient likes walking and decides to do more walking, that might benefit some aspects of their health. But walking will not benefit a man on ADT who has rapidly developing osteoporosis and sarcopenia (muscle loss). Walking will benefit his cardiorespiratory system, but that probably won't be what kills him. Most likely, he'll become dysfunctional due to low muscle mass and he'll have





an osteoporotic fracture. If it's in the hip, he probably won't survive it.

These generic recommendations are helpful generically, but if you have cancer you really need to be assessed by a specialist. That specialist can determine your life-limiting factor and then prescribe medicine tailored to reduce that factor.

Precision exercise medicine?

Dr. Newton: Exactly. We're working a lot with men with advanced disease, and the American Cancer Society guidelines are difficult for them, particularly if they've got cachexia, or muscle wastage. Most likely, 150 minutes per week of moderate intensity exercise is counterproductive. That makes for a greater energy imbalance; they will lose more muscle.

You've got to be a little bit careful, particularly with patients who are having a difficult time due to treatment or the stage of their disease. Exercise must be targeted.

That said, any exercise is better than none. The overwhelming clinical evidence and research show that men with prostate cancer—or anyone with any cancer—regardless of the stage of disease, even while undergoing difficult treatments, must be physically active on most, if not, every day of the week. If they adopt a rest strategy, then they will only deteriorate faster. We totally reject the rest strategy; it doesn't work.

Any amount of physical activity is beneficial and will likely increase survival, but a targeted exercise prescription will be far more effective and safer. We must move to the next stage where highly tailored exercise medicine is standard. Pp1

Greta Macaire
Nutritional Counseling + Cancer

Ms. Greta Macaire is a registered dietician at the University of California, San Francisco.

She spoke with *Prostatepedia* about the types of recommendations she makes for men with prostate cancer.

How did you become a dietitian for cancer patients?

Ms. Greta Macaire: I've been working with cancer patients for about 13 years. Before coming to the University of California, San Francisco (UCSF), 11 years ago, I worked at another hospital in the city for about two years. It just so happened that the assignment I was given at that hospital was in radiation oncology, working with people going through radiation treatment. I fell into it. I also worked with other diseased groups on overall wellness and nutrition counseling. And then the opportunity to work full time in oncology nutrition came up at UCSF, and I was really interested in that.

I gravitated toward working with people going through cancer treatment for a couple of reasons. First, people with a cancer diagnosis are great to work with around diet, exercise, and lifestyle changes because their motivation level is often really high. Second, a cancer diagnosis is a time when everything feels like it's just really out of your control. Diet and exercise are something you can do to help feel as well as possible.

Where along the journey do you normally see patients: when they're just diagnosed, before treatment, or during treatment?

Ms. Macaire: It really runs the gamut. I see patients anywhere along the path, whether it's right after diagnosis, while they're going through treatment, or after they've completed some kind of treatment, such as radiation or hormone therapy.

Often, our prostate patients are diagnosed at a very early stage and are in our active surveillance group. We help try to slow or prevent progression of their prostate cancer through diet, exercise, and lifestyle.

I don't usually see people in prevention or risk-reduction situations since I work in a cancer center. Most of the patients referred to me have already been diagnosed.

What is the process like? Do patients meet with you once? Several times?

Ms. Macaire: My patients typically get a referral through their doctor here at UCSF. I look over their medical records before we meet so I have a full picture—at least from the medical side—of their prostate diagnosis and other health history. I combine that with more information I learn from the patient, such as where they are with their nutrition and goals. Then I come up with a plan.

Generally, we talk about how to manage the impact of the nutrition-related symptoms from the treatment they're going through. We also discuss overall healthy eating throughout treatment. We usually develop some kind of plan that the patient and I agree upon, and then they can follow up.

Sometimes patients come in just for a one-time visit. That depends on how savvy they are. Sometimes they've done a lot of reading and just want to ask questions and clarify information about diet. There is a lot of conflicting information out there.

In other cases, I'm doing a lot more guiding. I'll follow up with the patient multiple times as they go through their treatment. We're fortunate at UCSF because we can see patients multiple times throughout treatment.

If someone doesn't have a referral, can they see you independently and pay out of pocket?

Ms. Macaire: No. We don't charge for the UCSF system service and it's not usually covered by insurance.

So a man must be a UCSF cancer patient to come see one of the dietitians here at the Cancer Center. We want all of our patients to have access to nutrition counseling. If they're outside of the UCSF system, we can't see them. We direct them to other resources or help them find an oncology dietitian.

What kinds of recommendations do you make for men on active surveillance?

Ms. Macaire: In active surveillance, there are general themes and more in-depth, specific recommendations. Generally, I recommend a plant-based diet, which means the basis of their diet is vegetables and plant-based proteins. I encourage men to eat more cruciferous vegetables, like broccoli, kale, and cauliflower and cooked tomatoes

Dr. June Chan and colleagues at UCSF have done some research that found benefits for men with prostate cancer who regularly eat cruciferous vegetables and cooked tomatoes. (See *Prostatepedia* June 2017 for a conversation with Dr. Chan.) Reducing red meat, dairy products, and eggs also seems to be beneficial. They found that men should avoid processed meat and minimize highly processed foods.

Men don't necessarily have to cut out animal protein completely, but they should try to get more fish and plant protein from things like beans, tofu, nuts, and seeds. Try to make animal protein more of a condiment in the diet.

Based on a man's current diet, we discuss cancer risk reduction and overall healthy eating guidelines to see where he is meeting and not meeting his nutritional needs. I look at his body weight and suggest ways to reduce calorie intake and help him lose some weight if needed. Exercise is a key component. We have an exercise counseling program to ensure they're exercising properly. With active surveillance, there's not necessarily as much of an emphasis on resistance training like there would be for men on hormone therapy, but they definitely need regular cardio exercise.

I also look at vitamin D levels, if possible, to make sure it's at a healthy range. We know that low vitamin D has a lot of negative implications for overall cancer risk and health.

It seems like a low-risk prostate cancer patient on active surveillance who comes to see you might come out of the whole process healthier than he was before.

Ms. Macaire: Exactly. That's the goal. All of these recommendations would be helpful for heart health and to reduce the risk of diabetes. We hope to slow down prostate cancer, but we also want to keep men healthier over the long term.

What do you recommend for men about to start radiation, have surgery, or begin chemotherapy?

Ms. Macaire: I always tell men undergoing radiation, surgery, or chemotherapy that there will be side effects from those treatments. They may need to modify their diet.

For example, patients who get radiation to the prostate bed in the pelvic area (or if lymph nodes are involved) can experience side effects such as gas, bloating, loose stools, and diarrhea. To decrease these side effects, they may have to modify their diet. These are almost always temporary recommendations, though, so it can be really confusing for men.

As a good diet for men with prostate cancer, everyone would recommend a lot of broccoli and vegetables. But men who go into radiation might get gas, bloating, and diarrhea, so they may need to avoid gas-producing vegetables and acidic foods like tomatoes to decrease these side effects. We would also recommend less fiber and more cooked vegetables in that case. But I always let them know these are temporary changes.

Once they recover from radiation, they'll be able to introduce all these foods back into their diet gradually. It can be a little unnerving for them to think about backing off those foods that they feel are so important. The digestive tract usually heals pretty quickly from something like radiation, so it's just temporary. Typically, we incorporate those foods back in within a couple of weeks after treatment.

Surgery can also result in gas and bloating because of the pain medications. Constipation and gas can be really uncomfortable because of the surgery. Again, that's usually temporary.

Any dietary changes before chemotherapy?

Ms. Macaire: The most common side effect I hear about is taste changes: some foods are not appealing or taste like cardboard or metal. Nausea and decreased appetite are other common side effects.

You may have to plan out what you're going to eat. Eat smaller meals, and eat more often. That way, you're not getting too much so you're not going to feel bloated and uncomfortable, but then you're not going all day without eating, which will make nausea worse. If you experience a metallic taste, we can look at ways to tweak the flavor profile of foods to make them tastier.

