Welcome to our webinar tonight on prostate cancer screening, What Men and Families Need to Know.

My name is William Oh. I am the Chief Medical Officer for the Prostate Cancer Foundation. And I and I'm really looking forward to a very robust discussion today for this important topic.

Just as a reminder, Prostate Cancer Foundation is a 30-year-old organization with a mission to reduce death and suffering from prostate cancer. We fund some of the most promising research towards treatments and cures and have a global footprint in over 28 countries.

Many of the therapies that are used today for advanced prostate cancer were developed with early stage funding from the Prostate Cancer Foundation. In addition, PCF funds research on diet, exercise, cognition and also screening to improve patients' quality of life after diagnosis.

We have a lot of resources available to you online in addition to this webinar, which will be taped and available for you afterwards as well. If you or a loved one is diagnosed, you can find educational resources and community at some of the resources available at PCF.org as listed. In addition, there is a really wonderful website called Prostate Cancer Patient Voices, which in which you can hear from other men and families who are going through the prostate cancer journey.

We have funded $ 6 million in awards this past year to Young Investigators. A key part of our mission is to support young scientists and doctors as they go into the field in order to allow them to really develop new treatments and new advances in the field in the future. So please consider really our program of supporting investigators and supporting the best research and consider a donation at PCF.org.

So I'm really delighted to invite two of our speakers tonight who are experts in this field, Sigrid Carlsson, who is the Director of Clinical Research at the Josie Robertson Surgery Center at Memorial Sloan Kettering Cancer Center in New York. She's also an Associate Professor of Uurology at Gothenburg University in Sweden, and she's really an expert on screening, a urologist by training and an epidemiologist as well.

And Dr. Isla Garraway is a Professor of Urology, Director of Research for Urology at the David Geffen School of Medicine at UCLA. She's an Attending Urologist and PI at the VA of Greater Los Angeles and really is an expert, both as a urologist but also as a scientist in understanding the causes of prostate cancer, as well as its interactions with the environment.

So welcome, Dr. Carlsson and Dr. Garraway. Thank you for joining me tonight.

So great to be here.

Thank you.

So thank you. So I'm going to start by talking a little bit about the process of screening, and then we're going to jump into some cases so that we really are able to talk a little bit about the differences, because people are very confused by prostate cancer screening and what they hear from different organizations, different people, even from their own doctors. They get confused, as you guys know. So we're going to try to clarify some of this tonight in the next hour.

So, first of all, just as a reminder, and you both know this very well, but for our audience, prostate cancer remains the number one cause of cancer in men. About 288,000 cases last year, which is almost a third of all cancers in men, and about the second leading cause of cancer death, About 34,000, over 34,000 deaths last year in 2023. So we can talk a little bit about this discrepancy between the larger number of diagnoses and the smaller number of deaths and how that plays into the screening question.

And I want to start by asking you both to comment on this algorithm that was published in the New England Journal last year. So we know that there's a lot of questions about how you should be screened for prostate cancer, but maybe I can start with you, Dr. Garraway. Talk a little bit about this algorithm that a doctor or a patient may really consider in terms of what a positive PSA test, a PSA test is and how they should go down this pathway.
We'll talk more about this, obviously, in the context of the patients that we're going to be using as cases and examples. But could you just walk us through a little bit of this right now?

So as you are pointing out on this, in the slide, prostate cancer screening really does begin with a blood test, with a PSA test specifically. And so based on the value that we, you know, find out from that blood test, we're going to make recommendations.
And so that recommendation may be that, okay, your test looks fine. We will follow up with that test in another year or two.
Or it could be that, the test looks a little bit troublesome where … we're a little bit concerned about the result. And so we need to do something, another action as opposed to just, you know, seeing you back in a year or two to do another test.

So basically what you see at the top of the slide is a PSA test greater than 4 as being that kind of trigger to either basically go back to screening and say, see you next year or do something else. And I do think that, you know, one of the things we can discuss is whether or not that level of 4 is still the level that we are using as our cutoff.

So I think that might be a little bit different, because when I look at the PSA results as I think a lot of my colleagues feel the same way, the cutoff for when we feel like something's okay versus when we feel like something needs to be looked into further through either another confirmatory test or moving on.

And then, you know, before moving on to more of a workup is, you know, not only is the PSA value, but how old is that patient? So a PSA of 4 for somebody who is 69, you know, it means something totally different than a PSA of 4 for somebody who's like 45.

So there is a little bit of discrepancy probably….people treat the actual value differently than just having a straight cut off of 4, or we usually take into account age as well. And there's other things that we take into account when we're trying to interpret that first PSA test, such as, for example, the size of your prostate. So someone could have a very large prostate and their PSA is 4, and that's actually kind of pretty normal for the size of their prostate that they have. And the prostate might not be cancerous at all. So a lot of times, you know, a very large prostate is just large because of just benign reasons, meaning that your prostate just starts to grow when you get older. A lot of men will experience symptoms related to that growth, but it has nothing to do with cancer.

Then there's other factors that we need to consider when we're interpreting the PSA test. But in general, if that PSA test is high, then we basically will almost always get a confirmatory test and just make sure that value really is true, and it wasn't a spurious test.
And then we will move on to do a further workup to make sure that you know, that that this is not a cancer that we're detecting.

So typically, when do you do a confirmatory PSA test? So one important part of this is you never just use a single number as an abnormal PSA. And we're going to talk a lot about whether this cut off of 4 is….what you're saying is, there's a lot of nuance there. And we'll talk about some of that nuance today but when do you usually do a confirmatory PSA if somebody had an elevated one for the first time?

