

Doctor Charles J. Ryan:

All right. Well, hello. Good evening. Good afternoon, everybody. Welcome to our webinar for February of 2023. It's the first of two webinars we're doing in the month of February, the shortest month of the year, but we're going to fit two in. It is Black History Month, and we are going to commemorate that and speak to the issue of prostate cancer in Black men, which is not only relevant for the month of February. It's a very topical issue right now, given new data that we're seeing.

I'm delighted to have a couple of guests to present in a moment, but let me just, again, highlight the Prostate Cancer Foundation that funds research around the world. 28 countries, we're funding research on prostate cancer. We support transformational prostate cancer research to accelerate our goal towards curing this disease. We are most proud of funding teams of scientists across multiple disciplines and institutions. We've got some pictures of some of our great teams from around the world shown here. We're also quite proud of our ability to bring young researchers into the field to study prostate cancer as their life's work. We will see one of those wonderful young researchers in a few minutes.

Black History Month is relevant for many reasons, but it is particularly relevant this year because of this graph that I'm showing right now. We saw, in the latter part of 2022, a publication that looked at epidemiological data from men in the United States, that shows us significant inflection and an uptick, not an uptick, a significant rise in the number of men being diagnosed with distant metastatic prostate cancer. This is somebody who does not have the disease confined to the gland and, by extension, has a more difficult treatment path for them. It's not one where we're choosing between a curative surgery and a curative radiation. It's one where we may have multiple modalities of treatment that are needed.

Of course, the implication is that the risk of dying from this disease is significantly higher in a situation where the disease has spread outside of the prostate at the time of diagnosis. As you can see, the graph here demonstrates that this is happening across the board. Men of all races are affected by this increased risk of advanced prostate cancer. We believe this is due to a lack of screening and a lack of early detection. We are addressing that at the Prostate Cancer Foundation, but it is quite stark to see the significant difference in the incidents. Almost a threefold increased risk for distant metastatic prostate cancer in Black men versus men of other races. That's what is stimulating the conversation tonight.

It's worth pointing out that the mortality from the disease is leveling off in all groups, which is heartening. That does mean that, although men are being diagnosed with advanced disease, we are not currently seeing a significant rate of rise in the number of people dying of this disease. This means two things. One is it tells us that our treatments for advanced disease are working and in some populations are getting out into the patient population where they can benefit from them. But as we'll talk about, there are many populations where those treatments are not getting to the population, and as a result, the death rates are higher. But even with some optimism, it is also quite disappointing to see a significant racial disparity here, even though it's leveling off with the mortality from prostate cancer for Black men being about twofold higher than it is for men of all other races.

With that as a backdrop, we at the Prostate Cancer Foundation, for Black History Month and well beyond it, we will focus on prostate cancer disparities. We're doing a number of things in addition to this webinar. We are convening the first ever expert panel to develop guidelines for the screening diagnosis and treatment for Black men with this disease. We are putting up a lot of information on our website, [pcf.org](http://pcf.org), around the issue of prostate cancer awareness, other webinars and other events. So stay tuned to the website and other announcements coming from the foundation relative to this emerging problem and significant disparity for Black men with this disease.

With that, I am delighted to introduce my first guest, who is Doctor Leanne Burnham. She is from the Morehouse School of Medicine where she's an assistant professor of physiology. She has research interests that she will describe for you, but they include prostate cancer health disparities, genetics of prostate cancer, the biological underpinnings of prostate cancer tumor aggressiveness, and worse outcome in Black men. As I said before, she is a PCF Young Investigator awardee. For those of you who aren't familiar, the Prostate Cancer Foundation has a highly competitive Young Investigator program. We receive about 110 applications from multiple brilliant young faculty and postdoctoral fellows at institutions around the world for this. We award about 25 of them per year. Only about one in four people who apply for the Young Investigator Award are actually granted it. Doctor Burnham was fortunate to be awarded that. We're delighted to support her work at Morehouse. I'm going to take down my sharing and turn it over to you for the beginning of our conversation. I understand you have a couple of slides, so tell us a little bit about yourself.

