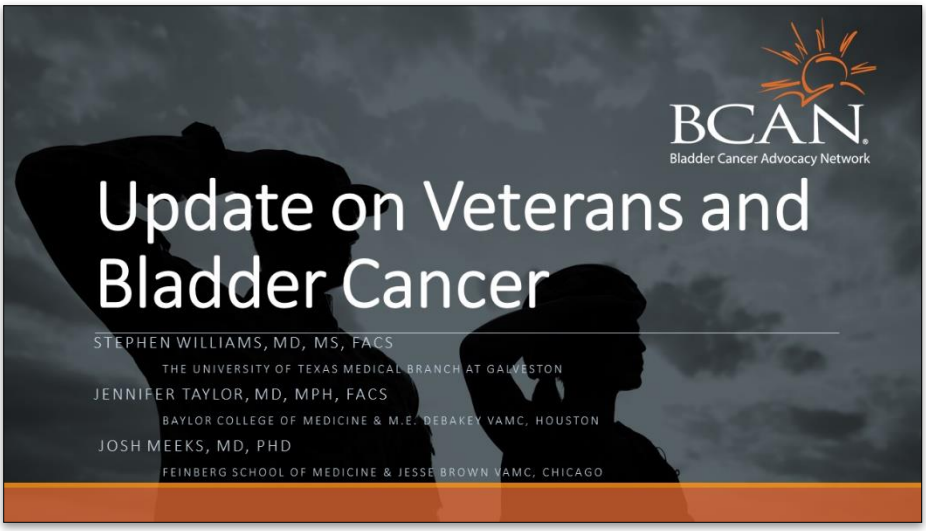

Meet Our Presenters:

Dr. Stephen Williams: Dr. Williams from the University of Texas Medical Branch, and is the Chief of the Division of Urology, as well as the Director of Urological Oncology and Urologic Research departments at his institution. He's heavily involved with many societies associated with bladder cancer across the world. His main focus in research is comparing the cost and effectiveness of bladder cancer treatments. He's going to talk about some of the work that he'd been doing in understanding the impact on the veteran community.

Dr. Jennifer Taylor: Dr. Taylor is an Assistant Professor of Urology at Baylor College of Medicine, and she also concurrently practices as the ME DeBakey VAMC in Houston, Texas. So she's working within the Veterans Administration. She serves as an Associate Residency Program Director and Director of Preclinical and Clinical Urology courses for medical students. Dr. Taylor's involved in clinical research in multiple genitourinary malignancies with a focus on bladder cancer and the research in medical education, and she's involved in the national medical communities.

Dr. Josh Meeks: Dr. Meeks is an Assistant Professor of Urology at the Northwestern University Feinberg School of Medicine in Chicago, as well as the Section Chief of Robotic Surgery at Jesse Brown VA Medical Center. He is a urologic surgeon with expertise in the diagnosis and management of bladder cancer. So I am going to turn my screen over to you, Dr. Williams. Let me just give you the mouse.

Dr. Williams:

All right. Thank you very much, Stephanie. And I'd like to think specifically the Bladder Cancer Advocacy Network, as well as importantly, and as you pointed out, all of the veterans that we are giving this particular webinar to. Thank you for all of your service and particularly this special day. Hopefully, you'll find today's webinar suitable but more importantly, provide some interesting information on where we stand and what we know at this particular point.

As previously mentioned, I'm the Professor in Chief of the Division of Urology at the University of Texas Medical Branch. In addition, Medical Director for High Value Care at my institution.

So, bladder cancer statistics, where do we stand in 2020? Well, with bladder cancer specifically, it affects both men and women and is the sixth most common cancer when we compare against all cancers in the United States. However, as I previously alluded to, bladder cancer affects both males and females. However, bladder cancer is approximately four times more common among males than females. In addition, among males, it's the fourth most common cancer. However, when we looked at... I didn't do it.

However, what we need to be mindful of is, that cancer incidence, particularly among those veterans and what we know from looking at large data particularly in the VA health system. And when we try to compare versus those that are, as I previously mentioned, to the general population in the United States, versus those in the VA population, bladder cancer is the fourth most common cancer overall. However, what we have found is that bladder cancer is more commonly diagnosed earlier among our veteran population, however, also is the fourth, most common cancer among males.

And I think one of the key questions that a number of veterans, as well as investigators, we want to understand why. Is this a nature versus nurture or environment versus genetics? And when we also come down to the research particularly, we're focused on exposures versus actually understanding the genomics, and my colleague, Dr. Meeks will talk more specifically in regard to subtypes, mutations and other interesting research that is really exciting work currently under way.

