Let's Talk About Men: Hereditary Facts and Figures

National Webinar Transcript

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Presented by:

SHARSHERET®
The Jewish Breast & Ovarian Cancer Community

About Sharsheret

Sharsheret, Hebrew for "chain", is an international non-profit organization, that improves the lives of Jewish women and families living with, or at increased genetic risk for, breast or ovarian cancer through personalized support and saves lives through educational outreach.

With regional offices in the Midwest, Northeast, Southeast, West, and Israel, Sharsheret serves 275,000 women, families, health care professionals, community leaders, and students. Sharsheret creates a safe community for women facing breast cancer and ovarian cancer and their families at every stage of life and at every stage of cancer - from before diagnosis, during treatment and into the survivorship years. While our expertise is focused on young women and Jewish families, approximately 25% of those we serve are not Jewish. All Sharsheret programs serve all women and men.

As a premier organization for psychosocial support, Sharsheret works closely with the Centers for Disease Control and Prevention (CDC) and participates in psychosocial research studies and evaluations with major cancer centers, including Georgetown University Lombardi Comprehensive Cancer Center. Sharsheret is accredited by the Better Business Bureau and has earned a 4-star rating from Charity Navigator for four consecutive years.

Sharsheret offers the following national programs:

The Link Program

Peer Support Network, connecting women newly diagnosed or at high risk of developing breast cancer one-on-one with others who share similar diagnoses and experiences

- Embrace™, supporting women living with advanced breast cancer
- Genetics for Life®, addressing hereditary breast and ovarian cancer
- Thriving Again®, providing individualized support, education, and survivorship plans for young breast cancer survivors
- Busy Box®, for young parents facing breast cancer
- Best Face Forward®, addressing the cosmetic side effects of treatment
- Family Focus®, providing resources and support for caregivers and family members
- Ovarian Cancer Program, tailored resources and support for young Jewish women and families facing ovarian cancer
- Sharsheret Supports™, developing local support groups and programs

Education and Outreach Programs

- Health Care Symposia, on issues unique to younger women facing breast cancer
- Sharsheret on Campus, outreach and education to students on campus
- Sharsheret Educational Resource Booklet Series, culturally-relevant publications for Jewish women and their families and healthcare Professionals

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Speaker 1:
I want to encourage anyone who hasn't filled out the poll to please do so. We'll give it one more minute and then we'll post the responses and get this webinar started. This looks like a pretty knowledgeable audience so far.
Okay, why don't we end the poll? We have over 50% of the people in the webinar participating, so thank you for that. Can we share the results? Okay. Like I said, it's a pretty knowledgeable audience, but let's make sure that you understand the reasons for all of these answers. A special shout-out to those who answered the fourth question that had no actual question in it. I love your enthusiasm. Okay, let's get started.
I want to thank you for joining us tonight. We're so excited to have you here. This is a topic that you might not expect a woman's cancer organization to address: men's health. Over the past few years, Sharsheret has really worked to ensure that men's health, especially as it relates to hereditary cancer, becomes a priority.
So let's begin by answering the most common question we received in advance of tonight's webinar: Why would Sharsheret, an organization that supports women facing breast cancer and ovarian cancer, host a webinar on men's health? Well, we know that many of the genetic mutations that increase diagnostic risk of breast cancer and ovarian cancer increase the risk of other cancers as well. Those include prostate, melanoma, pancreatic cancer, and male breast cancer. We know that men and women carry these mutations in equal numbers and pass them down to their sons and their daughters in equal numbers. So therefore, we know that this isn't just a woman's issue. This is actually not just a men's issue, this is a family issue. This is a community issue. So once again, thank you for joining us tonight to be part of this important conversation.
Before we begin, I have just a few housekeeping details that I'd like to share. I want to start by sharing our gratitude for the sponsors of this program, whose generosity allows us to continue to provide support and education to you: AstraZeneca, the Basser Center for BRCA, Daiichi-Sankyo, Merck, The Max & Anna Baran, Ben & Sarah Baran, and Milton Baran Endowment Fund of the Jewish Community Foundation of Los Angeles, and The Siegmund and Edith Blumenthal Memorial Fund. And I'm excited to say that we have so many organizations that have chosen to become program partners on tonight's webinar because they understand the importance of this topic. So thank you to AnCan, the Federation of Jewish Men's Clubs, FORCE, JScreen, the Male Breast Cancer Global Alliance, Men of Reform Judaism, and the MSK Catch Program.
The webinar is being recorded and will be posted on Sharsheret's website along with the transcript. As always, participants' names and faces will not be in the recording. We received an incredible number of amazing questions before today's program, and we already have them included in a planned Q&A session toward the end of the evening. But we're going to do questions that arise during the webinar a little differently, so please pay close attention. If during

the program you have a question that would benefit all the participants, please enter it into the chat box. We will work to answer as many as possible during the Q&A. If you have a question that is specific to your own particular situation, please place it in the chat box specifically to an account named Sharsheret Genetics, who just waved so thank you for that. That is Peggy, our genetic counselor. Or if you have questions about or need some support surrounding issues related to whatever's going on tonight, Sharsheret Support, right there, one of our amazing social workers, Erin. So reach out to one of them specifically and they will message you back privately.

Okay. As a reminder, Sharsheret has been providing telehealth services to the breast and ovarian cancer communities for more than 20 years. As we move into tonight's webinar itself, I want to remind you that we are a national not-for-profit cancer support and education organization, and we do not provide any medical advice or perform any medical procedures. The information provided by Sharsheret and tonight's speakers is not a substitute for medical advice or treatment for a specific medical condition. You should not use this information to diagnose or treat a health problem. Of course, you should always seek the advice of your physician or a qualified health provider with any questions you may have regarding a personal medical condition. Let's move into the webinar.

Stories are so important to us at Sharsheret. They inform our work, they inspire us, and frankly, they make it easier to understand complicated information. And tonight, we are really fortunate to have Bill Harris with us. Bill has been married to Karen for 45 years. He is also the proud father of Eric, and in the very near future, soon to be the proud father-in-law to Megan. Congratulations. He spent 25 years as a photojournalist and an ABC News editor and is a two-time Emmy Award winner. Bill also wants you to know he's a dogaholic. Bill, thank you so much for joining us tonight to share your story. Can we get Bill spotlighted?

Bill Harris:

Perfect. Thank you very much for that, guiding the introduction. I'm very happy to be able to be here. I really admire the work this organization is doing, and I'm actually a member of three or four of the organizations that you mentioned as sponsors and supporters here. So let me quickly tell you what my story is. I'd never heard of breast cancer in men. And in April of 2012, my wonderful dog started poking me in the chest, something she had never done before. And two weeks later, a small dark spot showed up on the T-shirt that I had been sleeping in and I didn't really think much about it. The second morning I knew I had a clean T-shirt on and there was that little bloody spot again. I was online at 6:00 in the morning looking for what causes a man's nipple to discharge something that was like that and found only three things. One of them happened to have ductal cancer. And that scared me a whole lot because I didn't know men could get cancer in the breast.

I waited till 9:00 in the morning, called my doctor. After a little back and forth with the receptionist about him seeing me right away, he said, "Come in anytime today." He was able to palpate a lot more of a discharge. And within five weeks I'd had a mammogram and an ultrasound, a biopsy, and was under the knife for my first mastectomy, and still not terribly knowledgeable about all of this, and certainly not really aware of the genetic aspect of it. I started doing research, which is something that I was driven with and it was I think a way of coping with hearing this news and having a mastectomy and running around just like a woman with drains and the pain of recovery, and started to talk about it with other people.

