## **Risk Factors for Prostate Cancer Webinar Transcript**

Becky Campbell: Good afternoon. Good evening, and welcome to this PCF Webinar on risk factors for prostate cancer for patients, family, and friends. We thank you so much for taking the time out of your evening tonight to join us. My name is Becky Campbell, and I'm senior manager of medical content here at PCF. And just to let you know, during February we have been inviting people to "Give an Assist" to their family and friends. If you've already been diagnosed with prostate cancer, we encourage you to share this information with someone who might benefit. And if you are living with prostate cancer, we will have a section on recurrence and risk for recurrence that we hope you'll find helpful.

So please, whatever you take away tonight, please go out and share with loved ones who you think may be able to use this information.

So here's a little bit of our agenda for today.

We're going to talk about prostate cancer risk factors in general, we'll have some cases on family history, the importance of race and ethnicity. We'll talk a little bit about environmental exposures and military risk. We'll have a lightning round with some myths and facts about risk for prostate cancer. And then we'll close with a case about recurrent prostate cancer and risk factors and potentially ways to reduce risk of recurrence.

As you can see, this webinar is being recorded, we will send out a link to the recording by email in a few days.

If you have questions, please feel free to put them in the Q&A section at the bottom of your screen. We'll get to as many as we can. We also received some excellent questions in advance. Just to let you know that PCF cannot provide individual medical advice, so please be sure to consult your healthcare provider for that type of guidance.

And if you do have other questions that we don't get to tonight, you can find more information on our other recorded webinars on pcf.org, and I'll also be putting some links in the chat for other types of information.

Just a brief overview about PCF, in case you're not familiar. So our mission is fairly straightforward, but not a simple one. We were founded in 1993, with the aim of reducing death and suffering from prostate cancer. We do that through funding research projects - over 2,200, and counting - around the world.

Many of the therapies used today were developed with early-stage funding from PCF. And we continue to research new targets, new ways of delivering more precise medicines and

diagnostics. We also have been funding research to help improve survivorship related to diet, exercise, and those sorts of things to improve patients' quality of life now that patients are, in fact, living longer after a diagnosis.

We also aim to share knowledge with the community, such as through webinars like tonight's. You can go to pcf.org - there's a couple of examples of the guides you can find on our website. Our next webinar is March 27<sup>th</sup>, focusing on exercise and mental health, and I'm excited to announce that we will be launching a new pcf.org very soon to help you better find these resources.

I also encourage folks to check out our newest venture, Prostate Cancer Patient Voices, where patients tell their stories in their own words.

And you can also help support our mission, if you feel so inclined. In 2024, we funded over 34 million dollars in research awards. We have one in particular that I'm going to highlight - the Bayer PCF Young Investigator Award. And this researcher is addressing really community needs of patients with prostate cancer and involving those community members in the development of resources that are best going to serve that community and with PCF funding. And this is Dr. Samuel Washington, who is our host for tonight.

So you can go to support our mission if if that feels right to you.

Without further ado, I'd like to introduce our panelists. So our host is Dr. Washington. He's an associate assistant professor of Urology at UCSF. He is a practicing urologist, caring for patients with GU malignancies, and his research focuses on racial and ethnic disparities, including socioeconomic factors. And he'll be speaking a little bit more about his research later in the program.

We also have Dr. Leanne Woods-Burnham. She is a 2020 PCF Young Investigator. She is at Morehouse School of Medicine. Her research focuses on health disparities--prostate cancer disparities from the lab all the way into the community. She's very active in screening and outreach within the Atlanta area.

And then finally, Dr. Sokolova of OHSU. She is a medical oncologist, focusing on genetic risk factors and prostate cancer, and cares for patients there up in Portland. She is a 2022 PCF Young Investigator.

So I'm going to hand it off to our host, Dr. Washington. He's going to give us a brief overview of prostate cancer risk factors, and then we'll get into some of the details. So thank you all once again for joining Dr. Washington. Thank you.

Dr. Samuel Washington: Thank you. Excited to be a part [of this]...Let's talk a little bit about prostate cancer risk screening and steps beyond. Now, we know in 2025 alone, there's going to be over 300,000 new diagnoses of prostate cancer.

Prostate cancer continues to be the second most common cause of cancer deaths. For this year, there's expected to be over 35,000 deaths attributed to prostate cancer.

Since 2014 we've seen a consistent rise in cases over time and not just overall, but in more advanced disease. And we've seen that these increases for disease that's gone outside the prostate to areas close by the prostate as well as areas in the body. Farther from the prostate, or what we call "distant-stage disease" have also begun to increase.

And we know that some of this is related to diagnosis, better diagnostics, better evaluation strategies that we have, but also many other factors contributing big picture. We know that the number of cases have changed over time, and we see that that change over time is not impacting every group of people the same. We see some groups continue to harbor a higher burden of disease, such as non-Hispanic black patients, and we continue to see that over time. For some groups, it has changed and decreased, while for others that benefit has not been seen to the same degree.

And even looking within the same state, we're seeing differences based on where you live, drilling home the point that where you live, where you get your care, what type of care you get, are all things that contribute to the observations we're seeing, both in terms of new diagnoses and treatment and survivorship after diagnosis.