Sometimes animal protein brings out the metals in food. There's more iron and things like that even in chicken or fish. Choose alternative protein sources that don't have as much

of the metallic flavor. Lemon juice can brighten up flavor if everything tastes bland. These small modifications can help with the side effects.

I think it's comforting for people to hear that these changes are temporary. You're going to like food again. When you're done with chemo, things will taste good again. Hold tight.

One of the big side effects of androgen deprivation therapy (ADT) is that men tend to gain weight quickly. What do you recommend for men on hormonal therapy?

Ms. Macaire: We strongly recommend physical activity. The research is pretty consistent on physical activity. Cardiovascular exercise is important, but resistance training is also important. Resistance training maintains lean body mass, which keeps the metabolism higher. The more muscle they can maintain and not lose due to hormone therapy, the more they can keep their body composition on track.

Men on hormone therapy need to be careful about what they eat, especially with foods that can cause weight gain: white foods—which can cause abdominal weight gain—like refined grains and sugary beverages (soda, fruit juice), desserts, and pastries. It's really important to eat more green leafy vegetables, fill your plate with filling, high-fiber foods. Make at least half your plate non-starchy vegetables, fill a quarter of the plate with lean or plant protein and limit grains or starchy vegetables like potatoes, corn, or peas to no more than the other quarter of the plate.

I wouldn't recommend a low-carb diet by any means, but eating lots of vegetables and including a lean protein with each meal will help to keep blood sugar levels stable, to prevent spikes and drops.

Do you discuss stress management or mindfulness-based meditation?

Ms. Macaire: I don't particularly focus on that. We're so lucky here. Many people reading this may not have access, but we at UCSF have many great services here. We have a psycho-oncology program where patients can meet with a psychologist who deals with people going through cancer treatment. We have education modules on the cognitive changes with hormone therapy. We even have classes on mindfulness-based stress reduction and meditation. I don't necessarily coach them on that, but I make sure they're aware that stress is a normal side effect that can be managed.

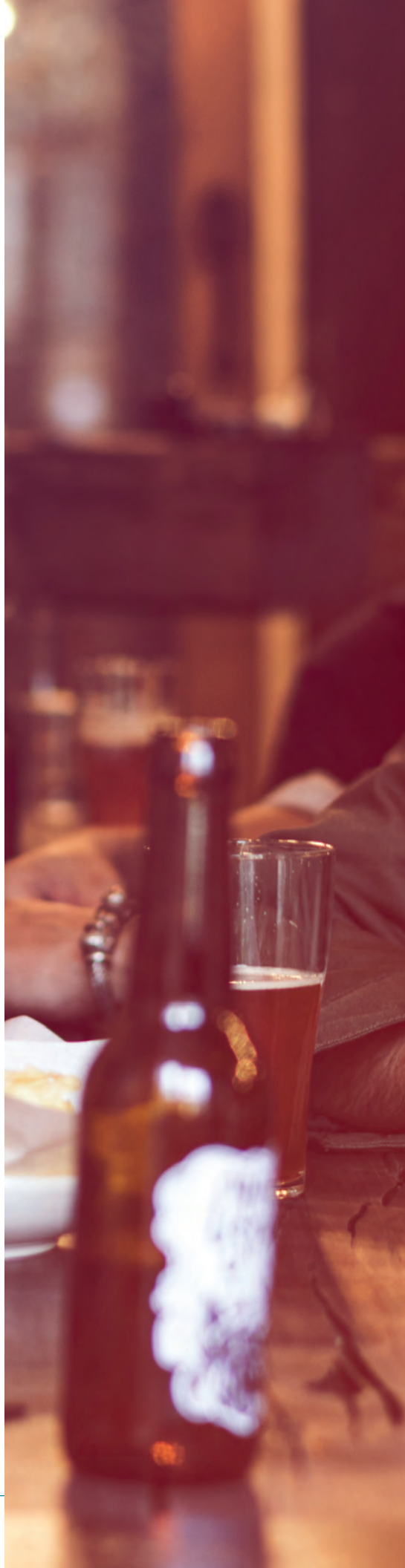
What would you say to a man who wants or needs this type of help? How would he find an oncology dietitian?

Ms. Macaire: The Academy of Nutrition and Dietetics runs www.oncologynutrition.org; they have a feature on their site to help find an oncology dietitian in your area. There's also a lot of good information on that website about some of the common questions regarding symptom management and healthy eating. Also, the cancer center where you get treatment may have a resource center that can help.

I would assume that most places have some kind of similar service for patients.

Ms. Macaire: Most of the National Cancer Institute-designated cancer centers offer free services, though not necessarily one-on-one nutrition counseling. But they might have a lending library with good quality resources or different classes that are open to the public.

At our cancer center, our classes are open to the public even though our



individual services are only available to UCSF Cancer Center patients. You should be able to find something like that in your area.

Are the UCSF classes available online?

Ms. Macaire: A lot of them are available as podcasts. We have podcasts of the nutrition classes that we've done on our website. Other cancer centers like Dana Farber and MD Anderson also have nutrition videos on their websites.

There is also the Answer Cancer Foundation. I did a nutrition and prostate cancer webinar with them not too long ago. The podcast is on their website, www.ancan.org.

What would you say to people who get conflicting information about diet from their doctors, online literature, and other resources?

Ms. Macaire: There's a ton of information out there, but you should always look at the source. Who's giving the information or recommendation and why? What support do they have for that recommendation? If it's on a website, the information in the "About" section will tell you who is writing the content and what their qualifications are.

Also, consider how the information applies to you. Your doctor might have recommended something that makes perfect sense for you, but if you went to your support group, it would sound completely foreign to others. It might be tailored to you.

Sometimes, it's not just prostate cancer that we consider. You might have other conditions, and a nutrition recommendation takes priority over what's the best thing for prostate cancer at that moment in time. We look at individual needs and your overall dietary goals.

We don't want to make recommendations from only one study. We want to look at the whole body of evidence and come up with the best recommendations that have the most research support. If you follow each study, you're going to completely change your diet every day because individual nutrition studies can be very contradictory.

The American Institute for Cancer Research has a quality website: www.aicr.org. Their whole mission is to study how food, physical activity, and body weight impact cancer, individually and worldwide.

It seems that news about diet and nutrition research makes it to the mainstream media a lot faster than other types of cancer research.

Ms. Macaire: Exactly. That's because the media is often after the headline. They publicize the studies that seem to go against what we accept as basic good nutrition. It's news. They're looking for something to wow people. It's not that sexy to say, "Another study came out that says eating vegetables is really good for you."

Is there anything else you think prostate cancer patients should know about diet and nutrition?

Ms. Macaire: It's never too late to change your diet no matter where you are in the process of prostate cancer. There's always something that your diet can do to help you feel well and improve your quality of life, and may even deter prostate cancer. Keep thinking about how diet can support your overall goals through the journey of prostate cancer diagnosis and treatment. Pp'

Clinical Trial: David Levy, MD Curcumin, Omega 3 Fatty Acids + Vitamin D

Dr. David Levy is a Clinical Associate Professor in the Department of Urology at the Cleveland Clinic.

Dr. Levy spoke to *Prostatepedia* about his clinical trial looking at the impact of vitamin D, curcumin, and Omega-3 fatty acids on prostate cancer.

Why did you become a doctor?

Dr. David Levy: From eighth grade on, every summer I worked in the hospital. That's basically what I did. I volunteered. I worked in the operating room. I was an orderly. I worked in the pathology lab. I worked in the hematology lab.

I pretty much spent all of my summers working in and around hospitals. No one in the family was a doctor, and I thought it was pretty neat stuff in terms of what doctors did for all the people that they saw. I gravitated to the sciences in college, but I majored in anthropology.

Why that choice?