I always do a confirmatory PSA if somebody has an elevated PSA test coming in.

Like a month later or two months later?

Yeah, No, just, you know, just I don't really wait a long period of time. I mean, depends again, it kind of depends on what's going on with the patient. So if there's like, things that can elevate the PSA, like a urinary tract infection, for example, or inflammation or something like that. So if I feel like there's something clinical going on, you know, if the patient has symptoms or other things, then of course we'll maybe treat that issue.

So, you know, if we test and see the patient has a urinary tract infection or something like that or prostatitis, I picture, you know, which is kind of an infection or inflammation of the prostate that sometimes can result in an elevated PSA that has nothing to do with cancer. It just is the fact that the patient is inflamed at that time.

And so in that case, we'll wait, we'll treat the patient for the problem, the issue. And then once they get treated, once they recover from that infection and everything's back to normal, no more symptoms, at that point we'll test their PSA again and see if it came back down to normal. And if it's still elevated, then we will move forward.

On the other hand, if somebody is totally asymptomatic and, you know, this is just kind of like they're just living their lives and are getting their PSA screening test and this comes back as abnormal and there's nothing else going on clinically with that patient, then probably there's no need to really wait. We can do another one right away and then move forward with the workup as needed.

Right. Thank you. Dr. Carlsson, Let's say the person has a PSA of 5 and another one, a month later is, again, 5. What does that mean? That it's positive and what would you do next in the setting?

Yeah, that's a great question. You know, it's interesting. I've been doing this for 20 years and it's so fascinating to see how the field has evolved. Back in the days, we used to only have the blood test PSA and then we used to jump straight to biopsy. But what you see here now in this algorithm on the figure is really what we call risk stratified screening.

So that means that we try to better determine a man's risk, and risk meaning risk of having a high grade prostate cancer or the type of cancer that we worry about and that we want to eventually maybe treat.
So we….the problem with the PSA screening, as Dr. Garraway mentioned, is that the most common cause for an elevated PSA is a benign enlargement of the prostate or BPH.

It's not cancer. And we also talked about how the PSA can jump up and down. So therefore, we need to do more things in between before we tell men to have a biopsy, because a biopsy can be a little uncomfortable and can lead to some bleeding or infection. So we don't want to put needles in prostates if we don't have to and so a simple way of doing that is just repeating the PSA.

And in many cases the value goes down to normal levels again. But if, in this case, a man has had two elevated PSAs, then we want to go onto to the next stage of the evaluation. And usually we start with the finger test. So it's a very simple test, but we can feel the prostate through the rectum, and that's another indication for us to move forward.

Now, there are also other tests and they can be in either blood or urine, and some of them are more what we call specific. And so they can add more information to us and we can use that together with a man's age and all the other factors to determine if he needs a biopsy.

And what really has been the gamechanger in recent years is MRI. So, multi parametric MRI and that means imaging of the prostate.

And so when I started this work, we didn't have that at all. So now it's really revolutionized the way we diagnose prostate cancer, because now you can see the prostate and you can see if there's a lesion and then your urologist might put needles towards that lesion that looks suspicious. And that helps us do a better biopsy, because back in the days we used to do a

fairly blind or random biopsy and we still do, you know, take systematic biopsies of the prostate also. But the MRI really helps us do a better biopsy.

So by doing this whole chain of things, we can better pinpoint those aggressive cancers and we can avoid finding those very slow-growing cancers because as you mentioned in your first slide, Dr. Oh, and the discrepancy between the number of cancers we find and the number of men who die from them is large and many men can live with prostate cancer without, you know, being harmed over a long time.

So using this type of algorithm, we can really find the cancers that we want to find.

I'm going to….we're going to probably come back to this picture, but sometimes it's a little confusing to people. You can see that you can go one of three ways. If you have a positive PSA or an elevated PSA, you could just go straight to a biopsy. Some doctors do this, but I think in centers of excellence, like where we all work, we would probably not do that. We would almost certainly do the MRI, as Dr. Carlsson mentions, because it's so much better not only to see the prostate, but also to help with the biopsy.

So you really want to think about going to a center of excellence where they would be able to get the MRI and also to do what's called an MR-guided biopsy.

And this, we'll talk a little bit about these triage tests. They're not always necessary. You can see sometimes they're used to kind of put people in to low or high risk, but they're not always necessary. So we're going to talk a little bit about this. So thank you both.

We decided, the three of us, to show some cases, some examples of people that we see. These are, I think, representative of the types of situations that we come across and that you, yourself, the patient and your family members will come across.

We know that many people who are on this webinar may have a connection to prostate cancer, and you want to talk about your family members, for example, or others, your friends and others who may not have that risk.

So let's start with case number one. Let's start with Mr. Williams, a 43 year-old white male who is overall healthy, very active, but he does have a very strong family history. His father was diagnosed at age 55 and died of prostate cancer about 14 years later. And his brother was diagnosed at age 57.

So, Dr. Garraway, what are the considerations for this patient? What would you say?

Yes, well, I think we could just start with his age. I mean, there's lots of interesting pieces of information in this case. But the first thing when we're trying to make a decision about PSA screening is we're going to take a look at the age of the patient.

Now, one of the things that's so confusing about PSA screening is that there are many different guidelines available out there. And they all and a lot of them have differing ages at which to start. So some guidelines recommend starting screening at age 45, some, you know, 45 to 50, others recommend, you know, waiting until mid-fifties actually to start screening and some recommend in really high-risk patients to start, you know, before the age of 45, even as early as age 40.