It took four tries to get my insurance company to approve the first genetic test available for the BRCA gene mutation. A company called Myriad was charging $3,500 for it in 2012. And finally, my insurance company gave in because one, I already had a mastectomy and had cancer found in my breast, and there was a history in my family both on my father's family side and my mother. So I came back positive for BRCA2. My son and my sister got tested. They were both positive as well. My mother got tested and she was negative.

My father had passed away by then and so we couldn't test him, but pure logic and the art of genetics showed that that gene mutation had to have come down from his family line where, as I said before, there were a large number of cancers that are related to that BRCA2 mutation. My son, I said, was tested. He came up positive, my sister as well. She chose to just be diligent in watching her health. My son decided at the age of 30 to do a prophylactic double mastectomy with reconstruction. He did not want to have to go through what I did, and this was pretty much all that he had in the way of tools to be able to cope with that.
My reaction to all of this was really to get very active and advocate for men and for the knowledge about male breast cancer and the need for people to get tested in terms of genetics. So they were informed, so they could inform their family, so they could look out for their children. I'd go to meetings that were primarily populated with women, and I would sit down and talk in this group and I'd say, "First of all, there's a man in every one of your lives, whether it's a father, a son, a brother, a husband, a nephew, anything of that nature, and it's important that this word get spread because even though only about 2,500 men are diagnosed with this each year, the percentage is five times from women's mortality, from breast cancer. And education really is the way to go about it.
I went nine years with no evidence of disease. I did take tamoxifen for a year and it was just a disaster, hot flashes and all. A year ago, a little over a year ago, I was diagnosed with ampullary cancer, also a BRCA2 related cancer. And I've spent the last year fighting that. I had a Whipple procedure and had a whole lot of my plumbing replumbed and some taken out and all of that. Unfortunately, the doctor couldn't do any liposuction while he was there, but I did lose a lot of weight as a result of the surgery anyway. Knock wood, I've been extraordinarily lucky. I did chemotherapy, and did not have to do radiation. The margins and the nodes were all clear, though it was staged as a T3N0M0 cancer. I'm healthy today. I'm getting my energy back from the chemo, suffering with neuropathy and such, but getting through it all. Thank God I'm alive and I'm here to say, you have to get tested, if there's a family history especially, and you need to inform your family members and stuff about this risk. So here we are.
Speaker 1:
Wait, I have one question that came up. So for those who don't know, can you please explain what ampullary cancer is and how it was detected in your case.
Bill Harris:
Yes, of course. So as a result of my breast cancer, I stayed very careful and diligent about being tested annually, and that included ultrasound and MRIs. About three years ago, my oncologist got me connected with a physician at UCLA who was doing a study where he is still currently trying to find an early sign of pancreatic cancer. It's a killer, pancreatic cancer, and there aren't any early signs for it. By the time symptoms show up, it's usually very late in the process and pancreatic cancer is a real killer. So I was in his study, and so I was getting imaged by him and ultrasounded by the other, and then they'd swap, and they all overlapped a year ago this past summer, and there was a shadow that was found on my pancreas. Turns out that there is a little reservoir called the ampulla of Vater, which lives right and shares a wall with the pancreas. And my cancer was there.
They did a biopsy with an amazing tool they put down my throat, and it was malignant. And then we scheduled this Whipple procedure, it's called, to remove that ampule. And what that ampule does basically is, it stores the enzymes that are used to digest fats and large proteins and the like. Its job is to squirt those into your GI tract when it detects that there's food there. It is filled up normally by the constant production by the pancreas and the liver and the gallbladder with, excuse me, I'm sorry about the dogs, with the enzymes that those produce, and it stores them until your GI tract needs them to digest. The Whipple procedure took all that out, took a bunch of my intestines out as well. I have a force behind me and I'm very sorry. Took all that out, replumed me and sewed me back up, and I was very fortunate in that the margins were clear. 33 out of 33 nodes showed no sign of a disease.

Speaker 1:
Amazing, amazing.
Bill Harris:
So that's really what ampullary cancer is all about.
Speaker 1:
Thank you for that. It's not a phrase that many of us are familiar with.
Bill Harris:
It's another rare cancer. So I've knocked off two of the cancers that are related to BRCA2, and hopefully I won't have to deal with the others.
Speaker 1:
Hopefully you've done your part and you're good.
Bill Harris:
Absolutely.
Speaker 1:
Thank you so much for sharing your story. I saw several people say how inspiring it was, and we're really grateful you could be with us tonight. Thank you.
Bill Harris:
Absolutely. My pleasure. And I welcome any questions during this or afterward as well.
Speaker 1:
Right. If you have questions for Bill, you can put it in and we will ask them at the end.
Okay. We have a lot to get through tonight. We are so fortunate to have our two medical speakers with us today. They are both from Memorial Sloan Kettering Cancer Center in New York City. Dr. Robert Sidlow is a board-certified internal medicine specialist and certified in cancer genomic risk assessment. His clinical work at Memorial Sloan Kettering focuses on three areas: pre and postoperative medical evaluation and consultation, managing the long-term medical complications of cancer treatment, and cancer genomic risk evaluation. Dr. Sidlow also leads a clinical program that addresses cancer risk surveillance and reduction needs of men who carry mutations in the BRCA1 and 2 genes. He earned his MD from Columbia University College of Physicians and Surgeons and an MBA from the University of Massachusetts Isenberg School of Management. His commitment to passionate patient-centered medicine has helped to develop a unique approach to care that emphasizes open communication, evidence-based clinical reasoning.
Also with us tonight, Dr. Alicia Latham is a board-certified family medicine physician who specializes in caring for people with genetic susceptibility to cancer. She provides long-term surveillance for cancer survivors with hereditary cancer syndromes and cares for both adults and children who don't have cancer but are at increased risk. Dr. Latham also has a separate genetics clinic where she provides clinical counseling and genetic testing for people who may have inherited predisposition to cancer. Her research is focused on identifying people with Lynch syndrome based on their tumor molecular profiles. Dr. Latham is also interested in developing biomarkers for the associated cancers as many of these types do not currently have proven effective screening methods, as we've heard. She received her MD from the Medical University of South Carolina. We are particularly lucky to have both of our doctors with us during November, a movement to raise awareness about men's health issues. We are going to start tonight's medical presentation with Dr. Latham.
Dr. Alicia Latham:
I'm going to share my screen. Bear with me. Okay. So I know that the larger focus of this group is certainly talking about BRCA, but I want to first start with a brief overview of genetics. So genetics overview to just give you some basic information for genetic testing and these genes. So when you think about genetic risk assessment, one of the classic models that we like to describe is represented here. And this is what I like to call really just simply the classic model. And that's that you have a patient that comes in that maybe has a family history of cancer that's

concerning, they go into a genetics referral, and then there's, after careful counseling, focused genetic testing for what seems to be suggestive of what's happening in the patient or the family. After their results, they may have or they should have post-test counseling where a genetic counselor or a geneticist like me would go through the results of their test and what that may mean. And then this starts what we call family cascade testing, meaning that because these syndromes are what we call autosomal dominant, meaning that there's a 50% chance that all close relatives, meaning siblings, children or parents have this risk, that you start really taking care of families. So that's where this idea and my passion in both caring for families and genetics is really molded together.

For this model, there's several benefits, meaning that these are the types of patients in this classic model that would traditionally meet what we call criteria for genetic testing. You can identify high-risk mutations based on what the family history looks like, but this also has limitations. What I mean by that is that sometimes there are little things that maybe make families look a little different from others. So maybe one family with a BRCA mutation has different types of cancers that are identified versus another. So that gets to this idea of the fact that sometimes we can underestimate how prevalent some of these mutations are in a population.

