New For You: Updates in Testing and Treatment Options for Hereditary Breast and Ovarian Cancer

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Presented by:

SHARSHERET®
Your Jewish Community Facing Breast Cancer

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Keith: Good day, everyone, and welcome to today's Sharsheret program. At this time, all participants are in listen only mode. Later, you will have the opportunity to ask questions during the question and answer session. You may register to ask your question at any time by pressing star and one on your touch tone phone, and you may withdraw yourself from the queue by pressing the pound key. Please note this call is being recorded. It's now my pleasure to turn the conference over to Shera Dubitsky. Please go ahead.

I. Introduction

Shera Dubitsky: Thank you, Keith, and good evening to all of you. Welcome to our national webinar, "New for You: Updates in Testing and Treatment Options for Hereditary Breast and Ovarian Cancer." My name is Shera Dubitsky, and I am the Director of Navigation and Support Services at Sharsheret. Before we begin, we'd like to thank AstraZeneca for their very generous contribution to tonight's program, and to the Cooperative Agreement DP14-1408 from the Centers for Disease Control and Prevention. We very much appreciate their support, particularly around these important topics that particularly are of concern to those in the Jewish community.

For those of you who are not familiar with us, Sharsheret is a national not-for-profit organization supporting young Jewish women and their families facing breast cancer. Our mission is to offer a community of support to women of all Jewish backgrounds diagnosed with breast cancer, or at an increased genetic risk. We are fostering culturally relevant individualized connections with a network of peers, health professionals, and related resources. I do want to say that although our expertise is in Jewish women and young women, we offer support to anybody who reaches out to Sharsheret, and we want to be there for all of you at any point in your journey, and at any time. Certainly, feel free to continue to be in touch with us, even after this evening's program.

In the general population, 1 in 345 individuals carry the BRCA gene mutation. Of those of Ashkenazi Jewish descent, meaning those who have ancestors from Eastern Europe, that number is 1 in 40. This is certainly very much a concern to the Jewish community, because those of Ashkenazi Jewish descent are ten times more likely to carry the BRCA gene mutation. What does that really mean? It means that those who are carriers of the BRCA gene mutation have as high as an 80% lifetime risk of being diagnosed with breast cancer, and as high as a 40% lifetime risk of being diagnosed with ovarian cancer. These are the kind of things that Sheila Solomon will be addressing in her presentation tonight.

Before I introduce Sheila, I want to say that we're very excited to have Sheila on board. She's been with us for several months, so this is an opportunity to publicly introduce her to the Sharsheret community. In addition to tonight's presentation, Sheila consults with women and families and answers individual

questions about family histories, the BRCA mutation, and personal risk of hereditary breast cancer and ovarian cancer. She also contributes to the development and implementation of Sharsheret's hereditary cancer resources and programs.

The other thing that Sheila will be able to do, and I want to encourage all of you to take advantage of it, is she can facilitate family conference calls. The value in that is that I'm sure many of you have families that live all across the country, and it's an opportunity for all of you to get on the phone at once and to have a conversation in real time. I encourage you to take advantage of this resource and the ability to have these family conference calls.

Sheila is also a customer service genetic counselor for GeneDX. With that, I am actually going to hand the floor over to Sheila, and I'm very excited for her to address many questions that we have received, both pertaining to this particular webinar and also throughout the year. Sheila, go ahead.

II. Updates in Testing and Treatment Options

Sheila Solomon: Thank you so much, Shera, and thank you everyone for attending this evening. I'm looking forward to speaking with you and sharing some of the updates that we know now in hereditary breast cancer and ovarian cancer. As Shera mentioned, I am consulting with Sharsheret and have had such a pleasure speaking with so many of you, and hearing about your stories and sharing your insights. I look forward to hearing your questions and conversations this evening, as well. Without further ado, let's get started.

Just a quick agenda for this evening's discussion. We've already had our welcome, and thank you very much for that. I wanted to review with you and update the newest, latest and greatest, if you will, in hereditary or inherited breast cancer and ovarian cancer, and really then bring everything back home to say, "Well, then, what are my next steps?" What are the next steps for you and your families? What does this mean for me? What does this mean for my family, and where do we go from here?

What is genetic about breast cancer? What is genetic about ovarian cancer? To give you a very quick answer, everything is genetic about breast cancer and ovarian cancer. Cancer in general is caused by genetic changes, or what we call mutations, that occur inside the cells of our bodies that make those cells unruly and unable to control how they're growing properly in the body, and that can ultimately develop into a tumor. But, not all cancer is hereditary, meaning that that genetic component is actually caused or inherited from parent to child.

Taking things to a global view, cancer is a common disease. Unfortunately, there are very few people who haven't been touched by cancer in one way or

another, meaning we know someone, someone close with us, someone in our family, even ourselves. Cancer can even occur in family members, even when there is no inherited cause specifically. We can oftentimes observe two sisters with cancer, two brothers with cancer, even though there may not be a hereditary cause. However, and where we're going to focus tonight, is on those families where there is a hereditary pattern to cancer.