Now, we know when we talk of risk, what's your chance of getting prostate cancer throughout your lifespan? There's going to be multiple things that are driving that overall risk that we're seeing -- older age, family history, biology. race and ethnicity, and how that's impacted by the society and areas in which you receive care, toxic exposures, particularly for those with military history, diet, lifestyle, exercise, as well as social needs, social drivers of health and structural barriers to care.

Now we know that the prostate cancer journey and process moving from screening doesn't stop there. You get the test--the PSA test--to know your number. Then you need to have discussions of what further testing should be done. Should you proceed to a biopsy? Do you need treatment, or can we surveil this safely with active surveillance, and even after treatment? It's still not the "one and done," so prostate cancer, its management and survivorship or "thrivership," as we call it locally, is a process and a pathway, and a journey that starts with screening. But every single step of the way must continue to proceed in a timely and high-quality fashion, to reduce the chance of worse outcomes.

Now I'm going to pass things over as we go over a few different cases. Our first case will be with Dr. Sokolova discussing family history.

Dr. Alexandra Sokolova: Hello, everyone. I'm really honored to be part of the webinar today and I'll be talking about role of genetic risk factors in developing prostate cancer. So, first we'll talk about a patient case. Mr. Z is a 58-year-old male who developed urinary retention in October 2023. As part of the workup for urinary retention, his PSA was checked and was elevated - 16. He decided to undergo a TURP procedure for his urinary retention, the transurethral prostate resection. And the biopsy showed--the procedure pathology showed Gleason 9 prostatic carcinoma. He was diagnosed with high-risk localized prostate cancer and chose to undergo radiation with a plan of two years of androgen deprivation therapy. He started treatment, his PSA started nicely declining to 0.13, and at this time he found out that his brother has a pathogenic germline--meaning he was born with it--mutation in BRCA2.

So let's look at Mr. Z's family history of cancer. We call this a family tree. And you can see right here this is a square with the arrow on it. This is our Mr. Z, who was diagnosed with prostate cancer at 58 with a high Gleason score and PSA of 16. And this is his brother who was an index case, meaning the first case in the family who was found to have a mutation. The reason his brother was tested, because his brother had male breast cancer. And so, his brother's doctor decided to test him, they found out he has a germline BRCA2 mutation. He shared with his brother and that prompted our Mr. Z to get testing, finding out that he also has the BRCA2 mutation. If you look at his family history, we can see that there's a lot of different cancers, actually on both mom's and dad's side. So, mom, there was prostate cancer in two uncles in their sixties. And on the dad's side there was--his dad had prostate cancer -two aunts with breast cancer, and one with ovarian cancer. So, when we see a lot of ovarian, breast, pancreas, cancer in the family, there's also suspicious with some sort of a germline component, inherited mutation that might be responsible for it. Because all those cancers could be associated with the same mutation.

So what do we know about germline mutations in prostate cancer? Well, first of all, we know that they--having the germline mutation, being born with a germline mutation, in the BRCA 1 or 2 gene, increases the risk of developing prostate cancer as long as other cancers. But focusing on prostate cancer, it's 4.5 to 8.6-fold increase of developing prostate cancer. Also, we know that if you already have prostate cancer, and we know that you have a germline mutation, BRCA 1 and 2 gene, it's also associated with a kind of more aggressive phenotype. So patients with those mutations have more advanced stage of

diagnosis, have metastasis at diagnosis, have a younger age diagnosis. They usually have worse clinical outcomes. They seem to have a shorter survival compared those who do not have germline mutations, those non-carriers.

So who should have germline testing? First of all, let me just kind of pause for a second as...what germline testing is. Germline means—was given through sperm through [inaudible] mom and dad, something that you born with, and usually tested by doing a blood test or by doing saliva tests. In certain scenarios, we can also do a biopsy of skin. But most of the cases it's either just spit in a tube and do saliva test or do a blood test.

So when do we think about germline testing in prostate cancer? So everyone who has highrisk localized cancer, PSA over 20, T3 and Gleason 8 and higher because--and everyone who has metastatic prostate cancer. Because we know that those two patient populations kind of enrich with germline mutation, they have a higher chance of having a germline mutation. So everyone who has those two stages of prostate cancer should get germline testing.

We should think about or consider it if there is evidence of intraductal/cribriform histology, because we also see potential slightly higher risk of having those mutations in this population. And then everyone has a family history. That meets certain criteria. And if the family history is suspicious for [inaudible] breast and ovarian cancer syndrome, so that's a cancer syndrome that's associated with pancreatic, ovarian, breast, prostate cancers. So we see a lot of those cancers in the family, as Mr. Z's family, or if we have families, what's considered to be suspicious for Lynch cancer. And those are colorectal, endometrial, gastric, ovarian, and others. So kind of what is considered close relatives and having those cancers in the family. So current criteria recommend germline testing in men with prostate cancer if he has at least one or more relatives with pancreatic, ovarian, breast cancer, colorectal. For prostate cancer, we think about either being kind of an earlier age prostate cancer, similar with breast and colorectal, or high-risk metastatic and high-risk. Or if there's two more relatives with any stage in any age of breast cancer or any age of prostate cancer. For Lynch syndrome, we're looking at three or more relatives with colorectal, endometrial, gastric, ovarian, pancreatic, urothelial, which is bladder, glioblastoma, bile duct, or small intestinal cancers. Anyone that has Ashkenazi Jewish ancestry, because again, in this patient population, there is a higher frequency of those germline mutations. If anyone has a known germline mutation, if you know, "Hey, my nephew, my niece, my uncle, someone in the family has a mutation," then we should test for this mutation. And if there's any personal history of breast cancer.