Doctor Leanne Burnham:

Sure. Let me share my screen. Hello, everyone. Thanks so much for joining this important call, this crucial conversation tonight. I always like to give a little bit of background as to why it is that I do prostate cancer research and why I'm concerned about studying it in Black men specifically. That is because about a decade ago, my dad was diagnosed with aggressive prostate cancer. He was 50 at the time and otherwise a very healthy person, and found out that he had prostate cancer on accident in the ER for another unrelated issue. When he was diagnosed, it changed the trajectory of what I was thinking in terms of my biomedical career. He's pictured there with me. That is the day I graduated with my doctoral degree. Also, if you look at the picture on the left there, my dad is situated on the right-hand side of that picture. He's pictured there with a group of men who are from the community that I grew up in, in Ohio.

What's interesting about this picture is there are other men besides my dad in the picture who have been diagnosed with prostate cancer, or who have men in their families who have been diagnosed with prostate cancer. So it really became apparent to me, once my dad was diagnosed and once there were others in the community that was diagnosed, that there was something going on that was different in terms of Black men being more likely to be diagnosed at younger ages and be diagnosed with more aggressive disease. My dad is still with us, thank God. He may be on the call right now. I'll have to check the participants. Anyways, everything that I do in terms of research is to help men like him in terms of being screened earlier and having the best treatment options available.

A little bit about what a day in the life of Doctor Burnham is. I do have a lab that I run at Morehouse School of Medicine. I'll talk a little bit about that during this call in terms of what specifically we look at, the scientific question that we're answering. But another major part of what we do is community outreach. What that is, is we go out into the community to make sure that men that are at highest risk for prostate cancer, which are African-American men, are able to be screened for prostate cancer. If you go to the clinic, if you go to your clinician and you were to be screened for prostate cancer, they would conduct a blood test that looks for a circulating biomarker called PSA, which stands for prostate-specific antigen. If you have an elevated PSA, it does not mean that you automatically are going to be diagnosed with prostate cancer, but it is an indicator that there is some suspicious inflammation that should be looked at a little bit more closely.

Well, what we know and what we've published is that Black men are less likely to have a discussion with their physician about whether or not they should be screened for prostate cancer, which is counterintuitive because if you are a person who's at highest risk for being diagnosed with prostate cancer, you should be more likely to have that conversation with your clinician. Since we don't see that

that is the case all the time, we want to make sure that we go into our surrounding communities and offer PSA testing.

Before I was in Atlanta, Georgia, I was in the Los Angeles area and developed, along with others, a community-based prostate cancer screening program where we were able, in about a year's time, to screen about 700 men for elevated PSA levels. What we saw was that a high percentage of men who were screened were Black men. We also had a percentage of Hispanic men. In the LA area, that is definitely understandable. We're looking to expand this community screening program in the Atlanta area. I just wanted to give you a little bit of background about why I do what I do and a little bit of details about what it is that I do. I'll stop sharing my screen, turn it back to you.

Doctor Charles J. Ryan:

Before you do, well, actually, I was just going to point out that on that slide, on that pie chart, you had percentage of men who were screened who had a high PSA. It was 65% for Black men?

Doctor Leanne Burnham:

Yes. Yes.

Doctor Charles J. Ryan:

Maybe that's a good starting point of how you interpret that number and how you would dissect that number and what it really means, and how many of them are going to have prostate cancer, et cetera. We can pull that thread a little bit. I guess what I'm getting at for your first question here is help us unpack this a little bit. A lot of people look at this data that I showed and the data that you showed. We're seeing a clear rise. We're seeing a clear disparity. I mean, there's no question. People are asking, "Why?" Is it a biology thing? Is it a sociology thing? Is it both?

Doctor Leanne Burnham:

Yes.

Doctor Charles J. Ryan:

Help us ground. What are the issues? Break it into its components for us.

Doctor Leanne Burnham:

Yeah. There's so many issues when we go in the community or even in the clinic, where, like you said, we know Black men are going to be more likely to have elevated PSA and have a subsequent prostate cancer diagnosis. There's a lot of different variables. There are social cultural issues. There are issues that are not genetic. We can look at diet. We can look at lifestyle. Of course, all of that is a cultural issue that would be related to race. But I want to point out in that instance that we're talking about race being a social construct and not talking about genetics. Every culture has their diet, their lifestyle, their customs. There's certain things that would make a person predisposed to or more likely to get prostate cancer. But when we're talking about genetics and things that we can't control, what we know is that there is a link between aggressive prostate cancer and West African ancestry.