We all have risk factors to develop cancer. What I wanted to focus on tonight is the risk factors for the two common cancers that we're speaking of, which is breast and ovarian cancer. One of the greatest risk factors is aging. As we age, there is an increased risk to develop breast cancer. If there's a family history of breast cancer or potentially other cancers, there's also an increased risk to develop that cancer. If an individual has already had a cancer personally, there is an increased risk for her to develop a breast cancer potentially. There are also certain environmental and lifestyle exposure based factors, such as beginning periods at young ages; having change of life or menopause at a later age, in the later fifties, sixties; not having biological children or having them later in life, perhaps, so hormonal factors that can also increase a woman's risk to develop breast cancer are in play. There are also genetic risk factors, which we'll talk about in a moment.

In speaking to the general risk factors for ovarian cancer development, aging, family history, personal experience of cancer previously, also fall in line with risk factors for this type of cancer, so very similar to the risk for breast cancer. Then what is it about cancers that are different when they are sporadic, meaning they just happen by chance due to personal risk factors, environment, unknown risk factors, and then the hereditary type? As I mentioned, all cancer is genetic, meaning it's caused by genes that are changed in our cells that increase that potential for cancer to develop; but not all cancer is hereditary, meaning it's inherited in families.

How much breast cancer and ovarian cancer is actually hereditary? Well, when we take a look at all breast cancers diagnosed, only 5 to 10% of all breast cancers are actually caused by a hereditary cause. If you flip that number around, we're talking 90 to 95% of breast cancers might be caused by other factors. Just right off the bat, it's a small portion of cancer that actually is hereditary. On the other hand, ovarian cancers are a relatively rare cancer overall, in the general population. A quarter of ovarian cancers may be hereditary, in fact. This is bringing it back to the audience here who's joining us this evening to say, "What does this mean for me?" Well, if you've had a personal or a family history of one of these cancers, it may be worthwhile learning more, because it could in fact be a hereditary cause. It may be a chance that you fit into that 5 to 10% or 25% of the population. Let's learn more about genetics and our genes before we get into these updates.

Our genes are like books. You think about a book sitting in a library on a shelf. That particular book has a particular job to do. What are our genes? Our genes are the instructions for our body to tell us how to grow, how to look, how our bodies function. In thinking about our genes similar to being like books, a book is almost like an instruction manual, if you will, just like a gene is the instruction code for our body. If you think about books, books are made of letters and words and so forth. In our English alphabet, we've got our 26 letters that we string together to make words and sentences and books. The genetic alphabet is made of four letters, and those letters are strung together in chemical version, if you will, inside the cells of our body, and those particular letters are the DNA. Those are the genetic code that make up our genes.

Now, our genes, just like a book, must be spelled properly in the correct spelling order so that the body can understand what that particular gene's instruction is to do. If there's missing letters or extra letters in that gene book, or missing pages or chapters, if you will, then that gene book doesn't make sense to the body and the body can't do its job properly to keep us healthy. The same thing happens in books, just like if you were reading a book and there were missing pages, it wouldn't make sense, and you'd put that book back up on the shelf and not use it properly. If that was important book for your job, or to do whatever it was that you were reading about, then you're going to be lacking information and can't do your job properly.

In thinking about the way that this affects Ashkenazi Jewish community, this is actually a diagram of the BRCA1 and BRCA2 genes. Imagine these gray bars as a book, and each one of these lines represents a different chapter in the book. There happen to be three different spots, noted here by the orange arrows, that are the common mutations or areas in the book where there are spelling mistakes, these mutations in the Ashkenazi Jewish community. There happen to be two different spelling mistakes that are common in BRCA1, and one common mutation or spelling mistake in BRCA2. As a review of the previous slides, given that the genes are like books, we want to see whether or not these particular changes are found at those sites in the gene. Individuals of Ashkenazi Jewish ancestry have the 1 in 40 chance of having one of these spelling mistakes at one of these three spots in the gene, and this is specific to our ancestry. This is what we call a founder mutation.

What is a founder mutation? A founder mutation is a little complex, and requires us to take a step back in time, if you will. Let's imagine, on the left hand side of the slide here, and you see these photographs, or these three pictures, and in many, many generations ago in Eastern Europe, let's imagine this shtetl where many families lived, where children played. In that particular town, there may have been a handful of families who had a BRCA1 or BRCA2 mutation. As we know, the Jewish families like for their children to marry into other Jewish

families, and then over time, the prevalence of the particular mutation may have increased, because the genes were staying within the community.

Now, as we also know, many Jews immigrated to other parts of the world, including the United States. On the right hand side of the slide, imagine that those two people, noted with the blue arrows, left Europe, fled Europe, and happened to also carry a BRCA1 or BRCA2 mutation. They arrived into the United States, they set up their lives, and established their families in a new, smaller Jewish community, where the prevalence of that mutation was no greater, because now those two people are setting up shop in New York or Philadelphia, or wherever they might have been in the world. Over time, as many of us know, again, firsthand perhaps, the Jewish children grew to adulthood, went on to marry other Jewish people, thus the genes stayed within the community. If that person carried a BRCA mutation, over time and many a generation later, the prevalence of that mutation grew, too. Once again, 1 in 40 Ashkenazi Jews carries one of these two mutations.