So how's germline testing done? It could be either referral to genetic counselor, you meet with a genetic counselor, and then they order the tests. It could be done by a patient themselves. A lot of companies offer patient-initiated testing such as COLOR or Invitae. They don't involve insurance. You kind of pay out of pocket. The average cost is about \$250, might be higher now. And there is some patient-facing research where patients can register themselves online. And the test gets--the test kit gets sent to their house. They just spit in the tube, send it back and get results, virtually as well. And so **Gentleman** is a study that provides testing for all metastatic prostate cancer patients. And PROMISE provides testing for anyone with prostate cancer. So if you are today listening and you have prostate cancer, you are welcome to register for prostatecancerpromise.org and get your free testing today.

Another important aspect is cascade testing. So we talked about Mr. Z's family where his brother got diagnosed with a germline mutation, and then he shared with his family, and Mr. Z got tested. So it's really important once we find a mutation of the family to get family members tested as well. We call it cascade testing. And PCF is--Prostate Cancer Foundation is supporting a project research that we're leading here at--which is [inaudible] to help do this cascade testing to help protect family members and loved ones of our prostate cancer patients, to find those mutations in the family and implement early cancer diagnosis or prevention strategies. So it's called cascade germline genetic testing in families with prostate cancer. Right now you see the email to reach out or phone to reach out if you're interested. If you are a patient with prostate cancer and you have a germline mutation, we can test your family members as part of this research study. The family members can be living anywhere in USA. We just, again, send the kit to them, we explain to them why they need germline testing, and we can test them for those mutations. So please reach out if this is something you'd potentially be interested in, and we're happy to help your family.

If you are a patient with prostate cancer, you should--and you haven't--don't think you've had germline testing done yet, talk to your provider, see if this is something that you would be eligible for and advocate to get the germline testing because it could also change treatment in prostate cancer. This is not the topic of today's talk, but it could increase-change the treatment of prostate cancer. If you have family members and you have a germline mutation, knowing that they have a germline mutation can change how we screen them, not for prostate cancer, but other cancers as well. So please share with your family, reach out if you're interested in cascade testing, and I'll be happy to enroll your family members if they're interested. Thank you.

Dr. Samuel Washington: Perfect. Now let's move on to another important topic of the impact of prostate cancer for men of Black race. Dr. Woods-Burnham?

Dr. Leanne Woods-Burnham: Okay, perfect. Thanks so much for the opportunity to join our other esteemed speakers today to talk about how prostate cancer impacts certain populations a little bit more aggressively or differently. And so, for my topic I'm introducing today, is prostate cancer among Black men. There's so many different reasons that go into why Black men are more likely to be diagnosed at a younger age, to be diagnosed with more aggressive disease. And if you look at the graph here, they are more than twice as likely to die from the disease as well. These are death rates here.

A lot of men in my family and family members of friends of mine, unfortunately, have a relatable experience of men in our family being diagnosed with prostate cancer at younger ages. And so that's really what sort of drives what I do for my career these days, which is looking at prostate cancer in Black men. So, there's biological and genetic drivers. And we spoke a little bit about genetic testing a little bit ago. But we know some genes we hear of like BRCA genes, SPOP genes. There's different tumor suppressor genes that are associated with genetic ancestry. And so some of those genetic variants, we know, are more likely to occur in Black men than other populations.

But if biology and genetics were the only contributing factor, that is something that we could target eventually and overcome by itself. And that would be really great. But there's these other factors that are shown here. For example, we have social determinants of health. This can include access to health care. Obviously, if you don't have access to quality health care, that's going to affect your outcomes over time.

There's also neighborhood risk factors that we have to think about. There's been an interesting study that's come out recently by Dr. Stefan Ambs, where he shows that some of these neighborhood factors, they actually can influence the association of genetic ancestry with prostate cancer risk. So that's interesting that there's this interplay between not only the ancestry, but what is going on in the environment around a person as--or growing up through life, and then in their current environment that is driving some of these differences that we see.

We know, of course, access to screening is going to drive some of these outcomes. Because, according to American Cancer Society, if we can detect prostate cancer when the disease is still localized, when it's early disease, 5 years out, there's a 99% survival rate. So that is extremely motivating incentive for us to make sure that we are screening all men at an appropriate age, but especially these populations that we know that are at higher risk to be diagnosed at a younger age. There's also a lot of studies to sort of look at these multiple factors. Right? We could talk about biology. We can talk about social determinants of health, I know, and would like to mention that Prostate Cancer Foundation supports what is called the "RESPOND Study..." It stands for research on prostate cancer in men of African ancestry, defining the role of genetics, tumor markers, and social stress. This is the largest scale study of this type, which is really interested in looking at these multifactorial issues that are driving worse outcomes in Black men. I encourage for men to sign up for that study. You can go on Prostate Cancer Foundation's website and look into that if you're if that's something you're interested in or for your loved one. But it involves completing a survey, also providing a saliva sample so that some genetic analysis can be done, and then also providing permission for tumor tissue that's already been acquired in the past to be accessed for research studies of different investigators who are interested in this topic and bettering outcomes.