Dr. Levy: I didn't want to concentrate in any of the hard sciences and anthropology provided a little different avenue. I took graduate level anthropology courses at the medical school at Washington University in St. Louis. I did research projects in the Department of Anatomy at the medical school in my junior and senior years. It was a different twist on the conventional approach for people who went to medical school.

Do you feel that that early coursework in anthropology informed how you now approach patient care?

Dr. Levy: I think it gave me a slightly different perspective on things. A different mindset.

Can you explain the thinking behind your clinical trial on vitamin D, Omega-3 fatty acids and curcumin in prostate cancer?

Dr. Levy: Well first let me say there are a number of people involved in this program without whom it would not be where it is today.

I was extremely fortunate. When I finished my residency in Cleveland, I went to MD Anderson Cancer Center in Houston, Texas to do a cancer fellowship.

At that time, we didn't really understand why cancer occurs and how to treat it. The attitude was: "Cut it out. Radiate it. Give chemo."

We're now twenty years down the road and while medical knowledge has advanced tremendously, what are we still doing? Cut it out. Give radiation. Give chemo. People with cancer keep coming and coming. It's like a conveyor belt. They don't stop.

About five years ago, I bought an abandoned farm here in Northeast Ohio. The goal was to make it an organic certified produce farm, which I did over three years. In learning about the process to make our farm certified organic, I had to review all the pesticides and chemicals that had been put into the soil and what we had to avoid for over three years to gain the certification. With all these pesticides and chemicals come known side effects.

There is a journal called the *Journal of Organic Sciences*, which ran a 25-page article on the use of a very common weed killer. Going back to the 1970s, there is a direct correlation of the increased use of this weed killer in commercial agriculture with an increase in liver cancer, colon cancer, kidney cancer, kidney failure, lymphoma, leukemia, thyroid, and prostate cancers. Every cancer went up. They all paralleled the increased use of this common weed killer.

When I read that article, I started to think that there has to be some correlation between environmental exposure and cancers. I started to ask: If you change the environment in which the cells live, do you change their behavior? That has been studied

a few times and the results published. Studies have shown the influence of vitamin D on prostate cancer behavior, the impact of Omega-3 and Omega-6 fatty acid ratios on prostate cancer behavior, and the impact of turmeric curcumin on biochemical pathways in the cells. I was thinking about all of that as I came to design the trial.

If you look at populations across the world, prostate cancer rates vary quite dramatically. India, China, and Japan have some of the lowest rates of anywhere in the world. The rate in India is 25 times less than that in the United States, England, France, Germany, Norway, Sweden, or Finland. Why is it that? Men in India all have testicles and testosterone and prostates, but they don't have prostate cancer. The same goes for Japan and China.

There are pretty interesting differences in terms of the eating habits of these populations and the disease processes that are common in the societies.

It turns out, as far as we can tell, that meat and dairy feed prostate cancer. What do we see in this country on NFL Sunday? What do they serve? They serve hot dogs, French fries, chicken fingers, chicken nuggets, chicken wings, and hamburgers. All of these foods are very high in Omega-6 fats. No one goes to the ballpark to get a bag of broccoli. That doesn't happen. No one goes there to eat apples.

When we look at our society in terms of the food choices, the foods that are heavily advertised are fast foods, pizzas, and sodas. High sugar loads, high glycemic index foods, and animal fats are all very well correlated with prostate, breast, pancreatic, and colon cancers.

I looked a little further into vitamin D and asked, "Is there a correlation with vitamin D and prostate cell behavior?" It seems there is. One published study

How To Get Involved…

For more information, contact, Dr. Levy at 216-692-8900, Option 2.

looked at 71,900 men—which is a pretty substantial population—for six and a half years. They found that the lower the vitamin D levels in the blood, the higher the patients' PSAs, the higher the likelihood of a positive prostate biopsy, and the more aggressive their cancers.

Another vitamin D study published by the SEER committee, which is a national organization that correlates hospital-reported statistics throughout the country, looked at 20,000 men. Again, they found low vitamin D, higher PSA, and higher odds of a positive prostate biopsy with significant disease.

Other studies correlate vitamin D levels with prostate cell behavior. It turns out that vitamin D binds on the prostate cell to the androgen receptor. That is where testosterone binds, and testosterone is the main food for prostate cells. Vitamin D binds to this receptor as well. As best we can tell, with low vitamin D levels, the prostate cell machinery churns along like a steel furnace. When the vitamin D levels go up, something happens to the cells' metabolic rates.

Across the country, almost all of the residents of the states north of South Carolina border and from East to West Coasts are low in vitamin D. I haven't tested anybody here in Cleveland in almost three years with a normal vitamin D level.

What about turmeric curcumin?

Dr. Levy: Tumeric is used in curry and it contains curcumin. Curcumin is a really good anti-inflammatory. It's a naturally occurring COX-2 inhibitor. (Celebrex was a COX-2 inhibitor.) It turns out that curcumin has a far greater impact on the biochemistry of cells than just an anti-inflammatory. Curcumin impacts what is called the Hypoxia-inducible factor 1-alpha. This is a factor made in the cells that is

involved in their ability to recruit new blood vessels to get more oxygen and more nutrients. Curcumin disrupts that cycle.

Curcumin disrupts the mesenchymal-epithelial cell transformation. The mesenchymal-epithelial cell transformation is a process that allows cells to gain the ability to climb outside the prostate and spread to the lymph nodes and bones. Curcumin also impacts the diclofenac acid pathway, which is part of the cell's Omega-6 metabolic pathway.

There are new publications that show curcumin increases cellular sensitivity to radiation treatment. There are some studies that show it increases the cell's susceptibility to chemotherapy.

There are over 300 publications in the National Library of Medicine on curcumin and prostate cancer right now. When I started this work about 3½ years ago, there were 13 publications on curcumin and prostate cancer. There were so few publications I couldn't even include them in my suggested regimen to patients. Now, there's no way we can ignore it.

In my opinion, to not include curcumin would be a disservice to patients because it has such a tremendous impact on cellular behavior without being toxic in any way to the kidneys, the liver, the intestinal system, or the cardiovascular system.

There are very few reported side effects of dosing curcumin. Patients have taken as much a 6 grams per day in capsule form in a study protocol to impact their prostate cancer. We give 2,000 milligrams per day, and in 27 months have not seen any side effects that would curtail our continued use of the supplement.

Are you giving men vitamin D, omega-3 fatty acids, and curcumin all at the same time and then measuring the outcome, or are you separating them out into different groups?

Dr. Levy: No. We're giving them all together.

After you give patients a combination of the three supplements what kinds of measurements are you doing?

Dr. Levy: We measure the fatty acid ratios in the body. We measure the three individual components of the fish oil: EPA, DHA, and DPA. We measure the Omega-3/Omega-6 ratios in the blood. We measure linoleic acid levels in the blood. We measure vitamin D levels, and then titrate their doses to get vitamin D levels up to our target range.

There is nothing you can do to measure curcumin except give the dose of the appropriate manufacturer's preparation. We spent a lot of time figuring out what was going to get to the cells most efficiently.

And of course, we change the diet.

But the end point of our study is genetics. We do a tissue biopsy at the time of diagnosis. Then the men go on nutrition modification and supplements for a minimum of nine months. After nine months, we repeat the prostate biopsy and do a side-by-side genetic comparison of the prostate tissue from before the diet and supplements regimen with the tissue from after the diet and supplements regimen. Then we see what kinds of changes we have caused by changing the environment in which the cells live.

What kind of patients are you looking for?

Dr. Levy: For the purposes of this genetic study, we are specifically looking at people with low-risk prostate cancer who are on active surveillance or who are candidates for active surveillance.

Angela Gaffney
Create Ease in Life

This time of year brings high expectations and a lot of hustle and bustle as we prepare for holiday festivities. When you consider the time and effort it takes to heal the body of cancer and create new habits for healthy living, there's very little room for stress. This is the perfect time of year to exercise healthy boundaries and create ease for you and your whole family.