For those individuals, Jewish or non-Jewish, who carry a BRCA1 or BRCA2 mutation, there are increased risks for cancer. Let's talk about that. In thinking about the risks for BRCA1 and BRCA2 mutation carriers, the cancer risks that Shera was mentioning are quite staggering. They're much higher than the general population risks. For BRCA1 mutation carriers, the risk for breast cancer is upwards of 85%, similar to BRCA2 mutation carriers. The ovarian cancer risk for BRCA1 mutation carriers is somewhat increased compared to BRCA2 mutation carriers. BRCA1 mutation carriers have up to a 54% chance to develop ovarian cancer, and a bit higher than the BRCA2 population. We also know that there are other cancers included in this spectrum, so that prostate cancer in men, pancreatic cancer, male breast cancer, and then some families have observed gastric cancer and melanomas as well. This is an important fact to think about. I mentioned prostate cancer and male breast cancer.

Thinking about the men, this is something that might be a misconception in the population in some cases. It's an important point to recognize that men are at increased risk for cancer if they carry these gene mutations, which also tells us that they can clearly inherit and pass on these gene mutations. It's very important, just as important to know your mother's side of the family history as well as your father's side of the family. I know that breast cancer tends to be a female disease. Obviously, ovarian cancer is a female disease. However, the risk to develop that disease may have equal likelihood to be passed from the father's side of the family or the mother's side of the family. When you think about the holidays coming up and Thanksgiving and so forth, and gatherings, it's important to discuss your father's family in addition to your mother's family's health history.

We see here with male breast cancer, BRCA1 and BRCA2 mutation carriers have an increased likelihood to develop a male breast cancer, so this is important for the men listening or for the women who have loved ones who are male in the audience here tonight. Now that we have the primer about hereditary cancers, about hereditary breast cancer, let's talk about the updates. Where are we now?

What I'd like to talk about are about five different points tonight. The first is the fact that BRCA1 and BRCA2, while I've reviewed those here tonight, they are no longer the only players in the inherited cancer genetic game, if you will. The idea of inherited cancer panel testing is here to stay, and I'll introduce what that means in just a moment. I also wanted to discuss the idea of lifestyle changes, as it's been something that has been brought to the media and to some of the scientific audiences; population screening for genetic testing; a brief update in treatments related to genetics; and then the concept of online research, databases, and research studies.

As I mentioned, it's more than just BRCA1 and BRCA2 anymore. This particular table represents a handful of relatively newer genes, not necessarily all new genes, but newer genes in the game of panel testing. These are a set of genes here in the left hand column that are listed below the word gene, and each of them is denoted with a different letter symbol, as you see. On the right hand side of the table, it represents the cancers that are associated with gene mutations in that gene. If you're looking at these rows and you see breast cancer and pancreatic cancer and colon cancer, if you think through your family history, "Wow, that sure sounds like my family," it may be one of these kinds of genes here that's associated with the family history, and something to evaluate.

How do you go ahead and evaluate these genes? What we can talk about now is how these tests are performed. Inherited cancer panel testing for multiple genes is available now, and actually more available now than ever. Many different laboratories around the country offer what's called next generation sequencing, which is a new technology that allows the laboratory to analyze many genes at the very same time. In years past, technology only allowed one or two genes to be tested individually, and it was more of a cherry-picking to say, "Which gene should we test for? Where should we go, based on the family history?" Now, because the technology has advanced, and the price of testing has been reduced significantly, meaning that now the cost of testing is a fraction of what it had been years ago, this next generation sequencing and looking at panels of multiple genes is able to provide more information than a single test every could.

It's very important to discuss these options with a certified genetic counselor, or with your genetic healthcare provider, before ordering this kind of testing.

Genetic testing is a very sensitive topic, and it's very important to be informed before having your test ordered and performed.

The next set of slides that I'd like to share with you are referencing some very new data that has come out in the past couple of months, either publications that have been presented at our most recent genetics conferences this past fall. This is a study here by Rinsky et al, who studied over 3,500 patients who reported having Ashkenazi Jewish heritage, and underwent this inherited cancer panel testing. If you think again, this is the series of many, many genes being evaluated beyond just BRCA1 and 2. What they identified is that patients who were tested, 20% of those individuals had BRCA1 and BRCA2 mutations which were not one of those three Jewish founder mutations. Further, they found approximately 17% of those patients who were Jewish had a CHEK2 mutation, which is another newer gene that has been identified in hereditary breast cancer, and further, 12% approximately carried ATM mutations. There were many other genes also that had been detected with mutations.

What does this mean for me? How does this study impact me as a Jewish person? Well, what this then tells us is that there are more players in the inherited cancer world than just the three founder mutations that I showed you earlier with those orange arrows, those three founder mutations in BRCA1 and BRCA2. If you had previous negative mutation testing years ago for BRCA1 and 2, it might be worth discussing the option of panel testing with your healthcare provider now. Next slide, please.

CHEK2 is another, more popular gene as it's coming out in the Jewish community, and in the general population as well. We've received many calls here at Sharsheret regarding cancer risks in CHEK2, and what does it mean to have a CHEK2 mutation. We do observe individuals of Eastern European heritage and Jewish heritage with CHEK2 mutations. Recently, Leedom et al studied the family histories of cancer in over 500 different people with CHECK2 mutations. What they were looking at is a founder mutation that is common in Eastern European individuals, specifically Jewish individuals as well, and looked to see if the cancer risks or the family histories of cancer were different between the type of mutation in CHEK2. What they found was the cancer risks, which are about twofold risk for breast cancer, were not different between whether a person had a founder mutation in CHEK2 or a non-founder mutation, meaning any other spot in the gene.