Now we're moving towards this new model where maybe perhaps the patient or the family has not had cancer yet. And there is something that you may have heard of called direct-to-consumer testing, meaning now we're getting into this age in which patients and families are going online and ordering their own genetic testing and taking it to their doctors. I'm not advocating for that, but I'm saying that it's a model that we are now becoming more and more familiar with, and this idea of multiple genes being tested at once. This also has its limitations and its concerns because you may get more uncertain results when this method is followed. This may reduce your pretest counseling, but it may also increase the complexity of your post-test counseling.

Now, even more past this, we're getting to this idea of universal testing. So I call this new model, if you will. What I mean by that is that several organizations have come out and have said that for certain cancers, that perhaps we should be testing all comers for genetic susceptibility. One of the most common ones that people may be familiar with or have heard about because it is rare, is something like pancreas cancer, in which there's universal recommendations for genetic testing for those patients. Ovarian cancer is another, and those are certainly two cancer types that are strongly linked to hereditary breast and ovarian cancer syndrome, which is caused by BRCA.

We've also had policy statements. So the first one that I popped up here was from The American Society of Breast Surgeons where they actually came out a couple of years ago and said that perhaps we should be considering this for all breast cancer. I don't think we're quite there yet, but that is a policy statement from that association. And then now, even in this year, and actually the last couple of months, the National Comprehensive Cancer Center Network has stood out guidelines to say that people could even consider genetic testing for patients diagnosed with colon cancer. So that's huge.

When we're thinking about cancer itself, I think it's important to take a step back and try to identify exactly what cancer is. So the way that I do this is a little bit of a simplification, but I think it's an important analogy. And that's, one, this idea of the two-hit hypothesis. So here you see kind of the normal scenario where you have one copy of each gene, and these genes are regulating cell growth and turnover, and you have a certain type of gene called a tumor suppressor. So that's this race car's brake, if you will. And that's kind of keeping this from driving into that wall of cancer.

The first mutation that happens, either if somebody's born with it or it happens sporadically in a cancer cell, is what we call maybe an oncogene here. So the gas, all of a sudden the driver is now pushing on the gas and it's fighting that brake and the car might be moving a little bit closer

and closer because it brakes, it's not quite catching up. And then that second mutation or loss is what actually leads to the cancer. So the driver has the foot on the gas and there are no brakes in the car. My definition of cancer is that as a geneticist, I like to think of this as, cancer is simply an accumulation of genetic mutations or DNA damage that's left unchecked, and sometimes we are born with that first hit.

So as far as the percentage of cancers, when you're thinking about this as a whole, if someone were to come into my office with a type of cancer, the probability or what we call the pretest probability of that being caused by a genetic predisposition can vary depending on the cancer type. That's why there's universal testing recommendations for rare cancers like pancreas and ovarian cancers, because those do seem to be linked more with hereditary predisposition. But the vast majority of cancer is sporadic, meaning it just happened. We see a small subset of what we call familial cancer, about 15 to 20%, and what that means is that we see a clustering of cancers in a family that doesn't have a known identified genetic risk that's familial. And then about five to 10% are true hereditary cancer predispositions, meaning that we know a genetic change has been identified in the family and that's driving the cancers in that family. And that's what we're talking about today.

So when you think about hereditary predispositions, it's important to understand what that means from an inheritance standpoint. So these are, the vast majority of the time, autosomal dominant conditions, which means that there's a 50% chance that the person affected with the mutation would pass that non-working or mutant copy to any child that he or she had. It does not matter if this is inherited from the father or mother, and that's actually something that is misunderstood or has been misunderstood in the past. So just with my diagram here that I've drawn, here we have two copies of the BRCA1 gene that this father has. One of them has a mutation on it. He has a 50% chance of passing that mutation just as he has a 50% chance of not passing. And the same thing for the mother who does not have a mutation. So each child, 50% chance of sharing this mutation.

When we're thinking about cancer in general and my definition of this being an accumulation of mutations that go unchecked, our bodies do have ways to try to prevent that from happening. Many of these systems are in place to help prevent or fix these DNA errors. And these are our key systems here. There are many more, but there are two that I want to focus on today. One we've talked about and that's what BRCA belongs to, and that's homologous recombination. The other is a system called mismatch repair system. So I'm going to segue into that a little bit because I do think it is important to go over.

The mismatch repair system. So this is what's called the body spell checker, and you'll see by my little Clippy here, for those of you that may remember, he was the Microsoft Office helper that if you ever had a spelling error, maybe he would say, "Hey, you need to come and fix that." So this is how I talk about him. For people that maybe are millennial or Generation Z, this is kind of the body's auto correct, if you will, spell check or auto correct. So basically what the mismatch repair system does is, it reads through the DNA as cells are dividing and replicating and making new cells, and it's scanning for errors. And if it sees an error, its job is to fix that mismatch. Well, what happens when you have a heritable mutation in one of these genes?

So that's what's called Lynch syndrome, and it's not our entire focus today, but I wanted it to go into it just a little bit simply because people of Ashkenazi Jewish ancestry may also have an increased risk here because just like with BRCA, there are founder mutations in this syndrome. So I think it's important to cover. This syndrome has classically been associated with a couple of cancer types. One of those is endometrial cancer and the other one is actually colon cancer. And colon cancer was really the first cancer that was described here. It's caused by, again, an autosomal dominant predisposition with a mutation in one of those genes that I just showed you, and they're listed here. And really what happens is that, because that spell checker's not working and it's not fixing those mismatches, it has a bunch of mutations that can accumulate over time in the now cancerous tissue. So that's a hallmark of the syndrome.

Again, previously called hereditary non-polyposis colorectal cancer, these are the cancers that have been associated. One of them being ovarian cancer. It's a little bit of a different... Not a little bit. It is a different type of ovarian cancer than what's associated with BRCA. The ovarian cancers associated with this syndrome look a little more like endometrial tumor or endometrial tissue. They think it's associated with endometriosis compared to the type of ovarian cancer and BRCA, which is more associated with high grade serous ovarian cancer. This is more common than we previously thought. In the general population, it's about one in 279, and unfortunately over 95% of people don't know that they have it.

These are the cancer risks. I'm not going to go into them in great detail, but it depends on the gene. This is really just putting this up to show you that this is real, that this is truly a pan cancer syndrome.

These are the screening recommendations. It's actually quite high intense screening, with colorectal cancer screening via colonoscopy, recommended every one to two years, beginning around the age of 20 to 25. You can see the gynecologic cancers here. Again for men, these are certainly all cancers that would impact men apart from the endometrial ovarian. So we know renal pelvis and ureter gastric cancer, small bowel cancer, pancreas cancer, and then prostate cancer has also been associated. They're not to the same degree as the BRCA gene.

One thing that I like to highlight is that this was a study that was done out of our group, and I wasn't involved in this study, but out of our institution, really highlighting that knowing one's genetics may actually have treatment implications. And this is one of those associations that was recently found in rectal cancer. So people with Lynch syndrome, because of the defect that they have, their tumors characteristically demonstrate something called mismatch repair deficiency. All that means is that the mismatch repair system is deficient. Because of that, they seem to respond exquisitely well to immunotherapy. And this study, even though it was a very small study, proved that in these 12 patients that did this immunotherapy upfront, they were spared the toxicity of chemotherapy and they were spared the quality of life issues of having the rectum removed by doing this immunotherapy upfront. And they all achieved a hundred percent complete clinical response, which is phenomenal. Now, this is a very small study and it certainly has to be followed long term, but I think it's important to highlight how genetics really is impacting not only prevention but also cancer care.