Stress feeds disease and illness in the body. In order to create an environment that supports your goal of healthy living, you'll need to learn how to honor the needs of your body. This exercise will help you identify those items that take up your time and create boundaries that let you choose how best to spend your energy for optimal health.

Let's begin by considering all the tasks and responsibilities you have on your plate and assess how each is impacting your health.

1. List on a sheet of paper all the tasks, relationships, responsibilities, activities, etc. that demand your time on a daily basis. Write whatever comes to mind.

2. Make three columns on a separate sheet of paper. Title the first column Must Haves, the second column Negotiables, and the third column Infrequent/Unnecessary.

3. Categorize each item from your list into its respective column.

- Must Haves are the relationships/hobbies/activities that you must have in your life; they are your number one priority. These are the items on your list you hold most dear to your heart. They bring you joy and you can't live without them.

- Negotiables are the activities/hobbies/tasks that provide value, but not without cost. These are such things such as social media, television, volunteerism, gaming, or shopping. You'll need to assess whether these items are positively or negatively impacting your health and whether they're taking away time you could be spending on your Must Haves.

- Infrequent/Unnecessary are activities/relationships/traditions that negatively impact your health or cause undue stress. These items must be given great consideration and may need to be placed in this category for you to manage stress and achieve optimal health.

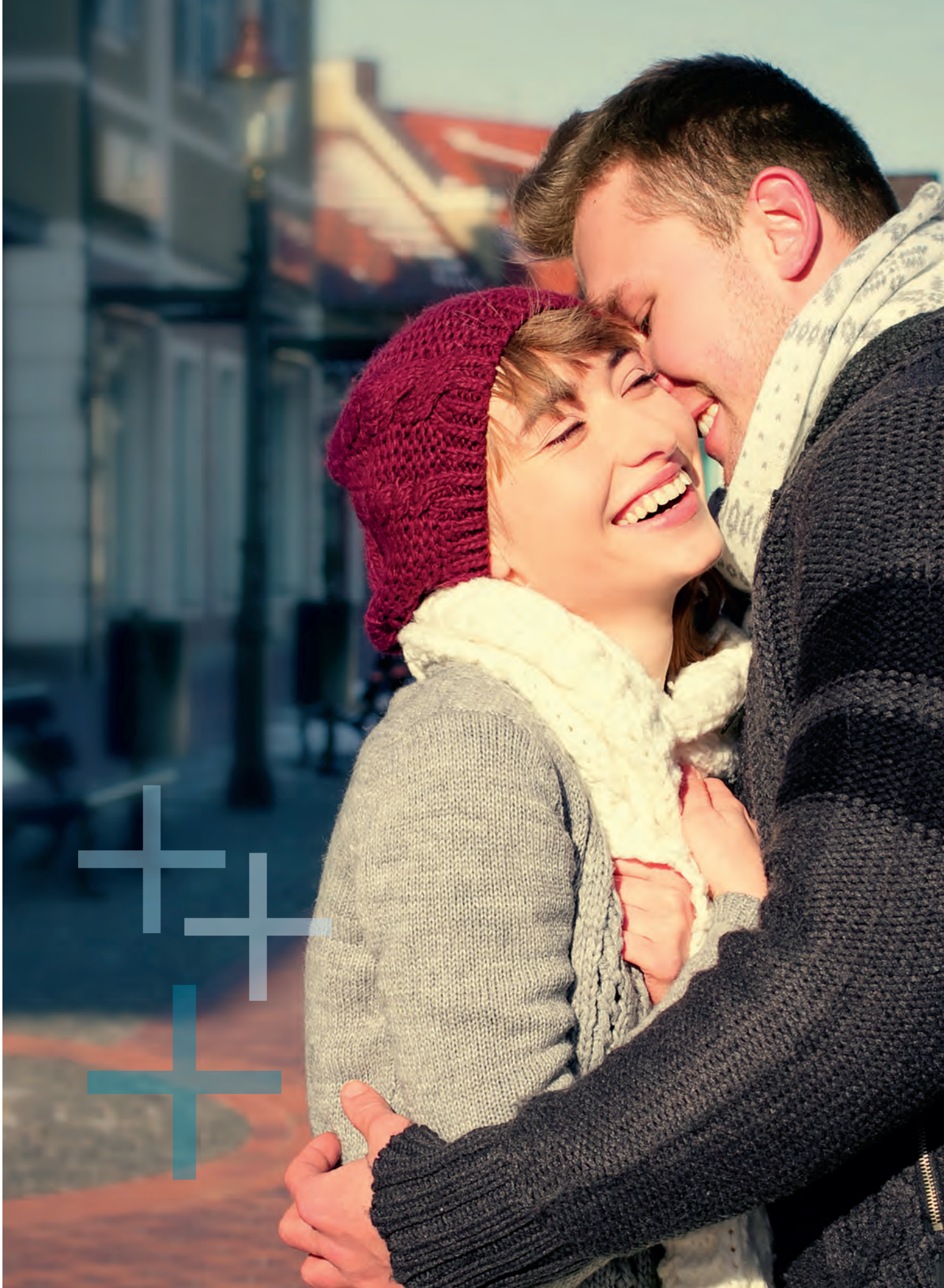
4. Review the items in your columns. These are the boundaries necessary for you to achieve optimal health. Honor those items in the Must Haves category and assess whether the Negotiable items are worth it to your health and happiness. For the items in your Infrequent/Unnecessary column, it may be difficult, but you'll want to honor the needs of your body by engaging with these items in an infrequent manner.

Your health is the greatest gift you can grant yourself and others. Please honor the needs of your body; create ease in life by identifying what's most important to you and making time for your "Must Haves." The other items on your list only need attention if they're fueling your health and happiness. Pp[1]

Want to know more?

Wellness speaker Angela Gaffney teaches simple and effective strategies to achieve health, increase productivity and live stress-free while reaching your 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. .



Patients Speak: Michael Meszaros

The Artist's Approach To Cancer

Mr. Michael Meszaros is an Australian sculptor with prostate cancer.

He spoke with Prostatepedia about the diet and lifestyle changes he made while on active surveillance.

What was your life like before prostate cancer?

Mr. Michael Meszaros: I was 70 when I was diagnosed. I've lived my life as a professional sculptor. A fairly normal sort of life. A wife, two grown-up kids. I've had a wonderful life in that I've made a living out of what would otherwise be a hobby. I've always felt that I've been blessed with being self-employed.

"My work as a sculptor is quite physical."

What kind of sculptures do you make?

Mr. Meszaros: Mostly cast in bronze or fabricated out of copper and stainless steel—anything from little medallions up to major public works. Two years ago, I won the Inaugural American Medal of the Year Award.

That's fantastic.

Mr. Meszaros: Sculpture has left me a bit more of an independent thinker than perhaps others because I'm always confronted with artistic problems, and I have to think my way through them to an artistic solution. In a sense, when I found myself confronted with prostate cancer, there were elements of my artistic thinking that I applied to my medical situation.

How did you learn you had prostate cancer?

Mr. Meszaros: I had been seeing a urologist since about 2003. My PSA was creeping up. I'd already had two biopsies in 2008 and in 2009. The

"I have tackled this head-on in my own way."

first one showed a focus, and the second one, they declared me clear. My PSA dropped quite significantly after the second biopsy, from 5.5 down to 3.2. Then it gradually crept up again until 2015 when it hit 6.8.

I had a third biopsy when they diagnosed two separate tumors within the prostate. After another two and a half months, it went up to 8.2, and it appeared like it was really taking off. My urologist said he wanted to operate within three months.

How did you react?