When we're talking about risk factors, which I will get to eventually, one of the most intriguing is looking at association versus causation. A large body of the research that is particularly being done in the VA at a population-based level is looking at associations. An association does not automatically imply causation, but also too importantly, as an example for this is, exposures. Exposure to arsenic is associated with a higher risk of bladder cancer. However, what's important is whether or not is it causative of bladder cancer? Important work is being done using animal models such as Dr. Meeks' excellent research that he has done, when looking at particular risk factors and bladder cancer.

And in specifically, as we all know, smoking is associated with bladder cancer and particularly with occupation and environmental exposures as well when considering smoking has about 50% of the cases, and then the occupational exposure is about 20% of cases. These are some common environmental or important occupational exposures to consider that have been associated with bladder cancer.

In addition, we also mentioned an infectious organism that is also associated with bladder cancer. Specifically smoking in itself, as we previously alluded to, when we're looking in the VA population itself,

in this data that is performed nearly about 20 years ago, 27% versus 21% of veterans versus non-veterans actually smoked. In the dataset that I'm going to present to you all today, we found roughly almost 80% of veterans are actually ever smokers, and when we assess over a 20 year period. So, a lot of the data that we are collecting today is very useful, but also owns to the fact of what time period you're assessing this information. And then in addition, we're also concerned as with bladder cancer more commonly diagnosed in a younger population of veterans, smoking rates are highest among young veterans.

As I mentioned before, risk factors and exposures, Agent Orange is obviously one of the topics of today's webinar. And today, as Stephanie alluded to, only limited data exists regarding a link or an association between Agent Orange and bladder cancer risk and importantly, death. Prior to 2014, Agent Orange was not even considered a bladder cancer risk factor. However, in 2014 this was upgraded from Agent Orange from no association to limited evidence. The Institute of Medicine concluded that there's actually an interplay between Agent Orange exposure and bladder cancer outcomes is an area of needed research.

Based upon this, the VA is considering bladder cancer as an Agent Orange-related disease. However, while some data suggest Agent Orange exposure increases bladder cancer risk, not all data agree. To provide a true measure of aggressiveness of bladder cancer, my group particularly found it crucial to study not only bladder cancer diagnosis, but also the long-term outcomes such as bladder cancer death.

In 2016, the DOD had the first time, the focus area of bladder cancer, and I was very lucky to team up with a group of Cedars Sinai UTMB, and in addition, within the VA and the Institute of Medical Research over in Durham, to leverage a team that actually also determined an association of Agent Orange and prostate cancer. What we were able to do is actually put together a team to very much determine the risk of Agent Orange and bladder cancer, but also death related to bladder cancer. However, in doing so, what we leveraged and what we were awarded to do, and what we have developed is, the largest, true nationwide cohort ever assembled to study bladder cancer according to Agent Orange exposure, which consists data of over 11.7 million veterans from the largest integrated healthcare system in the country, the VA health system.

This is a brief illustration of the grant's primary objective and secondary objectives looking at the link between Agent Orange exposure and bladder cancer risks, but also to Agent Orange exposure and whether or not it is linked with bladder cancer death. This is a brief illustration of the team. This is a career development award, and what we're able to develop is, the bladder longitudinal assessment database to direct epidemiology research. This was co-led by Dr. Stephen Freedland, as well as the team at the Durham VA Medical Center Institute of Medical Research. We were able to identify, as I previously mentioned, roughly 11.7 million patients, 181,200 cases of bladder cancer with tissue linked. In addition, we're able to identify almost a million patients that were exposed to Agent Orange, and then out of those a little over 16,000 had bladder cancer and Agent Orange.

With this data, we were able to also determine not only that a specific cohort of patients, but also analyze and assess and determine male versus female. And in addition, which is also important bladder cancer research, race and ethnicity. To put this in perspective, this population has a little over than

10,000 African Americans, is quite impressive from a bladder cancer database and to generalize our findings.

Today, unfortunately, I cannot elicit any of the analyses in whether or not Agent Orange is associated with bladder cancer. Preliminary analyses are complete and results and publications are expected in 2021. However, importantly, further veteran center studies are forthcoming, including health services research, mental health, disparities, and genomics. And this is a very exciting time for bladder cancer research overall.

I have to thank my team, particularly at the Durham VA Duke and the Institute of Medical Research, including Stephen Freedland, Amanda Deloitte, Lauren Howard, Megan Foster, Ruixin Yang who developed also to our natural language programming, which is critical to this large-scale study. And in addition, my team at University of Texas Medical Branch, my Department Chairman, Dr. Doug Tyler, our Director of Biostatistics, Yong-Fang Kuo, Director of Epidemiology Jacques Baillargeon, and most importantly, the veterans who provide the salient data to hopefully determine once and for all, is Agent Orange linked with bladder cancer.