Remember, we talked about genes being like books, so it's quite possible that person A may have the founder mutation in the gene, which is in a particular spot, but that maybe someone else has a different spot in the gene book that is abnormal or has the mutation. CHEK2 is a gene that can increase the risk for breast cancer, endometrial cancer, and other cancers as well, and is an up-and-comer in terms of conversations about cancer risks.

Something else to discuss is the idea of young women with breast cancer, which is also always a conversation that we're having here at Sharsheret, is how to address our young women with breast cancer and their concerns over genetics and many other factors in their lives. Andolina et al studied nearly 850 young women with breast cancer who had been diagnosed at age 45 or younger, and all of these women underwent inherited cancer panel testing. About 10%, 1 in 10, were found to have a BRCA1 or BRCA2 mutation, which is certainly in line with having an early age diagnosis of breast cancer. What was most interesting is that almost two-thirds of the mutations that were identified were actually not in BRCA1 or BRCA2, and in fact, half of the mutations detected were in newer described genes.

Again, when I talked about the panel testing being able to simultaneously evaluate genes, many, many genes, this study was able to say, "Look, we found surprising finds with panel testing." What it's essentially meaning for me, what does this mean for me? Well, it means having the conversation with your healthcare providers if previous genetic testing has been done and is negative, to consider the options of panel testing because BRCA1 and 2 may not be the only cause to the cancer in a family. Next slide, please.

Okay, lifestyle modifications. This is also something that has been discussed most recently. This is the idea of breast self-awareness. I'm actually pulling us a bit away from genetics at this point, but this is a really important piece of information to share with your loved ones, and to be aware of for yourself. The first idea is, it's not just performing a self-breast examination monthly. It is being aware of what the normal breast feels like, what it looks like. When do you notice that it changes throughout the monthly cycle? Being aware of your personal and family history risk factors, and of course, undergoing mammograms.

Now, regarding mammograms, the American Cancer Society recently published some updates in terms of screening guidelines recommending that women of average risk for breast cancer begin their mammograms and their annual screening at the age of 45, no longer 40, and screen every two years from the age of 55. They also suggested that women who have a family history of breast cancer, or those who carry a BRCA mutation, may need to begin screening between the ages of 40 and 44, and more frequently in the fifties. Most of the women in our Sharsheret community, including you here tonight on the call, Jewish women of Ashkenazi Jewish descent, we generally do not fall into these guidelines, because of the ethnic background in terms of the increased risk for a potential genetic mutation, so it's very important to speak with your healthcare provider regarding your risk and whether you fall into that average risk, or if you fall into an increased risk. That can help determine the appropriate screening management guidelines for you.

Another controversial and discussion point that has been brought to the public media and to the press recently is the concept of population screening for BRCA1 and BRCA2 mutations. There was a recent study published, if you look to the left of the slide here, looking at population-based screening considerations for breast and ovarian cancer due to BRCA1 and BRCA2, and this was a study performed with an international collaboration, in fact, that considered the possibility of actually performing population-based screening in the Jewish community. Further, there was a recent New York Times op ed piece that was also published that had brought quite a bit of discussion to the Sharsheret community in regard to population screening, and is this the right thing for me, is this the right thing for all Jewish women.

The most important take-home point from these recent discussions, and from these posts, is to speak with your family, speak with your healthcare provider and/or genetic counselor, to learn more about your specific risk. Everyone has a specific risk based on family and personal risk factors that we talked about tonight, and not all of those risk factors are family history based, or genetic based. Some very well may be environmentally based, some may be hormonally based, and so the risks are really personalized, and we recommend that you speak with your healthcare providers to better understand and pinpoint your risk and make good decisions from there.

I wanted to touch briefly on treatments updates, because that was also part of the discussion tonight about what are the new latest and greatest discussions in treatment of breast or ovarian cancer? As we discussed tonight, cancer is caused by genetic mutations, and sometimes those mutations can be inherited. We know that ovarian cancer tumors that have been caused by a mutation in BRCA1 or BRCA2, or another gene called PALB2, if you're familiar with that particular gene, those particular tumors may be sensitive to a new type of chemotherapy called a PARP2 inhibitor. This is an excellent example of how far we have come with genetic testing, and how genetic testing results can help personalize medical care and treatment for women with ovarian cancer. This allows us to better understand the causes of cancer, and to target those tumors for a better response, and hopefully for a prolonged survival.

Okay, so what's next? Well, we ask for you to stay in touch. This is a very young science, this science of genetics. We are learning more and more every day. Just in the past few weeks, as you see here, all of the data that I'm sharing with you has actually just been published in the past couple of weeks and months. This is all new, from the second half of 2015, for that matter. Please do stay in touch, because genetics is always being updated.