So moving into BRCA1 and 2. These two genes are part of what we call the homologous recombination pathway. So when the DNA damage like a double-strand break occurs, that's where this pathway goes into to repair it. There are many genes that make up this pathway, but these are two of the heavy hitters. And you can see here the cancers that have been described, divided by women and men, and Dr. Sidlow is definitely going to be focusing on the male group here. But you can see it's not just breast and ovarian cancer, there are multiple cancers related to this gene.

Importantly, there's three common mutations, what we call founder mutations, in people of Ashkenazi Jewish ancestry, two on the BRCA1 gene and one on the BRCA2 gene. And we know that people of Ashkenazi Jewish ancestry, about 2.5% will have a mutation in one of these genes. So that's about one in 40 regardless of family history. So it's actually quite prevalent.

When you're thinking about this from the cancer side of things, if you were to unselect these two female-associated cancer, serous ovarian cancer or triple negative breast cancer, you can see that the likelihood of having an underlying BRCA mutation in those two is quite high and much higher in people of Ashkenazi Jewish ancestry. Simply for the reason that I just shared regarding the founder mutations.

For BRCA1 management for women, again, just a brief overview, that's not the focus today, you can see that there are, for our cancer-unaffected patients, options for increased surveillance or screening for breast cancer with annual mammograms and annual breast MRI. Women may also consider a risk reducing mastectomy for primary prevention of breast cancer.

Unfortunately, there's no proven effective screening for ovarian cancer. So the recommendation

is for women to undergo what we call risk-reducing bilateral salpingo-oophorectomy, which is simply the removal of the ovaries and fallopian tubes. And that has been demonstrated to save lives. For women that present with breast cancer, this is a 10-year interval here, so at 10 years from their first breast cancer, their risk at the second primary breast cancer is about 25 to 30% in BRCA positive patients and their risk of ovarian cancer, about 15 to 40%. So it's quite high. Again, risk-reducing oophorectomy saves lives. It's been demonstrated time and time again. And the age at which to consider this for women that have BRCA1 mutations is 35 to 40, for women with BRCA2 mutations, they may delay this a little bit later because these ovarian cancers seem to be presenting a little bit later, proven a survival benefit and also seems to be some decreased breast cancer risk when it's performed before menopause. There is a small chance of primary peritoneal cancer even after what we call a risk-reducing surgery, but this is more commonly seen in BRCA1 mutation.
Again, genetics is not just about prevention, it also has implications for treatment, and this was a major one for BRCA. So this class of drugs, these are called PARP inhibitors, it's a pill that is used. These have universal approval for patients with BRCA mutations that have been diagnosed with ovarian cancer or metastatic breast cancer. And there are several trials that have looked at that. It's also recently been approved with a POLO trial for pancreatic cancer. So certainly implications for men as well. And at our institution, we are commonly, commonly testing for these cancers, not just for families, but in the event that they may absolutely have benefit from these drugs because they do work in BRCA, they do work better in BRCA positive patients.
So key takeaways from this. People of Ashkenazi Jewish ancestry have a one in 40 chance of having one of those three founder mutations. This syndrome has a high risk of female breast and ovarian cancer. Women may elect a prophylactic mastectomy or increased screening with breast MRI in addition to mammogram. There's no effective screening for ovarian cancer, so it's recommended to undergo risk-reducing surgery. There's certainly other cancer risks here too, which are pancreas and melanoma. And then men are also at increased risk, as Dr. Sidlow will now describe.
Dr. Robert Sidlow:
Thank you so much, Alicia. I'm going to share my screen. Give me a moment here. Sorry. Just give me a moment. Let me... Just give me one minute. This is not working, of course. Okay, can you see my screen?
Speaker 1:
It doesn't look like you're sharing at the moment.
Dr. Robert Sidlow:
Say that again?
Speaker 1:
It does not look like you're sharing at the moment.
Dr. Robert Sidlow:
Okay, sorry.
Speaker 1:
It was up twice before. If it's not happening easily, we can share your slides. Oh, looks like maybe you've started screen sharing again.
Dr. Robert Sidlow:
Okay, now can you see my screen?
Speaker 1:
We can see your screen, although we don't see it as a slideshow. We see that... There we go.
Dr. Robert Sidlow:
Okay, so I'm going to move my camera. Okay, so you see my slides now, correct?
Speaker 1:
Yes, we're good to go.

Dr. Robert Sidlow:
Okay, all right. I'm sorry about that, but okay, excellent. Good evening. My name is Rob Sidlow, and as was mentioned, I run the BRCA Cancer Risk program for men at MSK. This is a picture of me and my best friend David on a hike in New Mexico several years ago. At that time, David mentioned to me in passing that his father had died of metastatic prostate cancer at an early age, and my ears perked up and I was immediately concerned about the possibility of a hereditary cancer predisposition. I want to let you know however that David gave me permission to talk about his story. So since David is a card-carrying Ashkenazi Jew, I suggested that he get tested for a BRCA gene mutation. David sent off a saliva sample to 23andMe, and he tested positive for the BRCA2 Ashkenazi founder mutation, as Alicia just described. Presumably, he inherited this from his dad. Now, as a healthy cancer previvor, he didn't quite know what to do with this new health information and neither did his regular doctors.
Now, BRCA gene related cancer risks are generally seen as a women's health issue. This makes a lot of sense given the strong penetrance of this gene among women in its manifestations as female breast and ovarian cancer. And appropriately as a result, there are many systems of care available to women with inherited cancer risk. Now, men on the other hand, often fly under the radar screen. First, in general, most regular clinicians aren't trained to deal with genetic health issues and certainly not men's BRCA. Second, men are often not the most willing and forthcoming of patients. Often, men will only be seen by a medical professional when pushed to do so by their loved ones. And as a result, there are few, if any, systematic resources for the specific needs of men with BRCA.
After my conversation with David and seeing his difficulty finding someone to quarterback his BRCA cancer screening needs, I decided to start a program here at MSK to address his healthcare gap. And tonight I'd like to spend a few minutes with you to address two key questions. Number one, what are the cancer risks associated with being a man with BRCA? And two, what can be done to minimize those cancer risks moving forward?
So first, let's talk about male breast cancer. As was mentioned by Bill, it's a rare disease. There are roughly 2,500 cases per year that account for about 500 deaths per year. And the lifetime risk in the general population is really, really low. Roughly, one in a hundred thousand is one of the common estimates. It accounts for less than 1% of overall breast cancer cases per year. And the risk factors for developing male breast cancer have to do with an imbalance between estrogen and testosterone levels, so taking extra estrogen from outside the body would put someone at increased risk. Obesity, cirrhosis, alcoholism, a history of undescended testicles, or a presence of gynecomastia, which is breast tissue under the breast, actual breast tissue as opposed to fat under the breast, all increase a man's risk of developing male breast cancer. And in addition, prior radiation to the chest would also increase that risk.
Now, there's a strong influence of family history for male breast cancer. About one in five men with breast cancer also have a first degree relative with breast cancer. And the risk of male breast cancer increases as the number of relatives in that family tree increases up to five times. Male breast cancers are often detected at a later stage than women, and men have a poor 10-year survival compared to women. And that has to do with the fact that these cancers tend to invade the lymph nodes early and there's early skin and nipple involvement with men sooner than with women. Most of these cancers are hormone receptor positive. And triple negative breast cancer and HER2 positivity are much less frequent in men than in women.
Now, this graph highlights the modeled lifetime risk of developing breast cancer among men with BRCA. And we see that the general population risk is rather low, about 0.1%, one in a hundred thousand, and it remains so in old age. However, men with BRCA1 have a roughly 2% chance of developing the disease by age 80, whereas the BRCA2 men have a much higher lifetime risk of roughly 8%.
So we're left with a question: Does regular breast cancer screening prevent morbidity and mortality in men with genetic risk? And in contrast to female breast cancer, given the rarity of