Meszaros: My first reaction was that it was hugely expensive. I was put in touch with the co-ordinator of the local prostate group called Max Shub who runs our local prostate group and who is active in many committees regarding prostate cancer. (The prostate group has become very important to me and gives me a lot of support in what I am trying to do). He told me to get some other opinions. He gave me the name of a radiation oncologist and another leading urologist who I promptly consulted. The radiation oncologist said that he could fix me. I asked if I had much time, and he said: "You've got some time, but don't leave it too long."

On the same day, I saw the other urologist who looked at my pathology reports and PSA tests. He didn't think I was ready for an operation, and that I should go on active surveillance.

That's what I really wanted to hear. I figured that I had a window to try things like changing my diet and doing more exercise, even though I was quite fit to start off with. I started walking 30-40 minutes every day, I went almost entirely vegetarian, and started taking various supplements, like vitamin D. Immediately, my PSA stopped rising.

How is your cancer being monitored during active surveillance?

Mr. Meszaros: I have an annual MRI and quarterly PSAs.

Was exercise a part of your life before prostate cancer?

Mr. Meszaros: I played tennis and did Pilates once a week. My work as a sculptor is quite physical, and I'm on my feet all day, so I'm not overweight. By most standards of 70-year-olds, I was in pretty good shape.

What sorts of changes did you make after the diagnosis?

Mr. Meszaros: I went on an almost vegan diet. My daughter is a myotherapist and she has done quite a lot of her own research into diet. She told me about the effects of becoming vegetarian and that a lot of people with very serious diseases had shown remarkable recoveries by doing that. I read quite a lot about the benefits of keeping off red meat in relation to prostate cancer.

I thought I would change my diet, increase my exercise, and take a few recommended supplements and then see what happened.

What happened was that the PSA stopped rising. A year after, another MRI showed no progress in the cancer at all. The PSA had stabilized at about 8.6. One of the tumors couldn't be seen anymore, though I was assured that it would still be there, even if it did not show on the MRI.

I thought this was a pretty good situation, so I just went on with that. Then in April 2017, I did the regular PSA and another MRI. The PSA rose bit to 9.3 and seemed to stabilize. The second cancer was still not visible, but the MRI report said that the PI-RADS rating should be downgraded from a 3/5 to 2/5 because they had seen reductions in the cancer.

It seemed to be a very significant improvement. I asked the urologist if this happened very often. He said: "It happens, but it's very rare."

Last month, my quarterly PSA jumped to 11.6, which was a bit disturbing.

What did the urologist think?

Mr. Meszaros: He said not to get too concerned as PSA results fluctuate for many other reasons. The next test a month later showed that it had dropped back to 9.0. I may have done too many pelvic floor exercises or it may have come from some inflammation.

How have the diet and lifestyle changes affected your overall health?

Mr. Meszaros: I started getting fairly chronic diarrhea from the supplements, though so I've had to ease off on them.

How did you determine which supplements you were going to take?

Mr. Meszaros: Talking to people, looking on the internet and from others in the prostate group.

For instance, a friend of mine is a marathon runner and he recommended resveratrol, which is a derivative of red wine grapes. I see a naturopath who recommends turmeric. I researched these and found that, taken together and with a fat and black pepper, these have a greater effect than individually.

I drink quite a lot of pomegranate juice.

Very early, when my PSA started to rise, I was told about broccoli sprouts having a beneficial effect. I continue to eat them most days. There is quite a lot of research to back this up.

Do you discuss these supplements with your urologist?

Mr. Meszaros: Yes. I tell him what I'm doing, and he says: "Look, these are natural. They're not going to do you any harm. We'll wait and see if they do you any good."

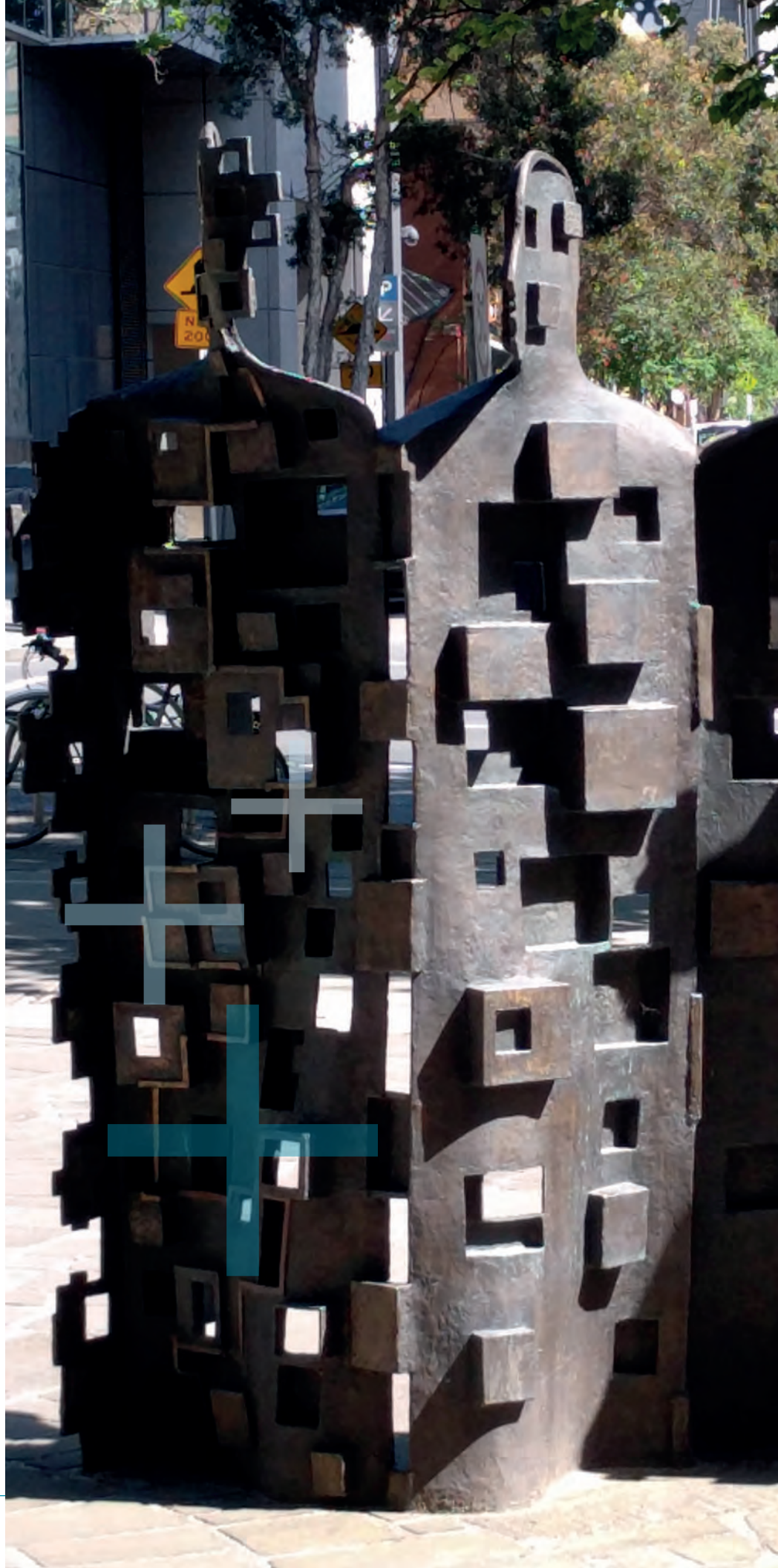
So much of this is uncertain. There are all sorts of rumors, myths, and possibilities in prostate cancer that haven't been investigated well. People like me are trying all sorts of things. I think there's a lot of interest in what people are trying, but there is no conviction as to what is really going to work or not. I get the feeling that my urologist won't positively endorse anything, but he's watching me carefully to see what happens.

This is an interesting time to have this cancer because there's so much happening all the time. Every time your magazine Prostatepedia comes out, I read something new.

Extraordinary things are happening. I think that if I can hold this long enough, who knows what miraculous cure might come out of the woodwork in the next few years?