With that, I wanted to comment on the fact that there is a lot of important research for genetics that's out there, so share your results with your providers. Share your results with public databases. There's accessible databases and

resources so women and men who have had genetic testing and have these variants and mutations that they're looking into more thoroughly, so the more we can share, the more we can learn. If you're interested in learning more, particularly for your own benefit or for that of your family, feel free to find a local genetic counselor by going to the website of the National Society of Genetic Counselors, www.nsgc.org. There's a very quick link, it's very simple to find, and it says, "Find a genetic counselor near you." You type in your zip code and it will locate someone who's very close to you, and you can meet with them for a personalized discussion.

We also would welcome you to stay in touch with Sharsheret. Sharsheret has counselors and information that is beyond your wildest imagination in terms of medical to emotional, psychosocial, supportive, in every way possible, so we are here as a resource for you all the time. With that, I would like to turn things back to Shera, and we will certainly take questions towards the end, but I do appreciate your time tonight, and hope this has been a helpful, informative session.

Shera Dubitsky: Sheila, it has in fact been very informative, and I was thinking as you were speaking really how far we have come, even since the last time we have done a teleconference on genetics. It's very exciting to think about where we're going, and where we will be over the next two, five, ten years. Thank you for that. I know that there were some technical issues for some of you in terms of the audio and the slides, so I want to assure you that the audio, the slides, and the transcript will be available on our website so that you can get it then.

Next, we have Lara, who is a Sharsheret link, a peer supporter. She will share her personal story about her genetic history and experience with genetic testing. Lara, the floor is yours.

III. Personal Story

Lara: All right, good evening, everybody. As Shera said, my name is Lara, and I have a different story than a lot of people, but ended up in the same place that a lot of people probably are. Basically, I'm interested in genealogy, and a couple years ago I decided to take a test called 23andMe, which at the time would look at people's genetics and try to match people in terms of cousins, and so I took it to find cousins. At the time, it also tested for those three founder mutations, and to my extreme surprise, I was told I was positive for BRCA2 mutation. It came as a complete shock, and obviously, I didn't have genetic counseling. I called my doctor, and luckily she sent me to a genetic counselor, who did a couple good things. She retested me. She also told me about Sharsheret, which is how I got to Sharsheret initially.

Unfortunately, the retest in the official lab came back that I was still positive for a mutation, so I was sent for some initial screening, and sent for my first-ever mammogram, because I was too young to have one before. It was fine, but then, because of the BRCA mutation, I was also sent for a breast MRI, which was not as clear. I had a biopsy, and I was actually diagnosed with breast cancer, which would not have been caught had I not known I was BRCA positive, because it was the last thing on my mind.

It was early enough that it didn't require chemo. I did have surgeries, and I had to talk, like I think Shera or Sheila mentioned earlier on, about talking to family members. I had to tell my family members that this was in the family, so I talked to a lot of them. Some tested positive, some tested negative, and some haven't tested, but they all are aware that it's something in the family, and something to be aware of. While it was very good that I did find out by mistake, it was difficult at the beginning because it was taken as a complete surprise when I first found out that I was positive. I didn't understand what it meant. Talking to a genetic counselor beforehand would have been wonderful. The fact that I had it afterwards did help me understand the ramifications, and the steps ahead that I needed to take.

That's my story. I think it shows how important it is to know, to at least think about knowing, if you are BRCA positive or not, or have one of the other mutations, just because it allowed me to be more proactive and find this cancer early.

Shera Dubitsky: Lara, thank you so much, and I think you're right. I think having the opportunity even to speak with a genetic counselor to decide whether or not genetic counseling is something that would be beneficial to you and family members is important. I think the big take-away message is that being able to speak with a genetic counselor, perhaps through testing, can be very empowering for many women and family members. Thank you very much for highlighting that.

IV: Question & Answer

We are now going to have a question and answer session, and to ask a question, please dial star, one, and your questions will be addressed in the order that they are received. We're going to ask that, when you do ask a question, to keep them somewhat broad in nature so that everybody on this evening's call can benefit from the conversation. We've already had several questions come in, so Sheila, I'm going to throw the first one out to you. Is it possible to have a BRCA mutation and also have another gene mutation?

Sheila Solomon: Good question, Shera. Yes, it is possible to have more than one gene mutation. As you know, we inherit half of our genes from our mother and half of our genes from our father, so it's possible that there may be one genetic syndrome or

hereditary predisposition running on one side of the family, and another on the opposite side of the family. If you do have a family history of cancer on both sides of your family, it's important to have that evaluated by a genetic counselor.

Shera Dubitsky: Okay, great. I guess on the heels of that, Sheila, somebody asked us, what should she do if she does not have her family history, or does not know her family history?

Sheila Solomon: That's a tricky question, because it is possible that there are a number of people who do not know their family's medical health history. It really comes down to your comfort level of where you feel you fit on that risk scale in terms of screening, and are you comfortable with the current screening that you're getting with your doctors? If you are interested in more information to pinpoint what that risk might be, it might be worth a conversation with a genetic counselor in going through the risks and benefits in having genetic testing without knowing one family history.

Not to get off topic outside of the clinical or medical angle, but from an insurance perspective, insurance companies oftentimes require some medical necessity, some indication or reason, to have this genetic testing. Usually that's based on the family or personal history of cancer, so not knowing your family history is sometimes a challenge to have a genetic test paid for by the insurance carrier if there's not an indication.