How that applies to African-American men is because of the transatlantic slave trade and how the Black population migrated to the United States, the DNA that is in the majority of African Americans comes from the West Coast of Africa. There's a link there with that West African ancestry to a lot of genetic variants that we know cause men to be more likely to develop prostate cancer or have an aggressive

form of it. What that means, we get asked a lot of times in the community, "Well, what if I'm doing everything right? I'm eating right, and I'm exercising, and I'm resting. I should be okay from not getting prostate cancer." But there's a genetic component. We can't change our DNA. Not yet. Maybe in the future with CRISPR or something like that. But we can't change our DNA. With that in mind, we have to keep in mind our own DNA, our own family history, and how likely we are to develop not just prostate cancer, but any disease. It's just important to know and advocate for yourself.

In the lab, what we do, which I'm so grateful, Prostate Cancer Foundation funds the research that my team conducts in Atlanta, is we are looking at genetic ancestry. We look at West African ancestry in Black men. Then we look at certain genes or proteins that we know are linked to more aggressive disease. Some on the call may have heard of a gene called HER2. HER2, actually, we hear about as it relates to breast cancer. But what we are seeing in our studies is that HER2 is also expressed in some men who have prostate cancer. HER2 is associated with more aggressive disease. It's associated with more metastasis. It's associated with worse response to treatment. We want to have good response to treatment, not worse response. What we're seeing is that if you take a Black man and you look at his percentage of West African ancestry, the higher or the more amount of West African ancestry he has, the more likely he is to have HER2-positive prostate cancer.

The reason that's important for us to find out is how amazing would it be if we could, in the future, target HER2 in these men? We already have drugs that are available to target HER2 in breast cancer patients. That's a potential that could translate into prostate cancer. We also have gene called BRCA. People also associate with breast cancer. What we see is that African-American men also have some genetic mutation, sometimes, some men, in the BRCA gene. That's also important for us to understand because if you can do genetic testing on men who have prostate cancer and see that there's a BRCA mutation, that opens the door to targeted treatment.

When you think about treatment for prostate cancer, there's a lot of treatments. There's radiation, surgery, chemo. There's a lot of things you have to dissect with your clinician, but they can be systemic. When I say systemic, it means if you're doing chemotherapy, it's going to treat your whole body. It's going to kill cancer cells in your whole body, but it's also going to kill some normal cells, too. You're just not going to feel that great. The goal of cancer treatment is always to find a way where we can target just the cancer cells and not be so toxic to the rest of the body. That drives what we do.

Before we move on to the next topic, I would like to point out, in 2020, Prostate Cancer Foundation, along with Robert F. Smith, announced an initiative that they have and that is ongoing, where they are developing a genetic-based test that is meant to identify aggressive prostate cancer in Black men specifically. So PCF, Prostate Cancer Foundation, is really leading the way with that. I'm very excited to see the results of that in the next few years.

Doctor Charles J. Ryan:

Well, thanks. That's quite a tour de force. You bring up the topic of genetics. We'll talk about social determinants in a minute, but genetics are fascinating because you've identified that there are obviously genetic links to that West African ancestry and that you can actually do a test for West African ancestry. Correct? There's essentially a gene or series of genes that says, "This means that this person's genome comes essentially out of West Africa." Correct?

Doctor Leanne Burnham:

Sure. Yeah. In the science world, we call it ancestry-informative markers. It's just a set of mutations or polymorphisms within the DNA that we know are not just associated with West African ancestry. There's

a certain set that we know that's associated with European. There's a certain set we know that's associated with Asians. You can look at these ancestry-informative markers and see where a person's DNA has delineated from.

Doctor Charles J. Ryan:

Right. The other thing is that you mentioned the BRCA gene. That makes a lot of news. There are populations where it's more common. In prostate cancer, we see it somewhere between 10% and 15% of cases. However, in the West African population, I believe the mutation in the BRCA gene is a different mutation than we see in people of Ashkenazi Jewish ancestry. Even when we're talking about a mutation, there's variants in that as well.

Doctor Leanne Burnham:

For sure. It's so nuanced and important to understand. That's why it's important for people from every race and ethnicity, when they have an opportunity to participate in a research study or a clinical trial that comes their way, that can help us better understand that genetic makeup, it's very important because there are so many differences, as you pointed out.