So looking at his age, he's 43 years old. He's definitely a young man. And so if he's a young man of average risk, he might even be a little bit on the younger side, you know, to start screening. We might, you know, might at first glance say, you probably don't need to start screening until you're between 45 and 50, and come back in a couple of years. But the thing about it is, the other piece of information that we see in his history that's really important other than the fact that, of course he's healthy, which is great, which again, you know, fortunately for his young age, he is a healthy person, physically active. But you see the family history here. That's a huge, huge red flag.

He has a dad who was diagnosed with prostate cancer at age 55 so that's a really young age to be diagnosed with prostate cancer, relatively young age. And his father died of that cancer in his late sixties. His brother was also diagnosed with prostate cancer in his fifties. So basically, this is a strong family history of two family members, direct family members, his dad and his brother with a history of prostate cancer.

So that makes me concerned that he might…there might be some heritable components to this prostate cancer history in the family, meaning that there are some genetic alterations that could be passed down in their family that increase the risk of prostate cancer.

So basically, this kind of shifts Mr. Williams into a high-risk category. He's no longer just your average guy with your average risk. He's high risk because of his family history. And so in this case, our most stringent guidelines, which are the National Comprehensive Cancer Center Network guidelines, recommend that we start screening him before the age of 45. So, age 40 to 45. That's when he should get his baseline PSA test. So that's probably what I would recommend in this person. Let's start screening now because of your family history.

Yeah. Thank you. And you know, these guidelines, obviously people don't know that difference… The guidelines are meant for doctors typically, although they sometimes address patients.

So, Dr. Carlsson, you're on several of these guideline panels. A lot of people, they go to their primary doctor. This patient might go to his primary doctor, and the doctor may say, well, you don't need to get screened until you're 55. Why would a doctor say something like that to a patient like this? And what else would you recommend for this particular patient?

Yeah, it's fascinating. You know, PSA is controversial, and it has been and remains and the guidelines they agreed to some extent, but they also disagree. So it can be very confusing,

even for us who've been in the field for a long time, when to start and when to stop. And….here's different consensus in the guidelines and how they look at the data and the studies. And so, you know, sometimes primary care physicians might follow one guideline that says it's okay to start at 55, but then you have other guidelines that focus on finding the aggressive cancers that really recommend starting early. So there are nuances and there's definitely benefits and harms of PSA testing.

PSA can, as we talked about, jump up and down and it can be a false positive and it can cause some anxiety and then finding those low grade prostate cancers. There's a risk of what we call overdiagnosis that you might find cancers that you otherwise wouldn't have experienced any symptoms from or would have otherwise harmed you during your lifetime. So that's why some guideline members feel that some of the harms might outweigh the benefits and other guidelines they really are convinced that the benefits are there.

So there are definitely nuance. And the prostate is unfortunately located in a place in the body where it's so close to important structures, such as the nerves that control erection and then it's close to the urinary bladder. And so if you have treatments, it might cause some side effects there.

So long-term, there are risks with treatment for prostate cancer. But a PSA test is a very simple test. So you don't have to think about that, you know, at this stage. But I think when you look at the whole pictures, some of the guideline committees might feel that, you know, screening might not be as good if you think about all of those things.

So would you offer this patient a PSA test?

I totally agree with Dr. Garraway. He has a strong family history.

What about genetic testing? What's the right time to do genetic testing with that family history? Isla, when would you offer this patient genetic testing? Is it too early? And would you wait to see if there was an issue for him?

Yeah, I think that's a great question. I think that the exact appropriate time for genetic testing is still something that our field is probably learning about and dealing with. Right now, I believe our guidelines say that if the patient ends up with a prostate cancer diagnosis, then we should do what's called germline genetic testing to look to see if there could be genes that are hereditary that could be passed down, and that maybe eventually could even impact the patient's care down the line.

But right now, I don't think I would necessarily do it. I would maybe recommend his dad get… his dad is unfortunately deceased. But the brother, I think, is still living….
So the brother could get genetic testing for sure. And then if it turns out the brother actually has a hereditary germline alteration, then that would be an indication for him. It's called cascade testing. If somebody in your family already has cancer and has a known hereditary

genetic alteration, then other people in the family should also be tested to see if they have the same gene and then, you know, offspring of those family members as well.

So you can understand and be able to mitigate your risk through screening.

We have a really good webinar on this topic of what germline or inherited risk is. And the most common inherited risk for prostate cancer is actually what is called the breast cancer gene, BRCA 1 and 2. And if the brother did have that, not knowing whether the father had it, if the brother had it, I think it definitely increases the concern you might have for this for this person to get tested, even though he's in his forties and the guidelines all support this.

While I'm pulling up the next case. Dr. Carlsson, I wanted to…you've mentioned DRE or digital rectal exam or the finger exam or maybe something that's not the most popular test for men, even though it can be done quickly in the office. Can you just comment on the value of that prostate exam or the digital exam and why it wasn't in that algorithm?I can show it again, but it wasn't really in the algorithm. But you mentioned it as something that the doctor may do after an elevated PSA. Can you just comment on the role of DRE?

Sure. And that used to be the test that we had before the PSA was discovered. So when PSA came, it really revolutionized everything. You could have a blood test, and it was very simple. And because by the time tumors are palpable, you know, that there they might have grown more. So the PSA test really offers the opportunity to detect cancers early.

So as a screening test, it’s not very good - the DRE or the finger test - because as we talked about, you know, you can feel an enlarged prostate. You can also feel cancer. But most cancers are not palpable at the low, you know, when they're in the early stages. So that's where the PSA test is much, much better because it can detect this protein in the blood. And so that it's a marker of cancer.