That's right. And the changes to your diet and lifestyle will only help your overall health.

Mr. Meszaros: Absolutely. That's what I've always argued, that these are all things which are good for all the ailments of age and affluence, from which we all suffer. If I ever need surgery or other conventional treatment, I will be in better shape to deal with it.



University of Melbourne Medical School 150th Anniversary Sculpture

University of Melbourne Medical School 150th Anniversary Sculpture

Did your diagnosis have any impact on your mood? Many people report feeling depressed or anxious when they receive a cancer diagnosis.

Mr. Meszaros: No. Remarkably. Everybody feels a bit down now and then for all sorts of reasons, but I don't think I got depressed. I suppose I got a bit tired. I took it on as a bit of a challenge.

There is an extra discipline you have to apply to your life to stick to a diet and an exercise regime. It's on your mind a lot because there are elements that will affect your life if you do or don't do them.

In that respect it has changed my life quite considerably. But in terms of living my life, doing my work, my family relationships, and everything else, I don't think it has had a great deal of impact.

My family didn't believe I could stop drinking my daily 2 glasses of red wine or stick to my diet. But I made the decision. Either I would have the operation, which has a lot of undesirable effects, or do this.

After I joined my prostate group and observed my fellow group members, of the people who have been operated, at least 1/3 have had recurrences of some sort. The operation was sold to me as the fix to my problem. Clearly that's often not the case.

I felt that if I could deal with prostate cancer in another way and not have the operation, then it may well be a more positive result than having the operation and then still being at risk of having all the complications of a recurrence, as well.

You can always choose to have the surgery later.

Mr. Meszaros: That's right. Because I'm trying these other means of treating myself, it doesn't mean that I have completely abandoned the possibility that I'll need conventional treatment down the track. That's all still there. Surgery, ADT, radiation, or brachytherapy —they're all there, and they're all evolving week by week.

I'm 72 and won't last forever. The question is whether prostate cancer will get me or something else will first.

Most men with prostate cancer die of something else.

Mr. Meszaros: That's right. The real trick is sorting out that 10-15% of men who have aggressive cancers that will kill them from all the others that won't.

Can you speak a bit more about your exercise program?

Mr. Meszaros: Last year I became aware of the benefits of weight and resistance training. Good Australian research [see this month's conversations with Robert Newton for details) has shown that weight training and resistance training stimulates the body to produce more killer cells. Killer cells go out into the system and kill off infections and mop up cancers or potential cancers.

My wife's had bowel cancer. Together, we consulted an accredited exercise physiologist who designed a weight-training program for us. About three times a week I will do 30-40 minutes of training with weights and rubber bands.

I've also designed this little sequence of exercises that I do and I've built myself up quite noticeably. They seemed to be paying off.

But even conventional medical schools recognize that mental attitude has a huge impact on the outcome of a disease or an operation.

Because I have tackled this head-on in my own way, that fact in itself might be having a positive impact inside the body.

You're engaged, talking to your doctor, talking to other patients, researching.

Mr. Meszaros: That's right. When my GP asked why I didn't get the operation I replied: "Most GPs only see one or two prostate patients a year." They don't have a lot of experience in this and they don't even understand recurrence rates. The operation is by no means proof against recurrence or further problems."

Do you have any advice for other men with prostate cancer?

Mr. Meszaros: It does take a deep commitment. I've found it increasingly difficult to stick to the diet because vegetarian food is often pretty dull. I do sin a little bit and have a bit of chicken, and once in a blue moon, I'll have a bit of red meat. I had pasta marinara last night, which my wife cooked. It was absolutely delicious.

Do you find your exercise program difficult to follow?

Mr. Meszaros: Sometimes it really takes an effort. As with many things, it's the starting that's hard. It's the effort of getting up from the television, getting the weights, getting myself organized, and doing the first five minutes. Then I'm into it and it's okay. I feel good at the end of it. Often the first step is the hardest.

If I stopped for a couple of months, I think that it would be hard to get back to it.

I studied architecture originally. I have lunch every now and then with the chaps I did architecture with 50 years ago. Most of them have sagging bellies, sagging shoulders, and poor posture. They all look like 72-year-olds. I'm not suffering from most of that. There is a satisfaction in seeing that I have actually maintained myself against the odds.

People routinely think I'm 10 years younger than I am. Not that I'm aiming for beauty contest wins or anything like that.

It's a visual indication that what you're doing is making a difference?

Mr. Meszaros: It is. It's a validation that what I'm doing is doing me good. I want to go on being able to do what I've been doing all my life for as long as I possibly can. I get a huge amount of fun and pleasure out of my work, and if you're not reasonably fit, you can't do what I do.

I've got a brother who's 10 years older. He recently had a pacemaker, but he looks about 15 years younger than his age. He has also worked diligently on keeping himself fit. There's a sort of philosophy that runs in our family that you look after yourself and take responsibility for yourself. He had a bowel cancer 23 years ago. He recovered remarkably well because he was fitter than average to start off with. When he came out of hospital he started taking himself to a gym and really worked hard at building himself back up to what he regarded as his normal. People were absolutely amazed at the way, firstly, how he recovered, and secondly, the diligence with which he got himself back into shape.

I suppose we are more independent thinkers than some people, and that independence translates into taking responsibility for yourself and your medical condition.

Taking ownership of your disease?.

Mr. Meszaros: It's up to me what happens to me. On the other hand, you have to be sensible. If things are looking really black, then there are conventional means, and I will run with that if that's what I have to do.

But my advice to other people? Everybody is diagnosed at a different point and a different degree of severity. One has to go with the situation at the time.

Then you've got to become educated about prostate cancer. When somebody comes to me to commission a sculpture, the first thing is I've got to do is become interested in the subject. The next thing, I've got to do is become educated in the subject. Once I've done those two things, I can form an idea as to what I think is important about the subject and then express it as a work of art.

Now, in principle, dealing with a medical situation is not that different. You've got to be interested in your own health. Then you've got to become educated in whatever issues you've got, and then you're in a position to form an opinion as to what treatment you should reasonably have.

There are some interesting parallels in life and medicine. The processes you put yourself through to reach conclusions have similarities in that respect.

You can't solve a problem if you don't understand it.

I've spent the last forty-odd years learning how my mind works in an artistic sense and then learning how to apply that knowledge in a conscious way

"You've got to be interested in your own health."

to find solutions to artistic problems. Now, I think I've done exactly the same thing with the prostate cancer.

It starts with being positive that you can do something for yourself. You don't just go along with whatever your doctor tells you without querying it.

Now, some people who are diagnosed much further down the prostate track may not have these options. They just want to stay alive.

The other element is this exercise regime. It used to be that people who were undergoing treatment were told to go home and rest. Now the recommendation in Australia is that they should go straight to the gym and do a workout. That apparently has a huge effect in minimizing the ill effects of radiation and chemotherapy as well as, as I said before, getting you in better shape generally to deal with what's going on in your body.

Australia is doing some world-leading research on exercise, cancer, and cancer treatment.

I will shortly take part in a monitored 12 week weight training program run by the Australian Catholic University with the aim of working out the effectiveness of weight training. Pp[1]

Visit https://meszarossculptor.com/ to see more of Mr. Meszaros's work.

Dispatches from the Hill: Cancer + Job Loss

Drew Salens, VP of Patient Programs at Zero - The End of Prostate Cancer, offers his insights on how a cancer diagnosis can impact job loss and financial burden.

At the time of their prostate cancer diagnosis, eighty percent of patients said that they needed more help than what they'd received from their doctor. Our new patient program, ZERO360: Comprehensive Patient Support aims to fill that need.

We launched the program just over a year ago in partnership with the Patient Advocate Foundation. ZERO360 is a comprehensive patient support service that provides free, confidential expertise to help guide patients through their cancer journeys. Each patient receives one-on-one support from a case manager dedicated to helping him navigate his prostate cancer journey.