Shera Dubitsky: We have actually received several questions about that in terms of the insurance company. One person said, "Do the insurance companies cover genetic counseling if you are BRCA positive?"

Sheila Solomon: You mean the genetic testing, or the genetic counseling piece?

Shera Dubitsky: They already know that they're already positive, so I guess some people may do some of these tests before ever having had counseling, maybe through their doctor. If they did find out that they are positive, can they now go back to a genetic counselor, do you know, and have the insurance company cover that?

Sheila Solomon: Right, very good question, certainly, and the genetic counseling meeting is really just like a doctor's office visit. In some cases, genetic counselors are not charging for the actual appointment. Other times they do charge, so it really depends on who you're going to see, but yes, insurance companies almost always will pay for the genetic counseling, and also nowadays the genetic testing if there is that medical necessity piece. I'd really encourage you to speak with your insurance carriers and your family doctors to find out what your coverage might be.

Shera Dubitsky: Okay. We happen to be getting a lot of questions, actually, about insurance. Another question related is, does insurance or Medicare also pay for the panel testing?

Sheila Solomon: Yes, good question. Yes, insurance carriers are starting to pay for the panel testing, as they're realizing that it probably will be more helpful for them to know this information up front, when a person is healthy and has not had cancer. Even if they have had cancer, it can be helpful information, so yes. Medicare does have criteria for genetic testing, and it can be coordinated in covered, as long as the patient meets the criteria.

Shera Dubitsky: Also related, we have received several questions actually about discrimination in terms of going for genetic testing. I'm wondering if you can just briefly talk about the GINA Act, and then I'll ask a part two after that, but go ahead.

Sheila Solomon: Sure, no problem. It is a real concern for the community; however, we know that there have been very few to no cases brought to the courts regarding genetic discrimination. As Shera was mentioning, GINA, G-I-N-A, is the Genetic Information Nondiscrimination Act, which was signed by President Bush. This is an act that prohibits group health insurance plans from discriminating their constituents over their genetic test results. Even if a genetic test was paid for by the health insurance company, that insurance carrier would not be able to access that result or make decisions about someone's plan based on the genetic testing results. Now, there are some loopholes to this, and that is the fact that individual health insurance plans, like those personalized or independent plans, are not covered, as well as disability and life insurance are not covered under GINA.

That being said, I wanted to reiterate that there have been few to no discriminatory cases brought to the courts based on genetic information and discrimination. I think this has been historically a concern in the community, but one that has really not been brought to fruition in real life in terms of action. If you think about the risks and benefits with the insurance carrier's perspective, the insurance companies are playing the risk game all the time. They're thinking that they're playing that game, and so in thinking about paying for a test that costs $1,000, and if it's positive, then they know that they have probably saved themselves hundreds of thousands of dollars in treatment costs, potentially, for detecting a cancer, as in Lara's case. If she had not known that she was BRCA2 positive, she may not have had an early screening test to detect the cancer at an early, curable stage. Then it may have cost many, many, many thousands of dollars in treatment for her, or worse, treatment side effects and so forth, over many, many years of follow up. This is where the genetic testing can be actually beneficial for the insurance carrier to know.

Shera Dubitsky: Okay, and so part two to that question talks actually about life insurance and long-term care. If somebody is testing BRCA positive, will that affect life insurance or long-term care insurance?

Sheila Solomon: That's a really good question, and it's hard to say. It might be, but it really is a hard question to answer. It would be based on that plan, and I would suggest that you really do speak with your insurance agent to go through the ins and outs. Every insurance policy should have some specifics in regard to that. Some young families determine that they would like to get their life insurance squared away prior to undergoing genetic testing, that way they can answer all of the questions honestly to know that they have not been tested prior to securing that policy. These are all really personal decisions, and I would suggest that you speak with your insurance agent or close friend to address those issues.

Shera Dubitsky: I now have three questions sitting in front of me, actually, about the next generation. One question is, if a woman does carry the BRCA mutation, what age should their daughter be tested or screened? What's the recommended age?

Sheila Solomon: For women who have a BRCA1 or 2 mutation, the age for the next generation, or for the younger women, or men, even, to consider testing would be age 18, when they are consenting adults. Now, these genes that I have spoken about tonight are not pediatric cancer genes. They don't affect children's development in terms of cancer risks. This is not even something that teenagers would develop cancers. We're talking adult onset conditions, thus we prefer, from the genetic community, if you will, that at age 18 or older, when that individual is of adult and consenting age, they can make that choice for themselves as to whether they would like to have the testing or not.

Now, an 18-year-old may not want to know that information right then at that time in his or her life, and that's okay. Screening for breast and ovarian cancer would begin in the twenties if that person was positive, or if that person decided they did not want the testing, because we wouldn't know if they were positive or negative if they weren't tested. Screening would begin in the twenties, but the genetic testing could begin as young as age 18.

Shera Dubitsky: Okay. If somebody is testing negative, but there is a family history, should they be getting tested, and I guess should it be the panel at that point?