But we definitely recommend DRE once the PSA is elevated and before proceeding to biopsies, which is part of the early detection pathway. But as a screening test, it’s not a very good test.

Thank you. Yeah, I think many men may feel some relief that they don't have to have what might be considered an uncomfortable exam.

So….I'm going to talk about the next two patients together because they bring up some of the different issues about particular race.
Here are two men of different races, Mr. Nguyen, who is 65, Asian, smoker, with a sedentary lifestyle but no family history.

And Mr. Brown, who's younger, 53, Black, identifies as African American, has some chronic health issues diabetes, hypertension, is physically active but doesn't really have a family history.mNot sure, but maybe his uncle. So maybe Isla, can you talk about the role of race and how it interacts with age and other considerations for PSA screening now?

So when we're thinking about consideration of PSA screening, as we discussed, we talk about age. So the older age, again, prostate cancer usually happens in older men. So the older you are, the higher your risk factor is in terms of age. But then like in the first case, we talked about how the family history also can be …can bring out risk factors, right?

So if you have a family history of prostate cancer, if there's a lot of prostate cancer in your family, the more relatives that you have impacted with prostate cancer in your family, the higher your risk and your risk goes up kind of multiple-fold. Then we definitely want to take a second look at screening in that population because it makes you a high-risk group.

Unfortunately, there are some races or ethnicities also, that can put you in a high-risk category, in particular B lack or African American race or African ancestry. That itself is ….that population is at higher risk for prostate cancer incidence. And this has been year over year very well established in studies, that we see in a lot of our data that is collected nationally that African Americans have like twice or two times higher risk of incidence of prostate cancer diagnosis, nearly a two times higher risk.

So basically, not only are patients of Black or African descent to have a higher risk of prostate cancer, they can often get it at a younger age than the average person, so that we just have to be particularly mindful of that as well when we're thinking about screening. So again Mr. Brown, because he's 53 years old, but because he's of Black or African ancestry, that puts him in a higher risk category.

So for sure, we want to be screening Mr. Brown especially…I mean, he does have….the other thing that of course, we need to think about in this case is life expectancy and other health issues that the patient might be dealing with because of the patient has a lot of health factors that they're contending with….

Prostate cancer is a very slow-growing cancer. It might not be useful to go and try to detect prostate cancer in a patient who has many other health issues. On the other hand, this patient, although he has diabetes, hypertension, those conditions can often be very well controlled and the patient can live a long life with these conditions.

We already know he’s physically active. So that tells us that, you know, probably PSA testing, again, would be a good idea because of his risk factors and the fact that he has some chronic medical conditions shouldn't deter us from doing screening in this patient.

On the other hand, Mr. Nguyen, he's 65, he's of Asian descent, so he's not in a higher risk category based on his ethnicity. He does have risk factors for prostate cancer that he's a smoker. I mean, smoking tobacco is kind of associated with prostate cancer incidence. But he doesn't have any other comorbidities listed. He lives a sedentary lifestyle. So, I kind of get the sense that maybe he might be not quite as healthy as your average guy, although he doesn't really have chronic medical conditions listed.

So you would just have a discussion with Mr. Nguyen, you know, again, all these things, all these discussions should happen between the provider and the patient. It shouldn't just be me, the provider, just checking a box saying, “get prostate cancer screening.” We always have to engage with the patient and I have to explain what I'm seeing about the history of the patient and factoring in the age and the risk factors.

And then the patient has to tell me what they want, you know, if they want to be screened for prostate [cancer], that's something that they want, understanding that prostate cancer is usually an indolent cancer.

Not in everybody, but it can be, and may or may not even need treatment and so maybe, you know, maybe it’s not something that they even want to deal with or look for at this point in their lives, depending on what's going on in their life and what their other health factors are. So these are the kind of discussions that I usually have with my patients.

Thank you. That's a really important point, which is it's ultimately their decision. But I think one of the issues here is that they rely on their physician and sometimes their primary care doctor is too busy.

So a lot of this is about educating yourself, understanding what your goals are in life. And it is only a blood test. And one of the things that maybe you brought up, Dr. Carlsson, was the idea that sometimes these cancers are indolent, slow growing, you may not need to treat them. So maybe if you find a cancer that’s like that, what would you counsel a patient, let's say if you had a low grade, let's say Mr. Nguyen gets a biopsy.

He has a PSA that's 5. He decides to get a biopsy and he has a Gleason 6 prostate cancer in one biopsy out of 12. What would you counsel somebody like that in this scenario? What are his choices?

Yeah, so it's really important to think about active surveillance or, to actively monitor those types of tumors.
And as we would say in Sweden, “There is no cow on thin ice,” meaning you don't have to jump to surgery or radiation or treat it immediately if you find a cancer diagnosis.

So that's the most important thing to really meet a doctor that that offers active surveillance. And we know that you can monitor these types of tumors very safely in these types of programs. And you come back for repeat PSA testing, you come back for the finger exam, you come back for MRI and repeat biopsy over years. And we know from many, many, many studies that these patients do really well without any treatment. For many, many years.

So if you were to treat this type of low grade and low risk tumors, you might only suffer from side effects from those treatments. So that's why it's really important to think about active surveillance and discuss that option with your provider.

So I think the whole point is, sometimes you will find a cancer that you may not need to treat, and you monitor and follow them on surveillance. Just because you find a cancer doesn't mean automatically that you have to treat it. And I believe in the United States, maybe up to a third, is that right? About a third of patients are now being monitored, even if they find a cancer, because their doctor and they decide that that's the best choice for them.