Doctor Charles J. Ryan:

As a tie-in the next part of the conversation, there is really fascinating data now to show that epigenetics alters over time. Individuals from a population with a shared experience, a shared traumatic experience, whether it's slavery, and we've seen this, it's been studied of the descendants of people who survived the Holocaust. They have different genes that are silenced and turned on and turned off. That's a whole new area of study. This may be something that as yet is undiscovered or undescribed, I think, as a link between the lived experience of the cultural experience of a group, as well as the genetics that come out of where the ancestry's from. That ties into the term social determinants of health, which I think is another huge component of your work. Tell us a little bit about how you define that and how you as a scientist approach this concept, really, this interface of social determinants of health and the genetics as you just described.

Doctor Leanne Burnham:

Sure. The genetics, like I said, there's only so much we can do with that. We're born with what we're born with. But there is a component that is unique to the United States when we talk about the African-American population and chronic psychosocial stress that is documented and observable and reportable. I became interested maybe about a decade ago in looking at is there a role of chronic psychosocial stress and worse disease, worse prostate cancer risk or outcome? What we know is that when we are under stress, our bodies have what is called a fight-or-flight response. It can be for something that's perceived as a smaller stressor or a larger stressor. But when we have this fight-or-flight response, our bodies make what is called cortisol. Now, there are studies that show that African Americans have higher cortisol levels beginning at very young ages. It's due to a lot of different reasons. We can talk about discrimination. We can talk about depending what neighborhood you grew up in, there's different neighborhood effects, depending on your socioeconomic status, depending on your access to healthcare. There's so many stressors that accumulate over time. What we see is that when you have excess cortisol in your body, your cortisol needs to bind into something in your body. What's inside of our body that the cortisol binds to is called glucocorticoid receptor. Me and others have published that African Americans tend to have hyperactive glucocorticoid receptors. It means that when there's so much stress over time, any sort of stimulus that activates that glucocorticoid receptor is going

to have all sorts of effects in your body. When we say, "Stress kills," we literally mean that. What we have seen is that there's also a link between this active receptor and chronic stress and actually resistance to treatment, resistance to therapy.

There's a study that we published where we found that there's certain genes and proteins that are linked to treatment resistance. When we were growing prostate cancer cells in a dish, because we do that in the lab, we have prostate cancer cells from patients, and we are able to treat them with drugs and cortisol and whatever we want to. What we saw is that we had prostate cancer cells from white patients. Then we had prostate cancer cells from Black patients. We treated them with cortisol to simulate what would happen in the body under stress. What we saw, the prostate cancer cells from Black patients had genes and proteins that started to magnify and amplify and be upregulated, and these genes and proteins we know are associated with worse response to treatment.

Some people say, "Well, my loved one had this type of cancer, and they survived. They had this treatment, and they survived. This other person had the same treatment, and they didn't survive. I don't understand. They both did this treatment. One survived, and one didn't. What happened?" What happened is the person who did not survive, their cancer cells figured out a way to circumvent that treatment. That's what we call treatment resistance. I have the utmost respect for cancer cells because the way they figure out is on another level of how to be resistant. If we see that stress is causing more treatment resistance in Black patients, that's definitely an area of opportunity for us to continue to study.

Prostate Cancer Foundation has a whole other initiative that I'm very excited about. It's called the RESPOND Study. You can find it. You can actually go to [www.pcf.org/respond](http://www.pcf.org/respond). RESPOND stands for Research on Prostate Cancer in African-American Men, Defining the roles of genetics, tumor markers, and social stress. To my knowledge, this is the largest study. It's going to be looking at about 10,000 men to look at biological reasons Black men have more aggressive prostate cancer, but also psychosocial reasons, stressors that I've just been talking about. I very much so believe in this study. I asked my dad to sign up for it, and he did. So go on there. It doesn't take much at all to participate in that study.

Doctor Charles J. Ryan:

That's a really important initiative. You've already highlighted the multiple components, the diversity and the variability of prostate cancer itself as a disease. One thing I've come to appreciate is it's just so many diseases, but you've really nicely detailed this one area where the glucocorticoid receptor, or the GR that we call it, plays a role. That ties in directly to environment, ties in directly to social determinants, another factor. The good part about all this is that it's not hard to figure out what could be the remedy and what could be the preventative medicine for this. Speak to some of the work that you're doing along these lines to identify, address, and mitigate some of these social determinants.