Sheila Solomon: Great question. There are a number of folks who are going to panel testing following negative BRCA1 and 2 testing. It really comes down to the strength of your family history in terms of how many relatives in your family have had cancer, and what types of cancer, and how old they were when they were diagnosed. I would suggest revisiting your genetic counselor who ordered your BRCA1 or BRCA2 genetic testing, and say, "Hey, I learned about this new panel

testing that's out there now." We're talking this is only about two years old, three years old now, and ask them to say, "Is this something that would be worth looking into?" It very well might be, based on some of these studies that have come out this fall. It's not just BRCA1 and 2 anymore.

Shera Dubitsky: I guess that that would also apply to the woman herself, that if she tested BRCA negative, that's very possible that in doing the panel it turns out that she is CHEK2 positive.

Sheila Solomon: That's exactly right. That's exactly right.

Shera Dubitsky: Okay. Sticking with the theme of the next generation, we did get a question about how do you keep from passing the gene on to the next generation? Maybe if you can just briefly talk about maybe the IVF, and anything else that would relate to that.

Sheila Solomon: My pleasure, and this is a really interesting and, I'd say, controversial conversation to have. When we pass on our genes, we don't get to choose which gene get passed to our children naturally, if we're going the biological, natural route. We pass on a lot of wonderful traits to our children, as well as a number of them that we just don't have the choice whether or not to pass along. There's a 50/50 chance, 1 out of 2 likelihood, that a person who has a BRCA mutation or any of these gene mutations we're speaking of tonight to pass that gene mutation on to their children. Each of their children, regardless of the gender of the child, regardless of the gender of the parent.

What Shera is mentioning regarding IVF, which is in vitro fertilization, is that there's actually a new technique that is called pre-implantation genetic diagnosis. Pre-implantation genetic diagnosis is also known as PGD, and it is a very highly specialized technique that is used with IVF treatment, whereby the sperm fertilizes the egg in a petri dish, or maybe not a petri dish, but within the laboratory. Then the pre-implantation genetic diagnosis testing will test the fertilized egg for the mutation that is in that one of the parents, and the physicians will only implant the fertilized eggs which do not carry the mutation in the family into the mother.

Now, this is a very controversial conversation, as I mentioned. It is a very expensive test and procedure, which I'm fairly certain is not covered by insurance, but it is available. It is something that can prevent this gene mutation from being passed to the next generation.

Shera Dubitsky: Thank you. We've received a couple of questions that I think may be more medical in nature, one having to do with the when to begin with the PARP inhibitor. I guess I would encourage all of you who ask maybe more medical questions to really bring those up with your treatment team.

Lara, we actually got a question for you from someone who wants to maybe know a little bit more information about how you decided to communicate the results to family members, and how you went about doing that, and basically how did that go?

Lara: That was probably one of the hardest parts of all this. First I talked to my parents and my siblings. My parents tested first, so we would know which side of the family that it was coming from. Once those results came back, I sent a long email, followed up by some phone calls, to some cousins, just explaining basically the whole story that I said, and if they wanted to get tested I gave them the name of my genetic counselor and asked them to come to me with any questions. I got a lot of questions, but most of them actually did get tested.

Shera Dubitsky: Okay, that's great. I think that that also highlights the service that Sharsheret offers in terms of being able to have everybody on a call at one time. I like, Lara, that you provided people with the name of a genetic counselor, but that's certainly something that we can do here at Sharsheret with Sheila to get all the family members on at one time, so thank you.

Somebody asked, Sheila, if there is a family history of breast cancer, are there any proactive treatments? I don't know if that's too medical, or if you can just briefly address that.

Sheila Solomon: Certainly. A family history of breast cancer, as you mentioned in the beginning of the talk tonight, of the webinar, is a risk factor for developing breast cancer. We know that right off the bat, whether or not anyone in the family has had genetic testing. Knowing if you have a family history of breast cancer can offer increased screening, and increased breast cancer screening program, which might include additional types of screening besides mammograms. In addition to mammograms, depending on the strength of the family history and how many women and who has had breast cancer at what ages, a woman might actually be eligible to have what's called a breast MRI in addition to the mammogram.

Now, while breast screening is not the same thing as prevention, and I know the caller's question was regarding prevention, we know that breast MRI's are highly sensitive and work very well in conjunction with mammograms in detecting early, early stage breast cancers. From the preventative standpoint, there are some chemo-preventive medications that can be taken to prevent breast cancer, but again, that's in a specific population of patients. I'm going to tell you something that I'm sure every physician and healthcare provider has always told you, is everything in moderation in terms of diet and your health and exercise and alcohol intake, and all of these things that are lifestyle exposures that we all can be aware of. I think you're probably catching my drift that there's really no easy answer for the preventative. It's really being aware,

and taking steps for screening early and often, and I think Lara is a success story of that.

Shera Dubitsky: When you talk about screening, is there anything else in addition to mammograms and MRI's, particularly if somebody is BRCA positive?

Sheila Solomon: There certainly would be, in the setting of a BRCA mutation, in terms of ovarian cancer screening or consideration for prevention. Removal of organs prior to developing cancer, so that means preventative mastectomies, preventative oophorectomy, which is removal of the ovaries. These are very personal decisions, and while they are the greatest risk reduction services, they also come with risks, so it's a conversation that's worth having with your providers. These are very personal and, while they are medically invasive, they also can be invasive to you in terms of your appearance and your relationships and so forth. These are not issues taken lightly, and so once again, Sharsheret can be there for you to answer those questions, to work through some of those issues. We're happy to help.