So it's important to recognize that just because you have prostate cancer, you don't always have to be treated for it. If the specialist tells you that that's one of your choices.

I'm going to do the last case and then we're going to have a series of questions both right now and also some people submitted some questions. And I want to kind of drill down on these different examples of hopefully everybody in the audience can identify with or understand kind of the situation of each of these four theoretical patients.

But let me let me go to you about Mr. Miller, Isla. 79 years old. He's white. He's a marathon runner. He has a mild hypertension and no family history. So what would you tell this person, and what else do you want to know that we didn't show here on this case?

So again, starting with age, 79. So I think Dr. Carlsson mentioned earlier like…for me, the tough question is not when to start PSA screening, because we have really good categories now of who's at high risk and who's at average risk. To me, it's like sometimes it's hard to figure out when to stop screening. So the question is, what has Mr. Miller's PSA screening history been like? You know, is this his first time coming in and he's never had a PSA test before? Or has he been screening his whole life, and the question is now, should I get my annual PSA test at 79 years old?

So generally speaking, you know, at some point, …. we probably should stop screening, right? Otherwise, we have the risk of overdiagnosis in cancer, meaning that we're diagnosing cancer that might cause some psychological stress knowing that you have cancer, but really isn't going to impact your quality of life or your quantity of life at all.

So I think when men get up to their late seventies, eighties, you know, that's when we really start to have to think about this really carefully and again, to have that discussion with the patient. So if he's had PSA screening his entire life or since, you know, his entire midlife, let's say, since he was like 45 or 50 and his PSAs have always been low and stable, you know, … I feel pretty comfortable maybe advising him he could stop PSA screening at this point, even if he does have a really long life expectancy. Even if he is going to get to 100 or beyond, you know, it might be okay.

Because he's had… you know, again, what we don't know is what his PSA screening history has been like. And what is PSA values have been like over that historical period. That would be really helpful because there's new data that suggests like if your PSAs are exceptionally low,

that you know, really you're at pretty much close to zero risk of developing a lethal prostate cancer.

So you might develop a prostate cancer, but it just…..all we care about at this point is like, is it going to be something that affects his quality of life, or his quantity of life, you know, really cut his life short. And so if we had a little bit more data, we might be able to counsel him a little bit better.

So I think there was a question about the fact that when we showed the algorithm, we use this cutoff of 4 and that's why you were so reluctant, both of you, to say that that's the cutoff, because there's really no such thing.
It's really the change in PSA, the age, the size of the prostate, other inflammatory or non-cancer related issues that that affect your decision about whether the person might have a prostate cancer or not.

So that is I think one of the key take homes is of course, it's not a single number. It's the entire story, including that person's whole history.

So, you know, let me just go to a couple of the questions, because I think some of them are quite interesting.

Dr. Carlsson, if a patient has prostate cancer, let's say, just like Mr. Nguyen actually has this low-risk prostate cancer, Gleason 6, one positive core out of 12. But he happens to be a carrier of BRCA2, which is what we know to be a higher risk disease. Do we know what the right way, what the right choice is for that person?

Let's say he is like the first patient, a young man, let's say his brother, in fact, does have the BRCA variant and he has it. And what they find is a very small cancer at the age of 43. Is there something, what's the right approach to a patient who does have this high risk genetic abnormality but actually a low risk prostate cancer?

Yeah, that's a good question. Maybe one that I would pose to our urologist in the room. Dr. Garraway, what would you say? I would say that we would maybe increase our vigilance, but not necessarily deter that man from active surveillance.

I just want to make sure we're that we're talking about a person with a BRCA2 alteration and prostate cancer, low grade.

Yes. And let's say he's in his forties.

I mean, these are hard questions. I don't know if we have the data to really show us what the answer is….. so I think the issues are that BRCA2 mutations are associated with more of a lethal prostate cancer. And right now this guy is in an early stage, which is great. That's the

whole point of screening, right? Screening high risk populations is to find them in an early stage.

So, would I feel comfortable putting him on active surveillance. I mean, I guess it just would have to be like a really reliable patient who we definitely can put on a very strict regimen of imaging as well as repeat biopsy over time, and then I probably would. Because the whole point is that these cancers are more likely to progress.

So definitely in a young man you want to preserve … Again, as Dr. Carlsson mentioned earlier, the prostate is in the worst location for men because it affects fertility and erectile function and all these things. And so somebody who's young, they might not be done having children yet.They might be starting their families. They might have you know, obviously they have a lot of other, there's a lot of quality of life considerations. Even if he does have this genetic alteration that puts him at risk for a lethal cancer. So I totally think that trying to preserve as much of that as possible is reasonable. But I think it would have to be a very, you know, very strict surveillance program.

Yeah, it's a tough question to answer, of course. And it gets to all the individualization because we believe that that genetic risk does increase the risk of the cancer behaving differently in the future, but not at the present time. There's no evidence for that. So that type of approach is … it has to be personalized.

Dr. Carlsson, there are questions about sexual intercourse and PSA and also bike riding and PSA. Can you talk about how those two activities might affect PSA and what's generally recommended to avoid confusion with regard to a PSA test?

Yeah, that's something that we also discussed a lot on the guidelines. There are multiple studies, and they say different things. So the bike riding hypothesis, I don't think it's been proven, to my knowledge, but some would recommend to abstain from bike riding and having sexual activities before drawing a PSA test.

I don't know how many days or weeks if there's really studies on that, but it's sort of kind of a clinical good thing to do. I don't know what you do in your practice.

Usually three days, I think, I hear 72 hours quite often. I don't think there's any science behind it. What do you usually recommend, Isla?