I was also asked to talk about what my lab does at Morehouse School of Medicine. So, I am an assistant professor in the Department of Surgery at Morehouse School of Medicine in Atlanta, Georgia, also very proudly funded Young Investigator with Prostate Cancer Foundation. And so they were really among the first to take interest in my research study, which looks at...the HER2 gene in prostate cancer. A lot of us on the call are familiar with HER2, as it pertains to breast cancer in women. But you may be surprised to learn that HER2 is a receptor on the cell that is actually associated with just normal expression on a cell. Right? It's not bad to have HER2 receptors on your cells.

But when we are talking about a HER2 overexpression of these receptors, so if you look in this figure here, when there is too many HER2 receptors, then they are binding to other HER2 receptors, and they are turning on genes in the cell that we know drive metastasis, we know drive cell proliferation, basically allowing the cancer cell to thrive and multiply and travel throughout the body, which we all know is not good for cancer outcomes. And so what my lab looks at--we have a lot of different approaches that we take in the lab, and it's not on our own. I wanted to make sure to show here a lot of our collaborative partners on the screen and other funders who are supporting this work. As we're interested in looking at HER2 expression in men with prostate cancer and seeing what are those associations with genetic ancestry? What are these associations with disease stage and clinical features and treatment outcomes? And evidence that we and another lab in the nation has shown is that we believe that Black men are more likely to have HER2 expression on their prostate cancer cells.

While we're talking about screening, it's very important to acknowledge that screening in the United States does not necessarily occur early enough in many clinics for our high-risk

populations. And so we know that the screening recommendation guidelines have fluctuated over the years, right? And so when these fluctuations happen, sometimes not every clinic is on the same page. Some clinics screen later, some clinics screen earlier. And so there's been challenges with uniformity. When we're looking at that Prostate Cancer Foundation released guidelines just last year espousing for screening in Black men between the age of 40 and 45 and definitely taking into account family history. But what we've done at Morehouse School of Medicine, is we have initiated what's called the "Prostate Cancer Precision Prevention Program." We call it PCP 3. This is done--this is codirected by Dr. Rick Kittles, shown there, who's an international leader in prostate cancer disparities and also genetic ancestry analysis as it is associated with disease progression, and also Ms. Pam Cooper who is the director of our program here in this PCP 3 program. What we do is we go out, we collaborate, and we leverage our community partnerships, not only in metropolitan Atlanta, but also in rural Georgia, and we provide free PSA testing.

And then we make sure that men receive their results back, and follow up is implemented various different avenues depending on the insurance status of men, and where they live at. In the first year that we developed this, we've been able to screen over 1,200 men in Atlanta, and, some of you may know, Dexter King passed away from prostate cancer, which to me was at a young age in his early sixties. And there's a lot of high public figures that are coming out, who are being diagnosed with prostate cancer, who are dying from prostate cancer. And so one thing that we were excited and honored to do, honestly, was to partner with the King Center and offer free prostate cancer screenings after following Dexter King's death last year.

I want to end by also talking about something that I'm very excited is going on in the Atlanta area for those of you who are from the southeast region of the nation. You may know of Grady. Others of you may not, but Grady is one of the largest public hospitals in the United States, and is doing amazing things when we're looking at addressing prostate cancer in these high-risk populations.

A little bit of background: Grady patients are serviced by Morehouse School of Medicine and Emory physicians, and they are known for their trauma center for one. But we also know that they are excellent at their oncology care, and looking at metabolic diseases as well. And so, Grady made the decision in 2023 to roll out screening for men who are over the age of 40 that enter into the clinic. And they built that into their electronic health system and so for men who we know they serve a very high-risk population for prostate cancer. We're really seeing amazing results where men are being able to be diagnosed in greater numbers at the earlier stage, right? Because what we really want to prevent is men being diagnosed in a more advanced stage, which, unfortunately, the treatment options are much more limited and much less chance for a cure at that point. And so I just wanted to highlight when I'm talking about what's going on at Grady. That's we're talking about clinical screening. Right? So at Morehouse School of Medicine we're working on screening in the community, but also partnering with Grady and what they're doing in terms of the clinic. And so with that, I encourage, if you're on the call, if you're a Black man with prostate cancer, if you have family members or friends who are at a higher risk to develop prostate cancer, Prostate Cancer Foundation offers a great resource online where you can go to www.pcf.org/knowyourrisk and it can break it down. If you go to that site, many more in much more detail of what your risk factors are and things that you can do to improve your outcomes, should you be diagnosed with prostate cancer.

Dr. Samuel Washington: Perfect. Now, I'll plan to go over a third case, talking about military exposures and a little bit about environmental exposures as asked about during some of our kind of pre-presentation questions.

Now, I think, for those of us who work clinically in the VA, we've all seen veterans who served in the military during Vietnam, and had some level of exposure to Agent Orange. We treat them the same in terms of our diagnostic steps. We still check that PSA. We still do a biopsy to understand what disease may be present and where it is. Is it contained inside the prostate? Is it outside the prostate? And then work together to find that appropriate treatment that's best suited for them.

Now for this patient, he underwent surgery. PSA remains undetectable, meaning there's no lab-based evidence of disease coming back. But we know things like Agent Orange, when we look at large studies of large groups of veterans who have that exposure...they were found to have an increased risk of prostate cancer. Not just that, but a higher risk of high-grade cancer as well.