this disease in men, there really have been no prospective clinical trials to answer this question for us. So we really don't know for sure.
Now, while we don't have clinical research studies to prove that regular examination of the male breast saves lives, we do have our common sense, and it simply makes good sense for men to regularly check themselves for abnormalities even in the absence of evidence. And what are those abnormalities? First off would be a lump that one would feel, any kind of nipple discharge would be abnormal, any unusual reddening in the skin around the breast, inversion of the nipples, and any kind of abnormal skin dimpling.
Now, the most common finding in men with breast cancer is a painless lump behind the nipple. Here are two examples of physical findings that we would find in someone with more advanced disease. Again, you see here the nipple is inverted and there's this abnormality in the contour of the breast here. In this example, you see a mark of asymmetry in the size of the breast from the left breast to the right. And again, there's this abnormal puckering, discoloration, and the nipple looks deformed.
Does mammography work for men? Now, the only published evidence we have comes from two retrospective chart audits from NYU and MSK, which looked at their imaging experiences from over a 20-year period. They looked at 328 men who were all high risk, who had mammograms, and they found, again, retrospectively looking backwards, that nine cancers had been found and these were all in BRCA patients. Interestingly, none of these cancers were detectable on a physical exam, which is what we're trying to shoot for, and all of these cancers were early stage, had negative lymph nodes and were curable. The estimated cancer detection rate, looking backwards again, was five per 1,000 examinations. And this really compares favorably with roughly the same cancer detection rate that we've established in average risk women based on prospective trial data.
So the NCCN guidelines for breast cancer screening in men with BRCA1 and BRCA2 recommend breast self examination starting at age 35, an annual clinical examination also starting at age 35 by a licensed medical professional, and to consider an annual mammogram starting at age 50 for men with gynecomastia, that's that abnormal tissue behind the breast, at age 50 or 10 years prior to the earliest male breast cancer. They state that there's only limited data to support imaging based screening for male breast cancer, again given the limitations of the data that we have.
My clinical practice is a bit more nuanced. Given the much higher 8% lifetime risk attributed to BRCA2 and given that mammograms are really relatively safe and pretty well able to identify these early cancers, I discuss the option of obtaining a baseline mammogram for my BRCA2 patients around age 50. And I found that most of my men opt in for this. The question remains when to repeat screening, and this really remains undefined. For both BRCA1 and BRCA2 patients, the presence of a strong family history of any breast cancer would also be a strong influencer in the shared decision making process. In general for BRCA2 patients, I don't necessarily recommend imaging because the risk is really quite a bit lower than that for BRCA2.
Now, it's important to realize that the male patient can experience psychological and emotional dissonance when engaged in a breast cancer screening plan. Now, this qualitative study of men with BRCA highlights the fact that more often than not, the embodied experience of men does not include the presence of breasts. Quoting one of the study participants, "In the medical profession, men have breasts, but in the real world, men don't talk about their breasts, they talk about their chests. There is a disconnect between the medical profession and regular people. And as medical professionals, it's important for us to address this issue up front and to normalize the screening process for those patients who opt to do so."
In addition, the breast imaging process can be a gendered-patient care experience depending upon the physical and demographic details of the facility you use. So you should be aware of what to expect if and when you get a mammogram as a man.

Next we're going to talk about prostate cancer. So prostate cancer is the most common cancer in men other than skin cancer. About one in eight men will be diagnosed with prostate cancer during his lifetime. It accounts for 269,000 cases per year and 34,000 deaths per year. It's the second leading cause of cancer death in men behind lung cancer. And most men importantly die with prostate cancer, not from it.

Risk factors include age, as one ages, the risk increases; being Black; having a father or mother with prostate cancer more than doubles a man's risk; and being overweight also increases the risk of having particularly deadly prostate cancer.

Now, a word about how to categorize prostate cancers. The Gleason score is the score that we use, and it's determined by adding the two most common cell patterns seen on prostate biopsy specimens from a low of six for well-formed prostatic glands to a high of 10 for poorly formed necrotic cells. The Gleason score correlates with tumor growth speed and aggressiveness, and in turn, overall patient disease-free survival. The higher the Gleason number, the long term outcomes.

Prostate cancer and BRCA. Men with BRCA2 develop prostate cancer at an average earlier age than others, with a mean age of 61 versus 64. For patients with BRCA2, the cancers tend to be more aggressive with 77% being a Gleason score of seven or above. These cancers tend to have increased lymph node involvement in distant metastases at the time of diagnosis. And there's an overall decreased long-term survival for men with BRCA2 and prostate cancer as opposed to non-carriers. BRCA1 has a much weaker association with the development of prostate cancer, and these men are more likely to have slow growing disease with Gleason scores around six. Some investigators question whether there is actually even an increased mortality of men with BRCA1 and prostate cancer.

Now, based on a recent large prospective cohort study, the estimated cumulative risk of developing prostate cancer by age 85 is 29% for BRCA1 and 60% for BRCA2 mutation carriers. BRCA2 carriers have a two to fivefold higher risk of being diagnosed with prostate cancer as compared to the general population. So is there any evidence to suggest that prostate cancer screening in high genetic risk men is helpful? To date, we only have interim data from the European impact study, which began recruiting men in 2005 and finished in 2013. They recruited 3,000 men in Europe with either a BRCA1 or BRCA2 mutation, and they conducted annual PSA screening and opted for a prostate biopsy if the PSA level rose above three. Now, the interim results that were published after three years of screening showed that indeed there's an increased prostate cancer detection rate, 3.4% for BRCA1 and 5.2 for BRCA2, which is higher than the controls one. So PSA testing does seem to capture patients more effectively. Now, the question remains if we could do better by adding MRI screening to the prostate protocol for high-risk men since MRIs are very capable of finding prostate abnormalities at an earlier stage. The National Cancer Institute in Bethesda, Maryland has opened the study to answer this question and is actively recruiting them with any of the high-risk prostate genes listed here to participate. Now as a shameless plug for this study, it's free for all participants and all expenses are paid for.

The NCI study provides men with any of those genetic mutations with a prostate specific MRI every two years along with PSA testing. Now, they have opted to use a lower abnormal PSA cutoff to prompt further workup, which should increase the overall capture rate. In the general population, PSAs are considered abnormal above the level of four, whereas you see here that levels of two for men between ages 30 and 49 and 2.5 for men above age 50 are considered abnormal. Again, a lower threshold.

Other important elements of this study hope to investigate new frontiers in precision-based early prostate cancer detection, looking at whole genome, whole exome analysis, cell-free DNA studies, RNA transcriptomes, polygenic risk score, derivation and validation, and overall biomarker of discovery.

Here's a real trial example that was shared with me, and this was a 55-year-old man with BRCA2 who had a normal rectal exam and a normal PSA. It was 1.68, certainly would not have been caught in the impact study. He underwent an MRI and he had a left peripheral zone lesion. He eventually underwent a radical prostatectomy which showed Gleason 8 cancer. And again, this man would've been missed using the impact protocol. The question still remains whether this man actually has a mortality benefit from this. But regardless, we certainly are capturing these cancers earlier so we can surmise that the patient will do better.