I actually….to be honest, I don't really necessarily make those recommendations unless it's like, you know, if somebody comes back with an abnormal PSA and he mentions to me, "You know what? I did go on this 45 mile bike ride, you know, the day before," and I'll say, "Okay, well, let's definitely … " That's why you do a confirmatory test, I think, in case these little things happen, you know, so that you can kind of say, well, was there anything going on or unusual at the time when you had your PSA test? You know, did you have symptoms of an infection? Did you go…..any unusual activity? And so then that type of thing comes out.

I don't usually again, because I mean…I'm a urologist, so I'm not the one usually ordering that PSA test. It's coming from primary care. So I fortunately don't have to make those decisions.

But I agree, I think you could say just like two or three days if you have that luxury, if you're the primary care doctor and you're saying, as far as getting your PSA test, make sure you don't, you know, maybe just try to reduce those types of activities to lower your chance of having an abnormal test.

Yeah, I think most of the time it would be the second test. So they're not going to tell everyone to stop riding a bike or stop having sex with the PSA - The first PSA. They're going to go in and get their cholesterol, get their PSA. And if the number comes back higher than expected, either because it was a change from the prior year, then a urologist or a primary care doctor should probably say, you know, let's try to get as clean a number as possible before we move forward.

There's a question about veterans. And you work at the VA, Dr. Garraway. Dr. Carlsson, you're an epidemiologist. Can you talk about veterans and Agent Orange and whether veterans are at higher risk?

Yeah, Yeah. So actually, this is a really great topic of interest to a lot of VA investigators like myself. And we are actively looking at this in terms of really trying to define the risk of veterans. So veterans in general have classically been thought to have a higher risk of prostate cancer specifically and other cancers in general, and because of their military exposures.

And so that could even be just like being on a base, like there are certain toxins now that we know from …. undergoing basic training on a base that might increase risk of certain cancers, not necessarily prostate cancer, there's not a clear link between prostate cancer.

But the one place where there is more of a clear link between prostate cancer in terms of military exposure is the Agent Orange situation. Right. So patients who….so there have been several studies that have shown that Agent Orange exposure is associated with an increased risk of prostate cancer incidence. And there's varying data to suggest that sometimes you have a more aggressive cancer with Agent Orange exposure.

It's not totally clear in terms of that, but for sure, there's pretty clear evidence that your risk of prostate cancer is higher with Agent Orange exposure. In fact, it's considered a condition that a presumptive cause of prostate cancer so people can get, you know, service connected. It's a service-connected condition.

So essentially, I think we've also kind of looked at this in the guidelines. I'm not sure I don't think specifically. I mean, we might have said that it puts you in a higher risk category.

But certainly if you've had Agent Orange exposure, you should be thinking about prostate cancer screening, or you probably have undergone prostate cancer screening because of…kind of the increased awareness about Agent Orange over the past several years in the VA system.

But I think one of the things to keep in mind is that……most of the veterans now from the Vietnam War era are kind of getting older. Right? They're kind of reaching their seventies or older. And so the question is….do they need any differences in the screening in terms of when to stop screening?

It's this question that just came up before, for men who are healthy, you know, in their seventies, eighties, you know….when do you stop PSA screening, and does the Agent Orange exposure factor into that because they're an increased risk of incidence.

So I'm not sure we have the total answer. Again, I think it goes back to looking individually and what the screening history has been, what the PSA has been over that period of time and making that decision….based on other health factors as well.

But certainly, being in the military increases risk of cancer. And so probably this should be factoring in in your decision whether or not to undergo prostate cancer screening.

Thank you for that.

Dr. Carlsson, there's a lot of questions about diet and whether certain kinds of diets can alter prostate cancer risk, you know, drinking beer, alcohol, smoking, plant based diets. Can you comment on what the data shows and what you might recommend to a patient or person who is concerned about their risk, let's say, because they have a family history?

Yeah, I wish I could say something, "Take this and you will never get prostate cancer." But unfortunately, we can't. And there's also controversies and the evidence goes in different directions. But I think there is consensus that what's good for your heart is also good for your prostate. But then, of course, there's different guidelines there, too. But it does seem like Mediterranean food or, you know, avoiding red meat or smoked food or processed meat, that can reduce the risk.

There are some associations with dairy or reducing milk consumption, smoking and alcohol, of course, also reduces risk. And it's good for your overall health. I would say those are the biggest ones, too, is if you want to reduce risk of heart disease and reduce risk of prostate cancer, kind of kill two birds with one stone.

Yeah, I think I think the problem is the data to prove these effects is very hard to show. But I think a lot of the same nutritional changes that help the heart, help the prostate, we believe.

And so those are very common sense. I think taking lots of vitamins or lots of supplements, there's really never been any good evidence for that. So it's really about a heart healthy diet

exercise, low animal meat consumption, low barbecue or barbecued meats. Those are things that seem to have been associated with less prostate cancer risk and maybe less aggressive prostate cancer risk.

So I wanted to maybe go back to the issue of …. when to start and when to stop. Maybe really go to basics. For an average man with no family history who is, let's say he's 50 years old now, what would you normally recommend to this person?

Pretend you're in the clinic right now, Dr. Garraway, and he's coming in for a regular follow up visit. He has none of these risks. He's not Black, he's White. He's not…either has no family history or one that he knows of. What is the main thing that you would tell that 50-year-old man about why he should or shouldn't do PSA testing at the age of 50, let's say?

Yeah, I mean, I think, again, it kind of goes back to the potential harms of PSA screening, right, is that there's this chance of overdiagnosis, there's a chance that we could detect a prostate cancer which will, you know, or go through the process of even detecting a prostate cancer.