Now, within the VA system, we didn't see differences in outcomes after diagnosis, and these were a lot of men who were already plugged in with healthcare in the VA to already get the diagnosis. So we don't see Agent Orange or other exposures like that being an inherent driver of worse outcomes as long as we identify that disease early enough to treat it appropriately before it escapes.

The other question that is coming up more and more in the literature and in the news is microplastics and their presence and prevalence both in the food and in the environment. And although we've seen correlations in other diseases, we're now finding microplastics present both in normal tissue as well as cancer tissue in the prostate. Now, that doesn't mean that there's a clear red herring there, that this is the absolute cause. But these

associations, these observations, where both of these things are present, does point to a potential higher risk. But we definitely need more information as we continue to understand not only where microplastics are present, but at what concentration, what amounts they may accumulate or store in the body, and how that storage of those plastics may impact outcomes in the development of cancer down the road.

Now we will take a few minutes and go over a few other risk factors for diagnosis that are commonly asked. A few kind of common myths, if you will.

Dr. Sokolova, I'd like to ask you the first one. A common question that happens both in clinic and outside is, "What is the impact of diet, exercise, or the lack of exercise and obesity on development of prostate cancer?"

Dr. Alexandra Sokolova: Thank you. I think it's a very common question and concern for [a] patient, is, "What am I, as a patient, can do to decrease my risk of recurrence and improve my outcomes?" And the short answer is there's no silver bullet that say, if you eat "this" sort of food, or you do "this" particular exercise, that will have very direct impact on your cancer, and we know that this cures cancer. But we do know that certain diets are beneficial, and certain diets might not be beneficial. So, talking about food, we want to be talking about a healthy food or Mediterranean-like diet, where we eat a lot of vegetables, specific vegetables that could be useful for prostate cancer. I want to be eating whole grain, want to be eating less of animal product and more seafood and plant-based diet.

Certain foods that might not be beneficial for prostate cancer are cured meat and any food that kind of has nitrous in it. Dairy products also has been associated with some increased risk for prostate cancer patients. We--so we want to be looking for something that will be decreasing inflammation in your body and yet nurturing your body with healthy vitamins and nutrients. It's also important to remember about bone health. You want to make sure you're getting enough calcium from your food sources and thinking about vitamin D.

Most of us don't get some exposure to produce enough vitamin D, and do need to be on vitamin D supplementation to help support our bones. When we talk about exercise, exercise is magical. It helps with most side effects that our treatments can cause. It also helps reduce risk of prostate cancer recurrence. It improves bone health. It improves mental health. So as little as 30 min a day, a kind of a fast walking has been shown to have beneficial impact on prostate cancer outcomes. And so I do recommend my patients to engage in exercise routine, and you want to be aiming to something that can be sustainable.

What we don't want you to be doing is going to the gym and overdoing it and hurting yourself so you can no longer exercise. So, starting slowly, whatever you think is feasible and kind of building your way up. But again, even 30 minutes of kind of brisk walking can have a significant impact on your health. [Inaudible] Visceral fat - the fat that's like around the belly and goes into your organs is associated with worse outcomes and higher risk of diabetes and other mortality causes, so kind of controlling your diet, controlling your exercise, controlling your weight could be beneficial for your overall health and prostate cancer health specific.

Dr. Samuel Washington: Perfect. Thank you so much. Another question that we have is about smoking and risk of prostate cancer. Dr. Woods-Burnham, do you have any insights you'd like to pass on to us.

Dr. Leanne Woods-Burnham: Yes. So smokers, we know, have increased risk for cancer in general, right? But when we're talking about prostate cancer, there is a 50 to 60% increased risk of developing prostate cancer - not only developing prostate cancer, but there's an increased risk of developing aggressive prostate cancer. So you really want to be considering that. And for men who are already diagnosed with prostate cancer, smoking increases the risk of recurrence after treatment. A lot of times when we think about smoking, we're thinking of cigarettes back in the day, but it's important to recognize that when we're talking smoking we're talking tobacco and nicotine, right, in any form. So you want to be cognizant of if it's not cigarettes, is it cigars? Is it chewing tobacco? Is it a tobacco wrap? You know, the verdict is yet to be seen on what vaping effects will be. But when we're just thinking about smoking in general, it is--it does increase worse outcomes for prostate cancer patients.

Dr. Samuel Washington: Perfect. A few other questions that we commonly get just in standard practices. "Well, I have a big prostate. Am I more likely to get prostate cancer?" Or, "if I'm concerned about prostate cancer, can I drive that PSA down?" And we know the prostate is a troublesome gland, because not only does it get big and cause urinary symptoms, difficulty with peeing, waking up at night, having to push or strain to get urine out. Other parts of the prostate are also areas where prostate cancer can develop. So just because you have symptoms waking up at night, difficulty peeing, doesn't mean you have prostate cancer. But it is worth having a discussion with your providers about those

symptoms and also talking to them about your risk of prostate cancer. So same gland, multiple problems.

Same reason why men who have a circumcision or a vasectomy are often seen, if you just look at broad numbers as being more commonly diagnosed with prostate cancer. Not that the circumcision or the vasectomy are causing you to get cancer, but you're also seeing people, like me who screen for prostate cancer, also do circumcisions and vasectomies. So all those things go together and kind of are clouded or confounded by the fact that you're seeing someone who does all those things in clinical practice.