So from the NCCN guidelines, they recommend for any man with BRCA2 to have a baseline digital rectal examination and annual PSA testing starting at age 40 using these cutoffs. The main modification to the NCCN guidelines in my practice is to use the lower cutoffs, that I had mentioned before, of two and 2.5. And I'm actively trying to encourage my patients to engage in the NCI study so that we can actually have some hard research on this question.

Now, pancreas cancer is the final major cancer, which should be on the radar screen for people with BRCA. And this affects both men and women. I'm not going to talk about melanoma. So pancreas cancers are rare in the general population, account for about 12 out of 100,000 people with cancer. It only accounts for 3% of all cancers, but it really rises to people's consciousness because it's very deadly. The average patient diagnosed with pancreas cancer will live for about one to three years after diagnosis. The reason for this is that these cancers are often microscopically or locally spread at the time of diagnosis. They're notoriously difficult to diagnose early. Once a patient has symptoms of jaundice, turning yellow, abdominal or back pain, or any kind of symptoms, that indicates that the tumors usually often advanced. And once the tumors advanced, there are no effective treatments for long-term survival. Theoretically, pancreas cancer is curable if it's caught early, when the tumor is very small or even better when it's microscopic.

Risk factors for pancreas cancer include age, as one ages all cancers become more prevalent. Obesity, smoking, family history of having pancreas cancer, recurrent pancreatitis, which is inflammation of the pancreas, and personal genetics accounts for five to 10% of pancreas cancer cases.

Now, it turns out that about 7% of all patients with pancreas cancer have a BRCA1 or 2 mutation. For an individual person with BRCA2, the estimated cumulative lifetime risk of developing pancreas cancer is around 4%. For BRCA1, the risk seems to be a bit lower, around 3%. And you see there are very wide confidence intervals here, although some people feel that the risk for BRCA1 and pancreas cancer is even lower than 3%.

Now, what tools do we have to screen for pancreas cancer? We discussed that physical examination is not helpful. The few blood markers that we do have have not been shown to help catch pancreas cancer at an early enough stage to be useful, specifically blood tests called CA19-9, which you might have heard. What's interesting to note is that new onset diabetes sometimes predates the diagnosis of pancreas cancer by six to 12 months. So perhaps, new diabetes should be raising our antennae.

Now, imaging for small early tumors or precursor cysts is currently the only option. Endoscopic ultrasound involves the insertion of a camera and ultrasound probe into the upper GI system, and it requires light anesthesia. Endoscopists can detect very small abnormalities and biopsy them at the same time if needed. MRI involves the use of IV contrast and doesn't have quite the same resolution as EUS. However, it's easier to tolerate, but both are expensive and time consuming.

So does pancreas cancer screening actually help? So this recent analysis of 1,750 high-risk people with genetic mutations or with a strong family history of pancreas cancer who were screened with EUS and MRI over several years shows that out of these patients, only 19 pancreas cancers were found out of 1,750 patients over a 20-year period. But what was very striking was that 60% were found at an early stage, stage 1, and these patients' five-year survival was 73%, which is unheard of in pancreas cancer. On the other hand, seven cancers

were found in patients who dropped out of the screening protocol. 86% of these cancers were stage 4 and all patients were gone by four years. Now, strikingly, the median survival time in the screen group was 9.8 years, and it was only 1.5 years in the onscreen group.
Now, it's important to note that all of the patients with cancers, whose cancers were found by screening, had also died within 13 years after the tumors were diagnosed. There's a question if the screening and subsequent surgery actually helped extend the lives of these patients, or perhaps the screening simply labeled these patients as having pancreas cancer sooner than they would've otherwise. And perhaps there was already microscopic spread early on. In research, it is just called a lead time bias. Now, since this was not a randomized control trial and there never will be one, we simply don't know for sure. However, given the huge difference between 1.5 years and 9.8 years of median survival, this study does suggest strongly that screening and surgery most likely can add years of life to those in the very highest risk groups who are destined to develop this disease. Importantly, 200 people need to be screened over several years to catch one pancreatic cancer.
We also see from this study that there was an excellent long-term survival among those patients who were found to have pre-cancers in their pancreas. This is called high-grade dysplasia, labeled here as HGD. These are not actually tumors. Pancreas cancer grows from microscopic abnormalities in pancreas cells that precede the actual development of a cancerous tumor. This is analogous to a precancerous polyp which can eventually grow into colon cancer. This excellent survival of the few patients who are found to have these precursor lesions in the pancreas emphasizes the need to find ways to detect abnormalities at the earliest time possible. And imaging simply has its limitations.
So, what is my practice? If there's a first or second degree relative with pancreas cancer from the same side as a man or a woman with a BRCA gene, this is what we call a very high-risk situation and this was a population that was studied in these studies that I had shared with you. The American Gastroenterology Association and the CAPS guidelines recommend the alternating MRI and EUS every year at an expert center like MSKCC. Everybody, regardless of whether they have a family history or not, should have an annual glucose in HBA1c drawn.
The question remains, what if there's no first degree relative with pancreas cancer? What about all the people with BRCA who have no family history? So this is really unclear at this point whether this population should have an EUS and an MRI. There's only one guideline which was recently published in July of this year actually that has a conditional recommendation to screen all BRCA patients, and it was based on poor quality evidence however. Some centers, namely Hopkins and University of Pennsylvania, and from what I understand from Mr. Harris, UCLA as well, some centers are moving away from requiring a positive family history. We're really not sure if it helps. We might be over testing and it would require millions more screening tests. And there are system capacity issues. This is clearly an evolving area.
We want to caution you, there are downsides of pancreas cancer screening. As I mentioned before, while there's a strong suggestion that screening is worthwhile, we're not entirely confident that it saves lives in the long run. It can be burdensome on patients in the healthcare system, costly, time consuming. There's gadolinium exposure, anesthesia for the endoscopic ultrasound, and there's a problem of over-diagnosing benign cysts. Now, about 50% of us walk around with cysts in our pancreas. And certainly if you're engaged in the screening program, if we see cysts, they're going to get biopsied and it could lead to more testing and possibly major surgery that could theoretically be unnecessary. The surgery can have complications and can result in major lifestyle changes. Engaging in a cancer screening program can either increase somebody's anxiety or also decrease someone's anxiety from developing this disease.
The reality is that despite everything I've discussed with you tonight, it's often very difficult to convince insurers to pay for the studies we order. As outlined in this recent commentary, the insurance barriers and personal costs associated with image-based screening after positive