So there's a there's a potential that by getting a PSA test, we might go down a road to a biopsy. You might have a complication from the biopsy and which, you know, obviously, you know, the complications from biopsies are pretty rare nowadays, but they still can happen, you know, So maybe 1% of the time somebody can get very sick from the biopsy.

They can get sepsis, you know, basically get an infection that requires hospitalization, and they can get very ill. Or they can lose blood for some reason from the biopsy and require a transfusion.

That would be very, very rare. It happens just so infrequently, knock on wood. But still, that's the harm that he could suffer from having the PSA test … and if that results in basically a clinically insignificant cancer, meaning that a very low-grade cancer that we're just going to watch anyway, then it's just like you might be wondering, well, why do I go down this route?

You know, now I know I have this cancer I have to worry about and maybe it won't ever impact my life in any way. So that's an example of like, a harm that could happen.

On the other hand, you know….we don't know everything about prostate cancer as clearly, it's been clear from this discussion. We don't know all the genetic components that lead to an aggressive prostate cancer that you might harbor, for example.

And so it's possible that we could detect a prostate cancer that could be lethal really early by starting screening at the age of 50.

And what we do and what we do see, like in the kind of preliminary data so far is that ..in the studies and the trials that we've done so far, that if we start screening early, it gives us an opportunity for early intervention and we can save lives from prostate cancer.

Unfortunately, it's not as many lives. The numbers are not overwhelming right now because these trials to kind of show that we can save lives through screening are very hard to do and they're really hard to control for. So it's really difficult to actually show how much of a difference we're making by screening. But yeah, that's the conversation I'm having with the patient.

And then hopefully the patient will be able to make an informed decision. But I think one more point, William, that you mentioned before is that a PSA test is just a PSA test. And so then we have to be really smart what we do with that information. So that's the thing. It's just like a PSA test doesn't mean you're getting a biopsy. It doesn't mean you're getting an intervention for prostate cancer. It's just a test.

So at that point, then we you know, we have the option of like, you know, deciding what to do after that.
So I think, again, as long as it's not just like a knee jerk response to everything along the pathway. You know, we're just obviously talking and interacting and explaining what the test results mean, what they could apply and, you know, and giving the choices at each step. I think that's when we can really make informed decisions and make sure we reduce the amount of harm that can come out of this testing.

And that's really, really, really important points. And the balance, really, we're talking about a balance of the pros versus the cons. That's why there's never a simple single answer for every person, for every man.

I want to talk about MRI. There was an interesting study from England where they screened everyone with an MRI and found a significantly more higher number of prostate cancers that are considered clinically significant, not those small ones that people don't worry about, but ones that really we all believe need treatment. Are we heading towards a time when MRI is going to be done as a screening test, Sigrid?

Yes, we're moving towards that. But I wouldn't start with an MRI because I don't think we have radiologists to look at all of them, right? So they would…technicians to do the scans, and it takes time and it's a little bit uncomfortable.

And so definitely the simple blood test, the PSA test, is the first start and that's something that we are studying now in a study in Sweden that I'm an investigator of that. We start with the PSA test, and if that's elevated, we could then go on to MRI and then we go on to biopsies where you put needles towards what looks suspicious on the MRI.

And it's really nice because you can then do a better biopsy and pinpoint those aggressive cancers and you don't find all these other low grade tumors that you otherwise would accidentally find by biopsy. So I think this is definitely the way to go in the future.

Yeah, I think this is a really important point. It's maybe in the future MRI will become more used and maybe become cheaper and faster. Right now, the first test is the PSA and the MRI is a follow up test, but it's become a really, really important one. It actually helps us to know where to put the needle.

And it's better than just doing what's called a standard or template biopsy because you're actually…a urologist is actually putting the needle in the right place. Sometimes they do the template biopsy in addition to the MRI guided biopsy. But the MRI guidance really has made a huge difference. And I believe it's really the standard of care. So everyone listening to this should really see a urologist who orders an MRI and who considers an MRI guided biopsy.

Not every urologist in the United States has access to this technology. So it's really, really important that you think about doing an MRI as something as an adjunct. That's something you do after a PSA comes back in a suspicious manner. Would you agree, Dr. Garraway?

Yeah, absolutely. The MRI is really helpful to me as a urologist because it basically gives me two, well, maybe three key pieces of information.

The first thing it does is, it tells me the size of the prostate, right? So it gives a really nice measurement of the size of the prostate. So if there's no lesion, if there's no suspicious area/areas at all detected on that MRI, but the prostate ends up being really big, then I can say, well, your PSA is probably elevated because your prostate is so large and it saves that person another rectal exam.

So anyway, so it does it tells you the size, it gives you some [inaudible] there.

But then it also as you're pointing out, William, it tells you exactly where areas are that looks suspicious for cancer. It gives them a grade. It tells how suspicious, how much they look like a….potentially could be a cancer in there so that we can decide, we can basically literally aim our needle right into that area and get a sample there.

So that's really important and, you know, in cases where, you know, unfortunate rare cases where you see these really large areas of suspicion that look very much like they could be a cancer, according to the radiologist. You can also see if there's any evidence that it's spread anywhere. So we can look at the lymph nodes, we can look at the areas outside of the prostate to see if there's any other evidence of disease anywhere else.

Or we can feel confident: Yeah, there's a really highly suspicious lesion here, but there's nothing else that looks like it's been…it's compromised from the cancer. There's no lymph node enlargement. You know, everything looks like it's contained in the prostate. So we can also give patients a little bit of prognostic information based on those kind of features from the MRI.