Recently, our case managers assisted a 56-year-old Stage IV prostate cancer patient who'd lost his job shortly after diagnosis. After moving in with his daughter, he had unpaid bills, no income, and no savings.

That's where ZERO360 came in. His dedicated case manager assisted him with applying for Social Security Disability Income (SSDI) and food stamps, and helped him sort out his Medicaid application so he could receive retroactive coverage for his unpaid medical bills. The work the case manager did on his behalf relieved the patient of worry about unpaid bills and helped him focus on his health.

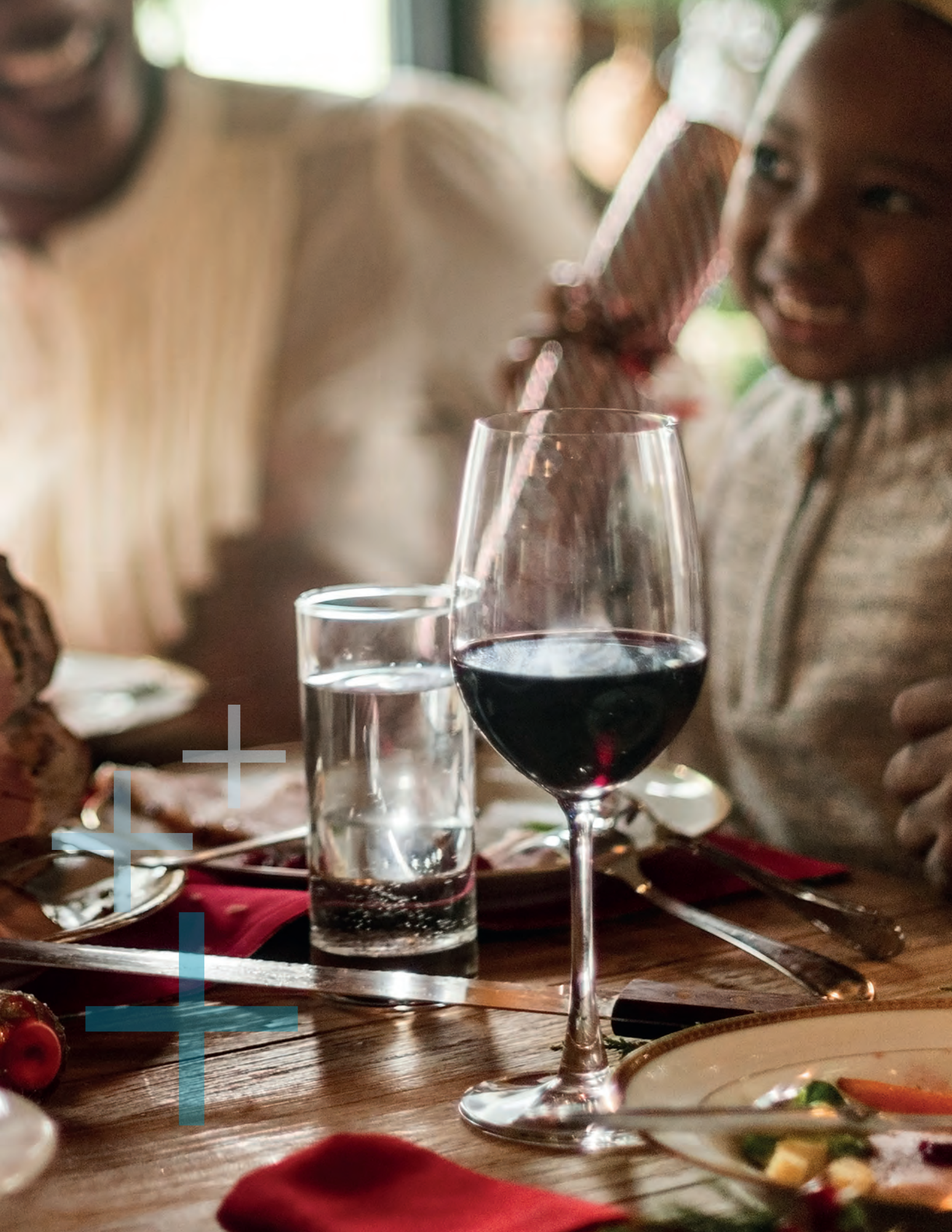
After helping him with his health insurance and SSDI needs, the case manager turned her attention to his prescription and nutritional needs. When the patient was again hospitalized, the case manager provided continued support via conference calls to ensure that all paperwork was moving forward. At the end of his experience with ZERO360, the patient was enrolled in SSDI and Medicaid programs, had retroactive health coverage, had his 12 prescriptions covered, and his food stamps application filed.

On average, 69 percent of patients enrolled in ZERO360 need insurance and financial assistance. Most of these patients are over the age of 55, and about 45% of them have Stage IV disease. This vital assistance to men battling prostate cancer allows them to focus on their health and fighting their cancer.

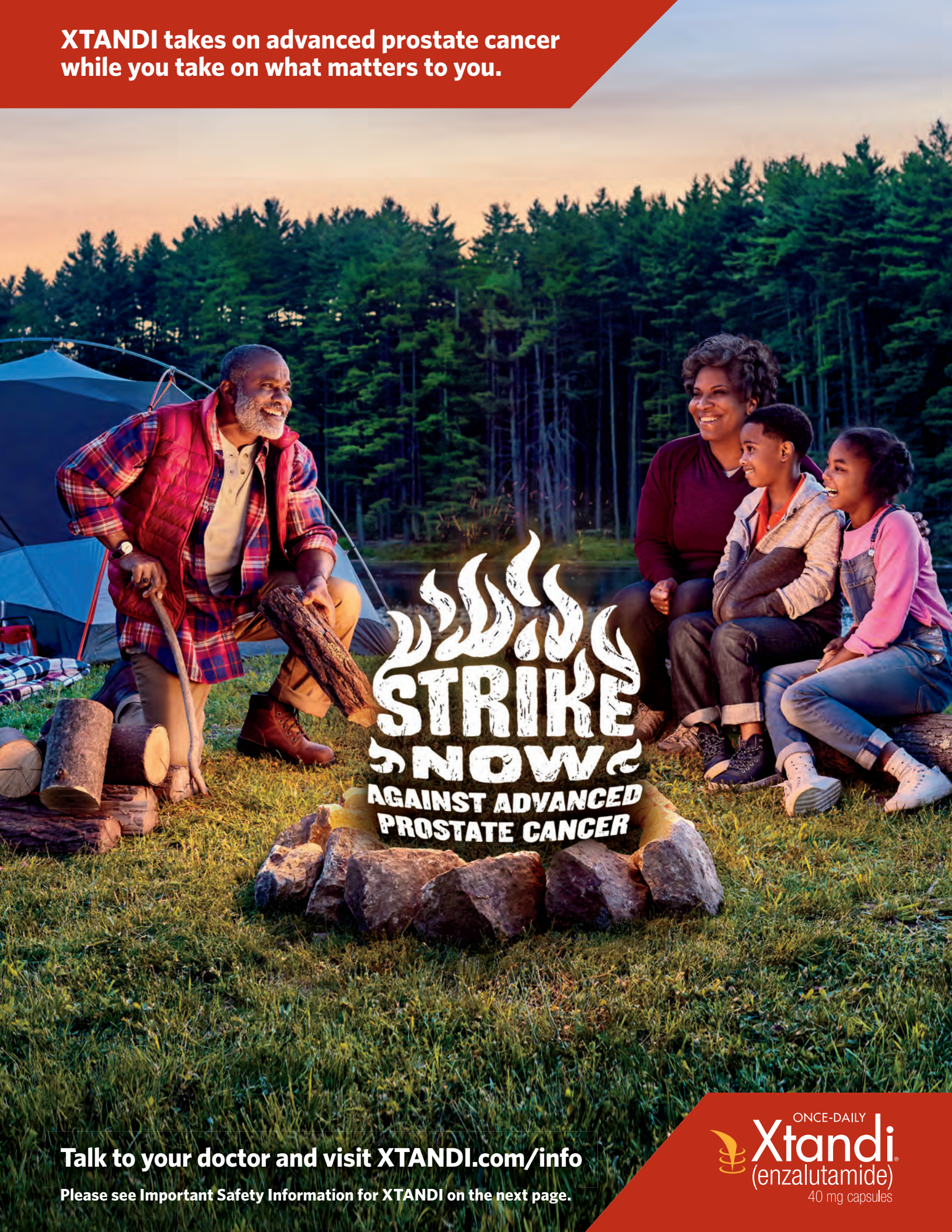
For some, that means consistent access to prescribed treatments and therapies, help making treatment decisions, and a better understanding of their coverage options. For others, it's help accessing financial resources to pay for treatment, and support for other needs patients encounter from diagnosis to survivorship. No matter where you are in your prostate cancer journey, ZERO360 can help you navigate it. Learn more at www.zerocancer.org/zero360. Pp

