Becky Campbell: We are going to have a chance now to go deeper into the treatments that are used for hormone-sensitive prostate cancer through a patient's perspective. We're grateful to Dr. Michael Holick for joining us to share his experience, along with his medical oncologist, Dr. Alicia Morgans.

So, Dr. Holick has performed extensive research in the field of vitamin D deficiency as it relates to metabolic bone disease. He has seen over 25,000 children and adults with metabolic bone disease during his career, and he is recognized as one of the most influential physician scientists in the world. He has authored more than 650 peer-reviewed publications and many, many review articles and book chapters.

Dr. Alicia Morgans is a clinician and investigator. She has expertise in clinical trials, patient-reported outcome measures, and incorporating patient preferences and beliefs into decision-making. She is a member of the Advanced and Localized Prostate Cancer Treatment Guidelines Committee from the AUA, and she has also received two PCF Challenge Awards and a PCF Creativity Award.

So, welcome Dr. Holick and Dr. Morgans. I know that we have some wonderful slides from Dr. Holick and then we'll get into a discussion.

Dr. Michael Holick: Thank you very much for that very kind introduction. It's a pleasure to be here. And as you've heard already, about ADT therapy. So I'm an endocrinologist and I have a nightmare, while trying to stay cool.

And so, I'm 78 years old, and I've been seeing men with prostate cancer and metabolic bone disease for decades. In 2021 I went to visit my PCP and I had a PSA that was mildly elevated. I saw my urologist and wound up having a biopsy, and lo and behold, I had a Gleason score of four plus five, nine and the MRI had demonstrated that it was already starting to advance into the neural bundle. But the PET Scan was negative. And so I saw my oncologist friend at Boston Medical Center and told me I had stage three prostate cancer, Gleason score nine, and that I was going to need really intense therapy. And what she also told me, which was really nice, and even though I'm a doc and I've seen lots and lots of patients, when she said "this is curable," it really gave me a wonderful sigh of relief, right?

But I knew I needed to be on androgen deprivation therapy, and the consequences are quite significant. On bone, it will reduce your bone density. For muscle, it'll cause wasting of your muscles. And more importantly, it also has an effect on your bone marrow, decreasing red blood cell production and causing you to be anemic. And so, the consequences of being hypogonadal, I knew very well, since I had seen a lot of men with hypogonadism and also men with prostate cancer on ADT, and this is what happens, right?

You wind up having your muscles become flabby. You become obese. You become listless. And you have a lot of other issues. So, in 2022, I knew I was going to be initiating my therapy, and I wanted to take advantage of this knowledge and to decide on ways of mitigating these consequences.

So I started walking five miles every day. It helps to maintain your bone density in your lumbar spine and in your hip. I weight lifted twice a week. I took 1000mg of calcium and 2000 units of vitamin D a day to help maintain my bone health, and I took up to 5000 later on, finding that it was actually beneficial. I was placed on Lupron to shut down my ability to make testosterone. But there's another problem. Your adrenal glands also produce androgens, as does your testes. And so as a result, initially I was put on bicalutamide which inhibits androgen activity because when you're on Lupron initially, your testosterone levels actually go up. You actually feel better. And you want not for your prostate cancer to start being more active. So, I was initially on that for 30 days. And then put on abiraterone.

And what are the consequences of these therapies? So yes, I'm hypogonadal because I have no testosterone. I'm anemic. I have a hematocrit at 36%. So I'm sure you've experienced this. Why am I so fatigued when I get up in the morning and late afternoon? Is it only due to my hypogonadism and my anemia?

Well, I'm an endocrinologist and I wondered about this because abiraterone is supposed to be specific for inhibiting this enzyme, and it's not supposed to have any significant effect on your ability to make cortisol and aldosterone. but I was concerned that maybe there was. And so I asked if to have an 8 AM cortisol. Your 8 AM cortisol is usually at your peak, should be between 10 and 20 micrograms per deciliter.

My 8 AM cortisol was 1, so it was 10% of normal. So I now knew another reason why I was so, so fatigued. Yes, you’re put on five milligrams of prednisone daily, but that was mainly to control hypertension and maybe to control your potassium, but not really to control your adrenal dysfunction, right? Because the half-life is only 3 to 4 hours. And so when you get up the next morning and if you have shut down your adrenal gland, you have zero prednisone in your body, and you have zero basically cortisol.

So am I adrenally insufficient in the morning and late afternoon? You better believe it. In fact, if you're severely distressed and you are adrenally insufficient, you could wind up having an adrenal crisis, and you should be aware of that. Adrenal fatigue - very significant. I would get severely fatigued by around 4:00 or 5:00 in the afternoon. And so I decided to take another--more prednisone, which would be great. The problem is prednisone causes insulin resistance. And even though I felt great, I wound up with diabetes.

And so as a result, I had to go back to my five milligrams of prednisone. So, I’m adrenally insufficient, hypogonadal, because testosterone is undetectable, and I'm anemic. New problem being hypogonadal: hot flashes.

Women with menopause can have severe hot flashes, but men with no testosterone can have the same. And hot flashes, now that I know that I experience them, they are devastating and there are really no good remedies. Yes, you can stay in the fan forever or you can go into a bucket of ice, right?

And I was having 1 to 2 per hour, so I was having up to 20 hot flashes a day. It causes you to have half your body in full-body sweat. It causes severe fatigue and you actually could almost not focus.

So what to do? And, well, you can move to the Arctic or Antarctic, but I found this device. It's called Kulkuf and when you turn this device on, it turns out it goes down to 47 degrees instantly.