Shera Dubitsky: That's great. We also got something about, is bladder cancer and other cancers an indicator for needing genetic testing? I think you addressed that by saying that probably the best bet on that is to make an appointment with a genetic counselor, or to speak with you. Would you agree with that?

Sheila Solomon: I would. For the most part, bladder cancer is not one of the common hereditary cancers, but there can be some rare types of bladder cancer that may be hereditary. If you're at all concerned, a conversation with a genetic counselor is not a bad thing. It's just a conversation, it's just a meeting. Meeting with a genetic counselor does not mean you have to have testing.

Shera Dubitsky: Great.

Sheila Solomon: The role of a genetic counselor is not to pressure anyone into such a decision.

Shera Dubitsky: Right. Actually, I want to emphasize that, that anybody calling in to Sharsheret, we don't have an agenda for testing, but we certainly encourage people to have conversations with a genetic counselor to see whether or not you would benefit from testing.

This is sort of an interesting question, Sheila. Do you foresee a time where panel testing may be part of the genetic testing when couples get married?

Sheila Solomon: That is interesting. I'm standing on my soapbox here, this is my own personal opinion, but I think this still comes down to the level of comfort in information that that person is interested in learning. There are so many different levels of panel testing right now, ranging from two to three genes all the way up through

many, many, 30, 40, 50 different genes. Depending on what that couple might be interested in, sure, it may be something, but again, it's very, very personal, and again would have to be consented by both parties, and understanding what the risks and benefits are and the limitations. We're working with a relatively young science here, so there may be changes, very much so, over the many years ahead.

V. Conclusion

Shera Dubitsky: Yeah, it looks like that. I want to encourage people to send questions or give us a call so that we can continue this conversation, and you can certainly call us to speak individually and have a one-on-one conversation with Sheila. You will be receiving an evaluation in your email. Please complete the online evaluation, because your feedback is very important to us, and everything that we do is driven from your feedback and to really identify the issues and concerns that are important to all of you. We want to make sure that we continue to address that.

As I mentioned earlier, the transcript and audio will be available, so you can go to www.sharsheret.org/resources/transcripts. We'd like to again thank AstraZeneca for making this evening's program possible, and for always supporting Sharsheret's programs. We ask you to also stay connected with us, and to continue this discussion or any other conversations that you would want to have with us. We also want to thank the Cooperative Agreement, DP14-1408 from the Centers for Disease Control and Prevention.

As we head into Thanksgiving, there is an American idiom called "talk turkey." On this American holiday of Thanksgiving, we encourage you to serve up a great conversation that sheds light on your family history. Since 2004, Thanksgiving has been declared Family Health History Day by the Surgeon General. This national public campaign encourages all American families to learn more about their family health history. We encourage all the families of Sharsheret and all of you on tonight's call to collect and share information about your family health history with one another, because on a day that focuses on gratitude, we can be thankful that we live in a time where preventative healthcare is integrated into standard health practices. As you head into Thanksgiving next week, the next time you ask Grandma to pass the turkey, also have her include a healthy side dish of family history.

Stay connected to us, you can give us a call, you can contact us on info@sharsheret.org, visit us on our web page, and you can like us on Facebook and follow us on Twitter. Thank you very much for participating, and we look forward to staying in touch. Thank you again to Sheila and Lara for really such an important conversation tonight. Good night, everybody.

VI. Speakers' Biographies

Sheila Solomon, MS, LGC, Genetics Program Coordinator, is a graduate of the University of Pittsburgh's Master of Science in Genetic Counseling program. At Sharsheret, Sheila consults with women and families and answers individual questions about their family histories, BRCA mutations, and personal risks of hereditary breast and ovarian cancer, and contributes to the development and implementation of Sharsheret's hereditary cancer resources and programs. Sheila is also a customer service genetic counselor for GeneDX .

VII: About Sharsheret

Sharsheret, Hebrew for “chain”, is a national not-for-profit organization supporting young women and their families, of all Jewish backgrounds, facing breast cancer. Our mission is to offer a community of support to women diagnosed with breast cancer or at increased genetic risk, by fostering culturally-relevant individualized connections with networks of peers, health professionals, and related resources.

Since Sharsheret’s founding in 2001, we have responded to more than 50,000 breast cancer inquiries, involved more than 5,300 peer supporters, and presented over 250 educational programs nationwide annually. Sharsheret supports young Jewish women and families facing breast cancer at every stage--before, during, and after diagnosis. We help women and families connect to our community in the way that feels most comfortable, taking into consideration their stage of life, diagnosis, or treatment, as well as their connection to Judaism. We also provide educational resources, offer specialized support to those facing ovarian cancer or at high risk of developing cancer, and create programs for women and families to improve their quality of life. All Sharsheret’s programs are open to all women and men.

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

VIII: Disclaimer

The information contained in this document is presented in summary form only and is intended to provide broad understanding and knowledge of the topics. The information should not be considered complete and should not be used in place of a visit, call, consultation, or advice of your physician or other health care professional. The document does not recommend the self-management of health problems. Should you have any health care related questions, please call or see your physician or other health care provider promptly. You should never disregard medical advice or delay in seeking it because of something you have read here.

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