Don't worry in terms of prostatitis. Another reason why the prostate is a troublesome gland. It can get infected, and you can start to have symptoms like it burns to pee. You have discomfort. You're peeing more often than you did before.

And in the setting of infection or inflammation, that PSA is going to skyrocket. So sometimes, if your PSA is very high and it changed very rapidly over a short amount of time, and you have these symptoms, it's good to make sure you don't have an infection or prostatitis. And then, also, once it's treated, to wait a little while and go back and recheck that PSA to see if it's coming down. That will also tell you this may not be cancer, but one of the other problems that the prostate can have.

Perfect. Let's see questions any other questions or concerns that were coming up from anyone. Otherwise we'll hop on to kind of the next question about treatment.

Perfect. Let's now move on to kind of the prostate cancer journey. I'm just going to share my slides here.

So after diagnosis, we have to kind of discuss what's happening. And this is kind of the broad--I'm excited to work with all of these people at UCSF, but in the broad spectrum of disease, what's happening. So after you get the PSA, you get additional testing, you talk about, "do I need a biopsy?" If you need one and get diagnosed, where is it on the spectrum of risk or aggressiveness? If it's low-risk, that doesn't mean you need to rush to surgery or radiation. Even though I like doing surgery, not everyone needs it. Not everyone will benefit from it right now.

And for that slow growing prostate cancer that may not change and impact your lifespan, active surveillance may be an option. If it becomes more aggressive, or we think it has the potential to grow or change, then surgery or radiation with other urologists like myself, radiation oncologists will be people you can talk to if we find that cancer outside the prostate or there's a chance that it's in the lymph nodes or other areas in the bone. For example, then we talk about medicines to treat the entire body. I don't think any of us would try to surge, as I call it, every single area of the body, no matter how microscopic, but our

armamentarium of medications to treat disease, even if it's outside the prostate, has gotten so much better even over the last 10 years that we've made dramatic strides in extending life and controlling disease.

And that's really when it comes to shared decision making--having an honest discussion with your provider and your care team, which may be more than one provider who treats prostate cancer in different ways and help tailor that treatment based on your disease characteristics. And what's most important to you. And that's why, having that frank discussion and honest discussion with your providers is so important.

Lastly, there are always questions about recurrence. And here I'm going to share a few slides. You guys can just screenshot because there's going to be a lot of information. And Dr. Sokolova went over some of this as well. Questions about ejaculation, vasectomy. We discussed before medications, statins, alcohol supplements, you know. I tell people when it comes to supplements, I don't recommend everyone go out and buy a full shelf of medications from GNC or some vitamin shop. We don't have a clear silver bullet from any of those, although it will have a dramatic impact on the wallet. A well-balanced diet, considering low red meat, low sugar, decreased processed foods and diet--dairy products have been shown to help. Exercise. Some degree of caloric restriction has been shown to help, and there are many other things that we've seen to correlate with better outcomes and a better trajectory. Getting plugged in with your primary care provider to make sure any other issues you may be dealing with--diabetes, high cholesterol, high blood pressure, depression, stress, are all treated--will improve your life and quality of life, no matter where you are on the prostate cancer spectrum, and provide more opportunities for you to enjoy life while having a potential diagnosis.

Let me stop there with sharing and let's see if there are any other questions or anything else any of the other speakers like to ask.

Dr. Alexandra Sokolova: While we're waiting for other questions, I do want to echo what Dr. Washington just shared. That stress reduction and kind of mindful practices have been shown some beneficial impact on overall well-being of patients, because when we decrease the stress, we improve our well-being, so exercise is really helpful. If you're willing to engage in any other mindfulness practices that could also be beneficial to improve your well-being, and potentially have some beneficial impact on your journey.

Dr. Samuel Washington: Perfect.

One question that's come up now is, "is there a link to toxic water exposure for prostate cancer?"

That I found interesting, and I'm not sure of the answer to that. If anyone has any insight into that at all?

Dr. Leanne Woods-Burnham: Don't have an answer. But I have a few friends that are looking into environmental contributors to prostate cancer, you know, ongoing. So it will be interesting to see. I see somebody put in the chat, too, "What are the--what's considered a normal PSA?"

So, you know, historically, in the clinic, it's been 4. 4.0 nanograms per milliliter is sort of the differentiation between normal and elevated. In the past few years, American Cancer Society has really espoused for anything over 2.5 in Black men to be a consideration for repeat annual testing.

At the scientific--at the bench-level there has been a study by Dr. Kittles and others that has shown that a PSA of a Black man at a younger age of 1.5 can be predictive of prostate cancer a decade out, if that man has a higher proportion of West African genetic ancestry. So that's not an easy cut and dry answer, but I'll let Dr. Washington speak more to PSA in the clinic. But what we do know as well is it's also age dependent, right? PSA is going to elevate as you get older. So if you want to add anything else.

Dr. Samuel Washington: Yeah, I was going to say, when we draw that test, the lab result comes back, is saying, 4 and below is quote, "normal" and above is "high," and that's usually the trigger for a referral.

So sometimes just that lab report and whatever is deemed normal on that lab report is what people are told is normal, but we know, exactly as you said, it's by age, race, and ancestry have impacts. Also the size of your prostate. I've seen men who have a massive prostate and no cancer. But their PSA is higher because normal tissues making PSA cancer makes a little bit more so that discussion with your providers is what's key, and I wish we had a cut and dry single limit for everyone. But we know, even across the United States, at a broad population level, if you're in your fifties versus your sixties, there are different levels of PSA that are more reassuring and ones that require more discussion and evaluation.