genetic testing can be very real. Insurers base their coverage for cancer screening through the lens of customers at average risk for cancer, not those at high risk.
Now regardless, it's important to note that the future of the field of early cancer detection does look promising. Here are examples of new tests on the market to detect abnormal cancer DNA, proteins, and other markers shed by cancer cells into the blood or urine, presumably at a very early point in the development of a tumor before it is visible with our current imaging tools. Now, while these tests are not ready for primetime use at all yet, we are hopeful that research technology and the marketplace will continue to advance and provide us clinicians with simpler and more effective tools to catch cancer early. In the meantime, we have to make an effort to do the things we can do to prevent cancer, like maintain a healthy weight, exercise, and avoid harmful habits like smoking or drinking too much alcohol.
As we near the end of this presentation, I'd like to take a step back and clarify who are the men who should get tested for BRCA. Number one, anybody with a personal history of prostate cancer that was either metastatic or a Gleason 8 or higher. Two, anybody who has a family history of one or more close blood relative with breast cancer of early onset, triple negative breast cancer at any age, male breast cancer at any age, ovarian cancer at any age, pancreas cancer at any age, prostate cancer with metastatic or high or very high risk group histology, or anybody with two or more close blood relatives with either breast or prostate cancer at any grade in any age. And finally, anybody who is an Ashkenazi Jew, as was mentioned, one in 40 Ashkenazi Jews is a carrier, and it's important to know that.
So, David is doing great. He exercises, he watches his weight, he doesn't smoke or drink. He's getting a regular PSA and prostate examination. And certainly, if his PSA rises above 2.5, he's going to get an MRI and be worked up for that. He's also considering enrolling in the NCI Natural History Study to allow him to get that MRI of the prostate beforehand. He had a normal mammogram and he regularly self-checks for chest, breast abnormalities. And he is really on the fence about engaging in a pancreas cancer screening program. He has no family history of this problem, and he's willing to wait for better noninvasive tests to develop. In the meantime, he has an annual glucose and A1C test.
So in conclusion, men with germline genetic risks deserve specialized attention. For men, having BRCA2 carries more cancer risk than having BRCA1. Cancer screening and management requires clinical nuance and shared decision making. Currently, there's really limited high-quality research to help our decisions. And specialized programs to coordinate high-genetic risk screening and surveillance can be valuable to male and female previvors. I encourage all of your males to get tested, all of your male relatives to get tested.
And finally, this is just a plug for our program that Alicia and myself run. It's called MSK Catch. If you have any interest in getting any clinical guidance from either of us, the phone numbers are here. You can also Google us, and we're happy to help you out.
Speaker 1:
Thank you so much. Such great information. We're going to do some Q&A, but to be fair about the time, I see that our numbers aren't getting any lower, so I assume people will stay. But I do want to just say a couple of things in case somebody has to leave. So the two things I want is, if we can post the evaluation link in the chat box now, a little earlier than I originally asked for, but also there were a number of questions that came in that want the following information. We do want you to know that there will be a follow-up email by the end of this week or early next week that will include a recording, which includes the slides and audio, as well as a transcript for anybody who wants to review what was said tonight, or if you know somebody who would benefit from that. We'll also include some other helpful links. So that is coming.
Let's spend the next few minutes doing Q&A, and we'll see how many questions we can get through. Okay, an amazing number of questions here. I'm not sure who this is for, so whoever is the best one, but can you speak about the relationship between having a BRCA mutation, BPH, and other possible cancer risks?

Dr. Robert Sidlow:
There's actually no relationship between BRCA and BPH. BPH is a benign growth of prostate cells that just happens by virtue of growing older. There's no relationship.
Speaker 1:
That is actually wonderful news. Okay, a couple of questions about... I know we spent a lot of time on BRCA tonight, but what about prostate cancer or any of these cancers with regard to other mutations? For instance, a particular question came in about CHEK2, but if you have other mutations you want to add to that, that would be helpful too.
Dr. Robert Sidlow:
Alicia?
Dr. Alicia Latham:
Sure. So there's many genes that have been associated with prostate cancer. One perhaps that's very important to note is a gene called ATM. That gene has been associated with pretty aggressive prostate cancer, but there are many others. In fact, whenever we see a patient with prostate cancer, we actually typically don't just test through BRCA1 or 2, we do multi-gene panel testing. So I think that that's an important finding.
Speaker 1:
Thank you. That's helpful. For somebody who's already been diagnosed with prostate cancer, is there a heightened risk for male breast cancer? And I don't have the information as to whether or not that person has been genetically tested.
Dr. Robert Sidlow:
Absent an actual genetic mutation such as BRCA, not to my knowledge. There's no relationship.
Speaker 1:
Okay. Fantastic. For someone who has a strong family history, at what age do you recommend genetic testing?
Dr. Alicia Latham:
It depends on what the family history is and what we're looking at, to be quite honest. So what I will say is that in general, these cancer predispositions typically only affect adults. Unless it's information that would be used for perhaps family planning purposes, we don't typically test children unless the family history shows a very early onset, meaning before the age of 18. So I would just encourage anyone to speak to a genetic counselor about specifics. Define an adult.
Speaker 1:
Yes. I was going to say the same thing.
Dr. Alicia Latham:
Depending on the syndrome, adults, certainly no one under the age of 18. If we're thinking about things like Lynch syndrome for example, we would recommend testing for when actually intervention would take place, so the age of 20, because that's when we would recommend beginning screening. For BRCA1 and 2. For women, it's a little bit earlier because you would start breast cancer screening perhaps around the age of 20 to 25, and then men, it would be a little bit later, at least for their own health versus family planning purposes.
Speaker 1:
Somebody asked, for women and mammograms, sometimes dense breasts make it difficult to discover cancer on a mammogram. Do men have that same issue?
Dr. Robert Sidlow:
Not to my knowledge. The question of whether ultrasound should be used to screen men is completely unresearched, unlooked at. The current recommendations only look at mammograms, but ultrasounds typically can be more sensitive than mammograms. So I'm sure ultrasound would be probably just as good, but mammograms are really the only tool we are using.
Speaker 1:

Okay. That's good information. Okay. Are familial cancers simply genetic cancers where we haven't discovered the mutation yet?
Dr. Alicia Latham:
Maybe.
Speaker 1:
That sounds mysterious. Okay.
Dr. Alicia Latham:
So it could be but there is a gene that has not been discovered yet. It could also be that it's multiple factors coming into play. What I like to say is that families, they live together, they drink the same water, they eat the same food, they have the same habit, so you really need to be able to kind of tease that information out. So possibly.
Speaker 1:
That's great. Thank you. Can you discuss whether or not it is beneficial to test a parent whose siblings had cancers of concern, young, female breast cancer, older male breast cancer, if the person is not ready to test themselves? I guess, let me just... Should a parent of an adult be tested if there's cancer in the family, but the adult child isn't ready to be tested themselves? Is there benefit to that?
Dr. Alicia Latham:
If I'm understanding correctly, I want to make sure I have my generations here, so you're saying there's an adult child that is interested in genetic testing, but maybe let's just say an aunt or an uncle, there's hereditary cancer risk and we're trying to understand if the connection, the genetic connection-
Speaker 1:
Yes. That's what I believe is being asked.
Dr. Alicia Latham:
Yeah. Okay. So I think for one's own health, absolutely, I think that it's important information to have, particularly, say for example, this might impact someone's pre-surgical risk for such things like ovarian cancer. But also, I think it's important to have a conversation as a family so that people may understand, "Hey, for me, I want to do this. You may not want to do this for you, but it does open up a can of worms." So I think it's important to have that discussion as a family unit.
Speaker 1:
A couple more questions. A lot of questions about screening protocols and getting insurance to cover what is the screening protocol. So a couple of them. Will insurance pay for a mastectomy, no, I'm sorry, a BRCA screening if the patient's already had a mastectomy, a male mastectomy? Another one was, colon cancer screening recommendations have dropped in age recently, has insurance kind of followed that? Things like that. Can you just speak a little bit to insurance?
Dr. Robert Sidlow:
I will speak to one thing, and I'll let Alicia fill in the gaps. Most insurances follow what's called a US Preventive Task Force guidelines, which is an organization that reviews the data every couple of years and synthesizes it and determines a grade of evidence, A, B, C, or D. Any grade A or B recommendation from the United States Preventive Task Force, insurance companies generally adopt, so regular mammograms, cervical cancer screening, the usual types of cancer screenings. And if the US Preventive Task Force will adopt the new recommendation from the American Cancer Society to start colonoscopies at age 45, it will be routinely paid for. The problem is that, as I mentioned, this guidance is all through the lens of average risk. It doesn't speak to people at higher risk. So that's where some of the problems come in terms of getting these reimbursed. Alicia, I'm sure you have some comments.
Dr. Alicia Latham:
For colon cancer risk, yes, the general population guidelines have been lowered to 45, including the USPSTF, so that should be covered, that shouldn't be an issue. For some of these other