So it gives a lot of information, and if you can get an MRI, it just is really helpful in targeting the biopsy.

And there are cases if we don't see anything on the MRI and the prostate looks large, it can save a biopsy. I mean, like you could just say, hey, look, why don't we just follow your PSA a little bit more and see what that, you know, the trajectory of your PSA is, like how fast and how high it's going up, because it could just be this is just benign enlargement. Like Dr. Carlsson mentioned.

This is like one of the most common reasons the PSA is elevated is not due to cancer, but just due to the growth of the prostate and normal tissue growing. So sometimes we can basically save the person from going on a biopsy right away by just having an MRI.

Sigrid, there is a question about ejaculation and whether that actually decreases the risk of getting prostate cancer. There are general questions about prevention, like why we are talking looking for cancer, can't we prevent it? And that's a question that's much broader than the next five or 10 minutes that we have.

Unfortunately, right now, A, we don't really know what causes prostate cancer and B, we have no clear way to prevent it. So our general strategy is to detect it as early as possible if it's a potentially dangerous one, and if it's not a potentially dangerous one to leave it alone and to surveil.

So somebody had asked about what you meant by harms of PSA screening. And the main harm is that if you have a cancer that doesn't need to be treated, that overtreatment or taking out the prostate or radiating the prostate or doing a lot of biopsies may create anxiety and may create side effects that are not necessary. And it is a good topic to discuss at a future webinar.

But can you go to this concept of this Harvard study? Of course, any Harvard study always gets a lot of attention. Even though none of us are at Harvard right now. Can you talk about ejaculation and whether that's really associated with decreased risk of prostate cancer?

Yes, and I think that's what the study showed. I think it was Dr. Jennifer Rider from Harvard. *[editor's note: this is the study: https://pubmed.ncbi.nlm.nih.gov/27033442/]*

It was a couple of years ago. I don't remember exactly the frequency that they suggested in the study, but it was kind of the more the merrier. It's like Harvard studies are usually like: "drink a lot of…ten cups of coffee and ejaculate ten times a day. This reduces your risk."

But I don't know if you remember the exact numbers, but from my recollection, it actually was associated with the more the lower the risk for prostate cancer.

Yeah. Yeah. And I don't know that anyone's ever validated that study and I haven't seen much since then, but it did get a lot of attention at the time and I don't think it was ten times a day. I

think it was something like maybe 10 to 15 times a month compared to those who had less frequent.

So I just thought maybe we're going to go back just the to the basics of these cases and let you guys just talk a little bit about what the take home messages should be for the audience here in terms of PSA screening.

I know this is a very, very complicated topic. Unfortunately, we're not going to be able to cover every single person's particular scenario, but we what we try to do with these four cases was is kind of the most typical types of scenarios that we see. And maybe as you talk a little bit about your overarching thoughts about PSA screening, you can tell us what you think the future of screening for prostate cancer in general will be.

So I'll start with you, Dr. Carlsson, and then I'll end with Dr. Garraway.

When I started with this and was an investigator of the trials in Europe that we showed, that regular PSA testing reduces prostate cancer mortality. We started with at 50 and ended at 70, and some centers went up to 74. And we had a PSA of 4 and that we went to systematic biopsy and it was 6 to 10 cores. It was a very basic concept, but now we've moved into, as I mentioned, this risk stratified screening approach where we have kind of expanded on both ends of the age range, that we have lowered the starting age.

So we recommend starting the discussions between 45 to 50 and if men are at increased risk - so family history or African American or Black race - considering starting, you know, between 40 and 45.

And then in terms of ending, we can go up to 74 and then have discussions with the provider and depending on prior PSA levels and the man's health.

And then in between, as we talked about, if the PSA is elevated over 3 - and we have looked at going lower to 2.5 or maybe even lower - but not jumping straight to biopsy, but repeating the PSA, and then consider a reflex test, whether that's a biomarker and or MRI before proceeding to biopsy and then doing perhaps a little bit more extended biopsy to make sure you have covered the prostate.

And then, of course, a man is diagnosed with low-risk disease, then definitely consider active surveillance as the first choice and then monitor those patients over time. I think it's important to couple PSA testing with active surveillance. It's kind of a strategy that goes hand-in-hand. And so I would say that’s the future of risk stratified screening that we're in, and it's going to be even better.

Thank you. Dr. Garraway?

Yes, I mean, I agree with everything that Dr.Carlsson says. First of all, it's all about risk. So know what your risk is. Know your family history if possible. Know, obviously, your race ethnicity is pretty obvious.

So you can - if you're in a population that's at high risk, start screening early. Start, you know, before 45 and get screening regularly.

Anybody else, you can, everybody who's in our average risk category, if you're healthy and you have a long life expectancy, then you know, screening is probably a good idea.

And then be really smart about what you do with that information. Once you have that PSA value, if the PSA is really low, you probably don't need to get screening every single year.

You could probably skip a few years and just, you know, just check in periodically and get another PSA test to make sure it's remaining low. But so high risk, definitely screen early, screen regularly.

Average risk, you know, definitely a healthy person, long life expectancy, consider screening, and then you can decide what to do with those results, with the doctor, with your doctor and health care providers.

Well, I want to thank you both. You took a very complicated subject and really helped us to focus on how each person listening to this webinar can use this information for themselves. Maybe empower them to go back to their doctors, their primary care doctors or their urologists and really ask the right questions.

So I want to thank you for your time and I thank the audience for joining us tonight. Really interesting conversation and have a good night, everyone.