Dr. Alexandra Sokolova: I also would like to add how genetic testing kind of factors in when, if you look at NCCN guidelines [ed. note: National Comprehensive Cancer Network]and kind of the tree on what to do with PSA, and there is a risk that's called the "high-risk"

category. Black men fall under high-risk category, but also men with germline mutations fall into high-risk category. And so the guidelines for kind of repeat screening or more intensified screening. currently at PSA of 3, they were kind of looking to maybe a little more intensified screening. But there's some research suggesting that those thresholds should be redefined and maybe be a little more age-tailored because men at say 45 expect to have different normal PSA than men that are 75. So there is ongoing studies to redefine what should be a PSA threshold to initiate more workup for prostate cancer for men with germline testing.

PATROL is one of them, led by Heather Cheng from University of Washington. So if any of you have family relatives who have a germline mutation and male, and would like to kind of participate in prostate cancer screening, a PCF [inaudible] will be happy to connect you [ed. note: link to study]. There is sites open throughout the country. And another point I wanted to add about PSA - that it's different for men who have their prostate intact. And we're talking about diagnosis of prostate cancer versus those who have metastatic prostate cancer, or those who had their prostate removed. Our definition of normal will be very different in those two scenarios for men with metastatic prostate cancer. We don't worry as much about the number high or low, we worry about which direction its going. Is it going up, or is it going down, or what the trend overall is. So I would say the definition of normal will be really different, depending on which clinical scenario we interpret that in.

Dr. Leanne Woods-Burnham: You mentioned--I want to go back to genetic testing, too, because I see a couple questions in the chat about DECIPHER and some other genetic testing. It's important to realize that genetic testing is ever-evolving.

Okay, so we don't have all the answers either. Yet we've made tremendous strides, right? But in order for genetic testing to really advance what we call "precision medicine," which is tailored treatment for all populations in the future, which is the goal for every individual going into the clinic to receive the best personalized medicine for them, we really need to encourage all of us, but for the sake of this call those of you who have prostates to take part in genetic testing. If there's a part of a genetic research study or clinical trial at the hospital that you're at that's available that you can participate in and you don't feel overwhelmed or burdened to participate in that, I really encourage you to do that because we need everyone's genetic information to really be able to get better at this, the best way I can say it. I have a family member who is battling breast cancer right now. And she did genetic testing and came back negative, and she said, "Oh, I don't have to worry as much about my daughter," and I let her know that that's what we know right now. You know what I mean. That's just genetic testing that we have right now, and so there's always things to be discovered in the future. And so I was happy that she did that. But I also didn't want her to let her guard down and think "Well, her--you know, her daughter doesn't necessarily have that same risk just because that test was negative." So sorry for that tangent, but I just felt that's important to add to our listeners.

Dr. Alexandra Sokolova: I also want to echo that we've known that prostate cancer has genetic component way before we kind of had the germline testing. And currently, we think that probably about 30% of prostate cancer is kind of familial. It runs in the families, and we're able to identify genes that are responsible for that in about 12% of patients. So we know there's at least another 20% that's still genetic. We just don't know the gene yet. So when I tell my patients who have metastatic prostate cancer, even if their germline testing is negative, their sons and brothers should still know about it and be aware of these cancer diagnosis in the family.

Dr. Samuel Washington: Think that brings up a good point of there are a lot of questions of what happens after you get that PSA, what other tests can you do? And we know that there are tests based on the urine and the blood, and even imaging, like an MRI of the prostate that can help you better understand your risk. That's where questions around PSA density, so your PSA divided by the size of your prostate--that ratio or that density, can help us understand what's your chance of having some form of prostate cancer versus just a large prostate of benign, non-cancerous tissue.

What we often do are use those other tests like change in PSA over time, 4K blood test, exosome, Select mdx, MyProstateScore, there's a long list, so I won't be able to go through all of them, but all of them can help you at different points in the prostate cancer journey, understand if you need to undergo the next step, so help you understand what's your risk? Am I high enough risk to need a biopsy? Can I test the tumor tissue itself to see if I'm high enough risk to need one treatment over the other, even after treatment, can we do additional testing to understand what's your risk of subsequent outcomes? So a lot of the specific questions about tests and things like that are often good opportunities to discuss those with your providers so we can better tailor your management.

There are different discussions about different treatment modalities, and I think for each person. Be sure to talk about those with all of your providers. I tell people I'll be as a urologist. I'm inherently biased, even though I try not to be so sometimes when it comes to different types of radiation. It's good to talk with a radiation oncologist before you decide on treatment. So you can make that informed decision, and oftentimes we can use studies

and trials to tell what recurrence rates will be, the chance of disease coming back after treatment. But it's also worth asking your provider what's been their experience and understanding that will help you get insight into the local experience or management of cancer.

Any other questions anyone?

Dr. Leanne Woods-Burnham: I see a question about whether to take a vitamin D supplement. I think vitamin D sort of became a star in the news during Covid, when we realized that people who are vitamin D deficient were having worse outcomes, and vitamin D is so important to so many aspects of our health. But there is a vitamin D link with prostate cancer, actually. And we see this in men who are vitamin D deficient, which for the Black population in the United States, we've seen numbers where around 80% of Black men are either vitamin D deficient or insufficient, and that just has to do with how our bodies synthesize vitamin D, so the darker your skin, the more melanin you have, the more difficult it is for UV rays to penetrate your skin and vitamin D is synthesized in our bodies in response to sunlight.