measures for high-risk populations, sometimes it depends on the insurance carrier, and they do have their specific guidelines and criteria. What I typically do for my patients is, we have that conversation up front, and then if there's any concern and need for a letter of medical necessity, then we're always happy to provide.
Speaker 1:
Thank you. Okay, three more questions. So one is, actually this is a two-part, so maybe three and a half questions, if somebody knows they're at higher risk and wants to get into a study, what I'd love to be able to say is, if you have something really quick now to figure out how they can access these studies, but also if you could provide us a link, we'll put in the follow-up email because I think that's important. And then somebody did ask, if you carry a mutation, who manages this? Your program is pretty unique, so if somebody doesn't live within a subway ride to MSK, what type of doctor should they be going to? So that's that two-part question.
Dr. Robert Sidlow:
Alicia, you want to go? Oh.
Dr. Alicia Latham:
For the second question about who should manage, I think it depends on the syndrome. You need to make sure that whichever doctor is that you have looked at, I typically say start with your general doctor, engage to see what their understanding is of the hereditary predisposition. And then certainly there could be looking at subspecialties for BRCA, we think about for women, gynecologists, they're well versed in this field. They know these mutations very well. And I think for men, I think an internist for these mutations is completely appropriate. But again, it's important to understand medical knowledge. I would encourage people that don't live in the New York area to talk to a cancer genetic counselor. You can find that resource on the National Society Genetic Counselors' website, and they can guide you to providers that do this care in their state.
Dr. Robert Sidlow:
In terms of the question about how to access some of these clinical studies, I will provide the link to the NCI study. I think Anna-
Speaker 1:
Yes. It was put in there, but we'll include that. And we also have some Sharsheret information on how to access clinical trials. So we'll include that in the follow-up email as well.
Dr. Robert Sidlow:
Okay, great.
Speaker 1:
Okay, two more. Dr. Sidlow, you specifically said you're not focused tonight on melanoma, but can you give us a one sentence, if people know they carry BRCA mutations, should they be visiting a dermatologist every year to get a full body check? What's the process here?
Dr. Robert Sidlow:
It's very simple. The association between BRCA and melanoma is not quite as strong as people have thought in the past. The recommendation is just simply get an annual full skin examination, which is probably a good idea for anybody regardless. So that's why I didn't spend any time on it. Just go and get yourself-
Speaker 1:
Thanks for clarifying that.
Dr. Robert Sidlow:
Absolutely.
Speaker 1:
That's good to know.
Dr. Robert Sidlow:
Yep.
Speaker 1:

Last question. This is more of a general question. We know that men often ignore their health. The slides you showed indicate that. That being said, what can we do as a society to encourage men to seek the proper screenings for breast cancer or other cancers from their medical professionals? Listen, Sharsheret is doing our best to educate and we will continue, but any guidance you have may be for the people here who have men in their lives they want to encourage.
Dr. Robert Sidlow:
They just got to hock a chinik. (from Yiddish *hakn a tshaynik*) means to rattle on, nag, or talk nonsense, literally "to knock a teakettle".
Speaker 1:
Okay. That's the technical medical advice you have.
Dr. Robert Sidlow:
I'm open to suggestions. The loved ones in your family need to push you out the door and get you to go see a doctor.
Speaker 1:
When I go out and talk to groups, it's the same for men and women. If it's not enough to know that you should be caring for yourself, think about this as modeling behavior. How will the children or grandchildren in your lives, their daughters or sons, granddaughters or grandsons, know that they're supposed to care for themselves unless they see you doing it themselves? So if you don't do it for you, do it for your children and grandchildren. Okay. We really do need to wrap up, but I am so impressed at the... Oh, is there-
Dr. Robert Sidlow:
William has his hand up.
Speaker 1:
Oh, I'm so sorry.
Bill Harris:
That's okay.
Speaker 1:
Please join us.
Bill Harris:
I've been here all the way through. I'd like to point out a couple of things. One is that the recommendations for testing ages for examinations and that sort of stuff are just that, their recommendations and they're based on averages and statistics. An example of that, a young man whose slide was shown in one of the presentations holding up his shirt and his scar is Bret Miller, who is one of the founders of the Male Breast Cancer Happens Coalition Group. He complained about a problem with a pain in his breast from the age of 17 until a doctor finally took him seriously at the age of 23, and was diagnosed with stage 4 breast cancer. He is very healthy today. This was 10, 12 years ago. He's healthy, the father of two beautiful little children, and he is the co-founder of that organization.
So my recommendation is that, if somebody detects something and they're outside of those recommendations, that they shouldn't just say, "Oh, I shouldn't bother for another few years." They should definitely speak to their primary care physician and have it checked. Much better to be told, "Oh, it's nothing. It's a cyst or something of that nature,"rather than to miss something that could be really terrible later on. And I think-
Speaker 1:
Advocating for yourself is always important.
Bill Harris:
Absolutely. In terms of what can be done, I go to groups at least twice a month to discuss these issues, and education really is a key to doing good work in terms of getting people to speak to their doctors, to take care of themselves, and be their own best advocate.
Speaker 1:

Thank you. Thank you. Okay, we've got to wrap up. I just want to remind you quickly that Sharsheret has an amazing Genetics for Life program. Our genetic counselor, Peggy Cottrell, who has been answering questions also through the chat all night, consults with men, with women, with families, answers individual questions about family history, genetic mutations, personal risk, all free of charge. Our genetics program also educates through our website, which has a robust men's section, as well as through our national webinars. I want you to know that our next genetics-focused webinar is going to be at the start of January, and we'll focus on genetic variants of unknown significance. That is something that a lot of people we work with are dealing with and have to make decisions about. We'll let you know more about this in the near future as soon as we have that information.

Thank you Bill for sharing your powerful story. Thank you to both Dr. Sidlow and Dr. Latham for sharing your expertise this evening. Once again, I want to thank our sponsors AstraZeneca, the Basser Center for BRCA, Daiichi-Sankyo, Merck, Max and Anna Baran, Ben and Sarah Baran, and Milton Baran Endowment Fund of the Jewish Community Foundation of Los Angeles, and The Siegmund and Edith Blumenthal Memorial Fund. Thank you to our program partners, AnCan, the Federation of Jewish Men's Clubs, FORCE, JScreen, the Male Breast Cancer Global Alliance, Men of Reform Judaism, and the MSK Catch Program.

If you didn't yet take the opportunity to fill out the evaluation, the link's going back in right now. Please do. And if you fill it out, you'll be entered to win a Sharsheret swag bag, which has some really exciting stuff in it. We look forward to continuing this conversation with you.

I'm excited to let you know that as we continue our commitment to men's health education, we've established a Men's Leadership Council, which works to save lives through education. We've published in the past year our first men's health print resource, and we're now scheduling focus groups to explore how we can continue to best educate men about risks. If you're interested in learning more about any of those, you can indicate that on your evaluation and we'll get in touch with you.

Finally, a reminder that Sharsheret is here for you and your loved ones, men or women. We provide emotional support, mental health counseling, and other programs designed to help you navigate through a cancer experience, including pre-diagnosis, genetic information, risk reduction, as well as during the cancer experience and into survivorship. All are customized, confidential, and completely free, so please don't hesitate to be in touch with us. Thank you for joining us tonight, and have a good night.

Bill Harris:

Thank you.