It sends a signal to your brain and shuts off the hot flash. So I wear this all the time. I do not leave home without it. It's been magnificent. I initiated a clinical trial - six weeks, and, if some are interested, you're welcome to contact me at mfholick@bu.edu because we have openings.

It's a six-week study to see and demonstrate its efficacy. So, I'm adrenally insufficient, hypogonadal, anemic, and I have sleep disruption because I'm having a hot flash - one every hour.

But what about the brain? Well, it turns out that there's another major issue for the brain, which is suicide thoughts are significant - four times higher risk of suicide in men with prostate cancer.

You need to communicate your feelings with family and friends. Critically important. In 2023 I decided to step it up a little bit, and I suggested I'm going to run the Boston Marathon in 2024. I've never run in my life. My whole family thought I was crazy, right? But I decided I was going to do it anyway. I'm 78 years old, stage three prostate cancer, hypogonadal, hypoadrenal, anemic. I was going to challenge myself, but more importantly, I wanted to be an inspiration for all of you out there who have this disease that can really limit you.

And so, I ran the Boston Marathon this year, and I'm 78 years old. The next oldest person in my whole region was 65 years of age. And this Boston Marathon was one of the hardest ever. So here now, I just saw my oncologist, still able to lift the same amount of weight that I lifted before I went on ADT therapy, because I intervened by making sure that I did it twice a week.

I ran, this last week, ten miles. I'm planning to run the Boston Marathon in 2025. My testosterone is now gradually coming up. I'm anemic. I have normal adrenal function, but I still have hot flashes. I want to thank Alicia Morgans. She is my oncologist, and she's been fantastic and helped me, over these past two years, deal with many of these issues.

And I thank you for your kind attention. And you can go to my Facebook page where I share with you my journey with prostate cancer. You can go to my website - it has a lot of information about vitamin D and bone health. And you can text me and, contact me at my website, at mfholick@bu.edu. Thank you.

Dr. Alicia Morgans: Thank you so much, Doctor Holick. That's so helpful and really interesting, especially as, you know, because you're an endocrinologist and you're also someone who's, you know, being treated with all of these agents. If you had to give one piece of advice as the

main overarching theme to people who are listening, who have to go on ADT, whether it's short term, which we define usually as 4 to 6 months, or whether it's long term, which would be usually over a year to two years, sometimes even forever, what would your advice be to people?

Dr. Michael Holick: So two things. The first is just like I said, you want to keep your muscle strength, and the best way to do that is to remain very active. So, whether it's walking even half a mile, anything will really help a lot. Also, for your bone health, adequate calcium and, 1000mg a day, 500mg, twice a day, or three glasses of milk is great. And 2000 to 5000 units of vitamin D a day is very helpful.

Dr. Alicia Morgans: So, you're a vitamin D expert, and I wonder if you can tell folks who are all across the country, they think, you know, if they think, "oh, I'll just go out in the sun, I'll garden a little bit and I'll be good. I'll get all the vitamin D I need." Is that true? Or do we have sometimes trouble getting enough vitamin D from sun exposure alone?

Dr. Michael Holick: So, you cannot get enough vitamin D from sun exposure alone because time of day, season, latitude, degree, skin pigmentation. So, for example, if you go out even in the summertime at 8:00 in the morning, you make no vitamin D. You only make vitamin D from about 10 a.m. until 3 p.m. Also, you can't make any vitamin D in Boston, starting by the end of October, and you don't begin making it again until around March/April. And you only are really exploiting a small part of your surface area, so you can't get enough vitamin D from sun exposure alone.

Dr. Alicia Morgans: Well, thanks for reminding us of the wonderful winters we have every year in New England. That's stressful, but it's true. And I think, you know, as we're all thinking about supplements, you know, people think a lot about them. And there are supplements that are worth, you know, more than others. And I think vitamin D is probably one of those supplements. I think about, specifically supplementing that.

And then really, the final question I wanted to ask is, you know, how do you maintain mental health through all of this? Because, having low testosterone, seeing the physical changes, feeling the fatigue, this is all really difficult. And androgen deprivation therapy alone, having low testosterone levels, actually can increase the risk for people to develop things like depression. How do you advise that people try to combat that or face that and get help if they find that they're in that position where they may have low mood?

Dr. Michael Holick: Well, not only that, but of course, erectile dysfunction is with men and, I have a wonderful wife.

Dr. Alicia Morgans: Of course.

Dr. Michael Holick: And she's just been incredibly supportive. I mean, like I said, when I get severely fatigued in the afternoon, she's there to help me. We still have a wonderful personal relationship together, but it's obviously a little bit different in light of having no testosterone. And my whole family has been incredibly supportive. And my friends as well. Like I said, it's really important to be in touch with family and

friends and explain what you're feeling. I mean, males don't like to do that, but it's very important because it's true. I mean, men with prostate cancer, especially those that are alone, right? Are four times higher risk of committing suicide. So it's very important for communication and you have to really let yourself out. And it's very unusual for males to want to do that, but it's incredibly important. And like I said, I have a wonderful supporting wife, and she's helped me get through a lot of this.

Dr. Alicia Morgans: Absolutely. So one thing, just a comment there. You know, for anyone who is feeling in distress, 988 is a new national hotline for folks who need support around wanting to hurt themselves. Not that I think anyone here is, but I think it's always important to mention having that support, and also doing things like physical activity, engaging in a group exercises, or engaging at the gym and things that involve community can also be really helpful both in and creating endorphins, because you're being physically active. But also, of course, in giving you the the psychological and social supports that can be really, really important.