Doctor Leanne Burnham:

Yes. The first thing goes back to the slide I showed you at the beginning. The first thing is we know that, according to American Cancer Society, prostate cancer has an over 99% survival rate at five years, if you detect prostate cancer and handle it, treat it when it's still localized in the prostate. We are passionate about giving Black men specifically that opportunity to have prostate cancer detected at that stage. We don't want to have it detected when it's too late because, to be honest, a lot of men don't have any symptoms until we're already talking advanced metastatic prostate cancer. You can be walking around totally fine, and, oh, wait, you have prostate cancer. That's the first thing that we are adamant about, is the community outreach and screening.

We also collaborate with clinicians to develop clinical trials that are catered to and meant to especially benefit Black men with prostate cancer. We do that looking at, as I described, the genetic reasons, the cellular reasons that may be linked to ancestry, where we can look at cellular pathways and know this is more likely to occur in this population. If we provide patients with this certain drug, it may work great in everybody, but it may work especially great in people who we are targeting a certain cellular pathway. Prostate Cancer Foundation does fund a clinical trial that I'm a co-investigator on that is targeting PARP. It's a gene that's in the cell, using a drug called talazoparib. You don't have to remember that, but just know there are clinical trials that are targeting specifically to help every patient with prostate cancer, but we're really interested to see if this drug can perform better in people with aggressive disease.

When we talk about clinical trials, it's important to realize you're not a guinea pig in a clinical trial. When you hear people say, "If I join a clinical trial, I don't want to get the placebo." Placebo doesn't mean that you're not going to get treatment. What it means if you were in that group, you would be given what is the best standard of care approved in the clinic at that time. That means if your average person would go to the clinic and go to their doctor and say, "I have this stage of cancer," and they say, "This is your treatment," if you were placebo, you would be given that treatment.

But if you are assigned to another group, it's what I like to describe as VIP access to cutting edge treatment. Then we are testing a drug that has been in the works for 10-20 years, that we really believe and have a lot of evidence to think will work as well as the standard of care, or even better. I just think it's important to realize if you do enroll in clinical trials, what we know is, whatever group you're assigned to, you have greater access to your clinician, greater access to your care team. There's going to be more communication, more visits, and you could have much better outcomes doing a drug that is in the pipeline to be FDA approved.

The last thing that we do is we recognize and respond to calls from pharma to help recruit and retain disadvantaged or underrepresented populations to clinical trials because it's not going to be that great if you're trying to reach a high-risk population in a certain geographic region, but you have a clinical trial in some totally other unrelated geographic region that doesn't have the population that you're interested in. So it's important for pharma, when they're deciding on clinical trial sites, to realize, "If I want to reach this population, which I know is more likely to have aggressive prostate cancer, let me go to the part of the country or a clinic that is really servicing that type of a patient." We partner on that as well.

I would like to point out, too, just before I jump off, you can go on [www.pcf.org/risk](http://www.pcf.org/risk) if you want more tailored information about prostate cancer as a Black man. You can find out places to get screened for you or your family members. If you are a patient, you can find out about different treatment options, different genetic testing options. There's also support groups. I cannot underestimate the importance of support groups. I'm not going to give you the website for that because it's just so long. But if you go to [pcf.org](http://pcf.org) and just search support groups, it'll show up. There are support groups, and there's one specifically set up for Black men with prostate cancer. So keep that in mind.

Doctor Charles J. Ryan:

You highlighted the talazoparib study, which is a PCF-funded study. You highlighted earlier, and I'm just connecting these dots, the BRCA gene, and we talked about how the BRCA gene in Black men may be very different from the BRCA gene in the other populations where the mutation is located. We've already done a lot of clinical trials with these drugs, but Black men have been underrepresented in those trials. We don't know if they work in that population with that mutation. Critically important that we identify, really, this connection between groups and mutations and therapies. I applaud you for doing that work.

I'm really very proud that PCF has been funding you both in the laboratory for the work that you're doing, but also in the community support work and the epidemiological work that's being done, to really characterize what is likely to be not a slightly different disease, but a very different disease in some, and probably not that different in others. In other words, we need a taxonomy of what is prostate cancer in Black men because it itself is probably heterogeneous and different from within the population, as well as from non-Black men. Congratulations on your Young Investigator Award. You are what we go to work every day to try to do, to bring funding to ideas like yours. We look forward to your future success and the results of your work and seeing it disseminate around the world and impact the lives of so many people. Congratulations. Thank you for joining us.

Doctor Leanne Burnham:

Thank you.