So because we tend to be more indoors, you know, working at our desk and not outside in the sun, and then depending on your skin tone and the amount of melanin, we all process and synthesize vitamin D differently. And so I would definitely recommend for people who may be wondering their vitamin D level to get that checked by their physician and see what those numbers are, because that is something where supplementation can go a long way towards your health, and not just for prostate cancer. But, you know, your immune system and other things as well.

Dr. Samuel Washington: Another question, is there a limit to a safe number of biopsies?

Dr. Samuel Washington: That is an interesting question. Every biopsy has risks, as well as every treatment, risk of infection, risk of pain, risk of bleeding, risk of needing a transfusion. All of those risks should be discussed, and every time you have that procedure or a procedure you are at risk of any of those complications. It's worth having a discussion with your providers, definitely not worth having a biopsy every 3 months. I don't know many men that would sign up for that, but it is worth asking what that interval may be, particularly for patients who are on active surveillance. So we're not jumping immediately to treatment or radiation, but using a biopsy as a portion of a protocol to safely surveil your disease. It's worth a discussion to balance the risks versus the benefits of that biopsy. But there's no clear cutoff that I'm aware of thus far.

Dr. Leanne Woods-Burnham: I saw a few questions about Gleason score.

Dr. Samuel Washington: Oh, this is, so--I'll go over this one. So Gleason Score was designed to confuse everyone right out the gate. But basically what it does is allows us to understand what the cancer looks like under a microscope, and the way it looks under a microscope helps us understand its behavior, at least an overview of how aggressive, how likely is this thing to want to grow or change over time, and we use that by scoring it from 1 to 5 of how aggressive it looks. 1 and 2 is just normal tissue. 5 is the most aggressive, the most abnormal, the most likely to want to grow or change. We report the most common type, and then the second most common type, and that gives us our score. So if you're 5 plus 3, and the most common type you see there is Gleason 5. Second most common is 3.

And that became so confusing with the combinations that we've now tried to simplify it to grade groups. But that Gleason score, that Gleason grade group gives you the grading of your disease which again helps us understand its behavior, its risk of wanting to grow and helps us understand risk and impact on outcomes.

Becky Campbell: Thank you, everyone. We're about at time. And I appreciate that everyone has put in so many fascinating questions into the chat. It's just been really lively, and I appreciate that our panelists have been so actively providing those answers. Some were very specific and clinical.

So I have provided some links in the chat as well where you can go and get additional information. But please, please talk to your provider. Hopefully some of the general responses may equip you with a little bit more knowledge, with questions you want to take into the office. So just with the last 2 minutes here, any final takeaways from our panelists on considerations of risk and screening, And what patients--how patients can, you know, can think of some of these challenges that they're facing where they are in their disease journey. Dr. Sokolov. Any last words regarding your area of expertise?

Dr. Alexandra Sokolova: Sure. If you're a patient with prostate cancer, and you have either localized high risk for metastatic disease, talk to your doctor, have you had germline testing, do you think it will be beneficial for me and follow through. Make sure you have it done. If you have a known germline mutation, please talk to your family because it could be relevant to you. Know your family history. Talk to your family about what cancers have been

in the family, because that can inform your cancer risk and how we'll approach it in the future. I think germline testing is really important and can actually impact treatment.

Becky Campbell: Wonderful. Thank you. Dr. Woods-Burnham?

Dr. Leanne Woods-Burnham: Yeah. First of all, you're taking the first step by advocating for yourself by being on this call. I can't overstress the importance of community around you. Whether that's in the form of support group--I know, Prostate Cancer Foundation has excellent support groups, and some of you may have joined the call because you found out about this from a support group, but just leaning on community around you. If you already have prostate cancer, and then within your community, educating others around you, because, as we mentioned earlier, early detection is really key to the best outcomes, and so being able to influence others around you is very powerful opportunity.

Becky Campbell: Wonderful. Thank you for that. And again, we're going to be emailing out the link to this webinar in a few days. So please feel free to share this with family and friends who you think might benefit. And last, Dr. Washington, thank you so much for your hosting, and for answering all those questions in the chat. Any last words for our audience?

Dr. Samuel Washington: You know, I just remind everyone that prostate cancer happens. Life is still happening at the same time. So acknowledge the fact that this is a life changing event that's happening with life happening at the same time. It's a burden. It's heavy leaning on the community, both in terms of barriers to getting care or getting diagnosed or getting treatment, but also for—support is key, and having that discussion with your providers is also key. Community and institution can work together hopefully to--for the improvement of everybody, and we just have to move it closer to that.

Becky Campbell: Wonderful. Well, I think we're going to leave it there. I'm so grateful to everyone who attended. Thank you for your interest. Thank you for sticking with us here. It's getting late in the afternoon or evening. Thank you, Dr. Washington. Dr. Sokolova, Dr. Woods-Burnham, for all of your commitments to patient care, to research. Congratulations on your PCF awards and future research. And so we're so grateful to you for sharing your time and expertise this evening.

Thank you. Everyone take good care and be well. Good night.