About ZERO - The End of Prostate Cancer

ZERO — The End of Prostate Cancer is the leading national nonprofit with the mission to end prostate cancer. ZERO advances research, improves the lives of men and families, and inspires action. We're building Generation ZERO, the first generation of men free from prostate cancer, through our national run/walk series, education and patient support programs, and grassroots advocacy. ZERO is a 501(c)(3) philanthropic organization, accredited by the Better Business Bureau, with regional chapters across the country. We dedicate 84 cents of every dollar to research and programs. For more information, visit www.zerocancer.org



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.

astellas MEDIVATION

QUESTIONS ABOUT XTANDI?

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

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

What is XTANDI®?

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.

It is not known if XTANDI is safe and effective in children.

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.

What should I tell my healthcare provider before taking XTANDI?

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 effective 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?**"

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.

How should I take XTANDI?

- 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
- 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.

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

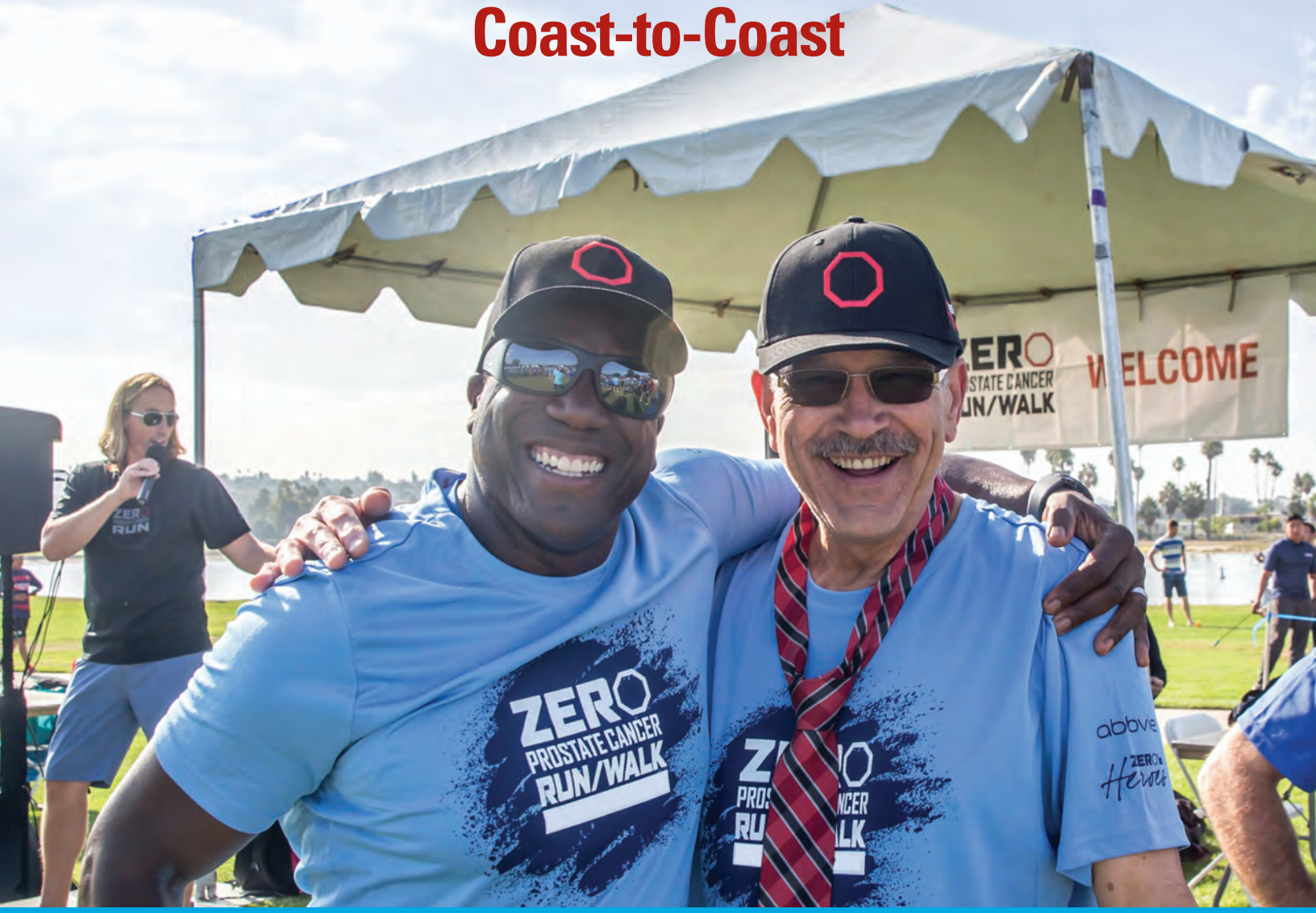
This Patient Information has been approved by the U.S. Food and Drug Administration.

Revised: October 2016

You can join the fight against prostate cancer!

2018 ZERO Prostate Cancer Run/Walk Events

Coast-to-Coast



Coming to a city near you.

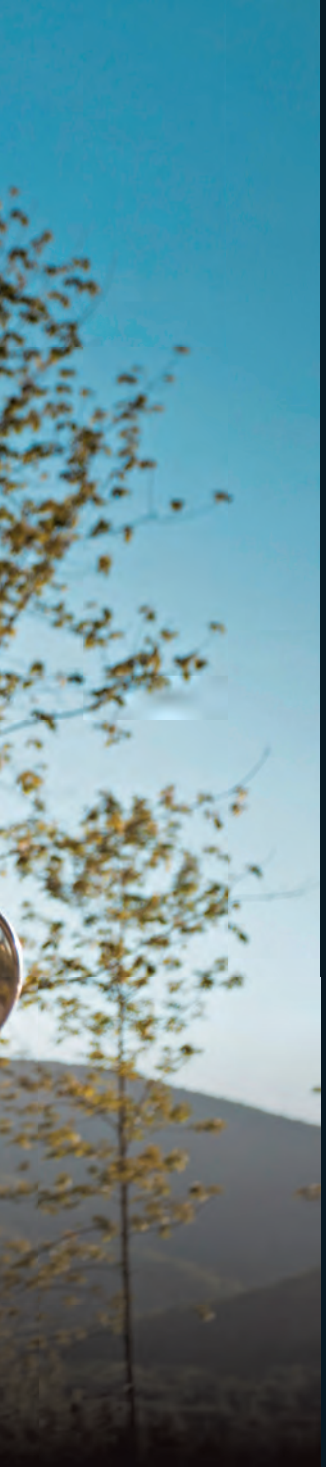
ZEROPROSTATECANCERRUN.ORG

ZERO

THE END OF PROSTATE CANCER

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!

January:
Immunotherapy

February:
Stress + Prostate Cancer

March:
Dealing With Recurrence