

Program Title: Genetic Counseling and Testing for Breast and Ovarian Cancer

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Guest Speaker: Nicole Boxer, MS. Certified Genetic Counselor at White Plains Hospital Center for Cancer Care, White Plains, NY. Ms. Boxer earned her Bachelor's degree from Cornell University and went on to pursue a Master's degree from the Joan H. Marks Graduate Program in Human Genetics at Sarah Lawrence College. Ms. Boxer has been practicing at White Plains Hospital for nine years, specializing in genetic counseling for hereditary cancer syndromes. Throughout her time at White Plains Hospital, she has worked with thousands of patients and their families to help them better understand genetic risk for cancer in their families.

Program Description:

This educational webinar will provide information about genetic counseling and genetic testing as pertains to breast and ovarian cancer, such as:

- Who should undergo genetic testing
- The genetic testing process
- New updates to genetic testing
- What to do with test results
- Myths and facts
- Case examples
- Discussing genetics with relatives/family members

NOTE: You may find it helpful while reading through this transcript to view and listen to the recording (audio and slides) of this webinar, which are posted on our website and YouTube channel.

Robin Perlmutter: Welcome. For all of you who know me or don't know me, I'm Robin Perlmutter, Peer Counselor here at Support Connection. I'd like to welcome you all to our nationwide webinar on Genetic Counseling and Testing for Breast and Ovarian Cancer with Nicole Boxer. This program is presented in partnership with White Plains Hospital. Remember that Ms. Boxer is sharing her expertise, and any information from tonight or questions pertaining to individual concerns should be discussed with your doctor.

It's with my great pleasure that we have Nicole Boxer, certified genetic counselor at White Plains Hospital for Cancer Care. Ms. Boxer earned her bachelor's degree from Cornell University and went on to pursue a master's degree from the Joan H. Marks Graduate Program in Human Genetics at Sarah Lawrence College. Ms. Boxer has been practicing at White Plains Hospital for nine years, specializing in genetic counseling for hereditary cancer syndromes. Throughout her time at White Plains Hospital, she has worked with thousands of patients and their families to help them better understand the genetic risk for cancer in their families. Ms. Boxer is also a member of the National Society of Genetic Counselors. Thank you, Nicole, for sharing your time and expertise with us tonight.

Nicole Boxer: Thank you guys for having me, and I look forward to discussing this topic with you over the next hour.

So, when we think about someone's risk to develop cancer over their lifetime, there are many different risk factors that are broken down into various categories that can increase one's risk for cancer throughout their life. So, there are lifestyle risk factors, environmental risk factors, biologic aging, so as we get older, our risk for certain cancers increases, and then genetic factors as well. And today we'll be focusing mainly on the genetic factors that can increase one's risk for cancer.

When we think about both breast and ovarian cancer, most of the time these cancers are not hereditary. So, 90% of the time, breast and ovarian cancer does not have any hereditary cause. It's only about 10% of the time that there is a hereditary cause for these cancers. And that is often different than what people tend to think. People often think that cancer always has to do with the genes that we've inherited from our families, but usually that's not the case. Again, only about 10% of the time is cancer hereditary.

So, the question is, what makes us concerned that cancer might be hereditary? What makes us worried that there might be some underlying genetic cause for cancer in a family? First of all, when we see cancers diagnosed at young ages. So, for example, when we think about breast cancer, when we see women diagnosed in their 30s or 40s, that makes us concerned that there could be some underlying genetic reason as to why it's happening so young. When we see women that have developed bilateral breast cancer or cancer in both breasts, so two primary -- two separate primary cancers in an individual, either at the same time or sometimes at different times. For example, a woman that had left breast cancer when she was 45 and then right breast cancer at age 60. When we see bilateral breast cancer, that makes us concerned that there could be some underlying genetic reason to why that woman developed two different breast cancers.

Individuals who are of Ashkenazi or Eastern European Jewish ancestry have a higher likelihood of carrying certain genetic mutations. And therefore, our threshold for offering genetic testing is always a bit lower when the family is Jewish just because we know that there are certain mutations that are more common among that particular ethnic group. That being said, we know that mutations can be seen across all ethnicities, but again, some mutations are more common amongst people who are of Eastern European Jewish ancestry. Additionally, when we see male breast cancer, because it is so rare, that is an automatic red flag and should trigger a referral for genetic testing.

When we see triple negative breast cancer, that should also trigger a referral for genetic testing. So triple negative breast cancer is when we do a biopsy and we find breast cancer, they test the breast cancer for certain receptors and proteins. So triple negative breast cancer means that the breast cancer does not express estrogen receptor, progesterone receptor or has very little HER2/neu protein. And we call that triple negative breast cancer. We know that women with triple negative breast cancers are more likely to have an underlying genetic cause for their breast cancer.

When we see ovarian cancer at any age, that is a red flag and should trigger a referral for genetic testing. And when we see an individual that has more than one primary cancer over their lifetime. So, similar to the idea about why we want to test with bilateral breast cancer, when we see a woman that maybe develops breast cancer in her 40s and then goes on to develop melanoma or colon cancer at a later age. When we see someone that develops more than one cancer throughout their lifetime, that is concerning that there could be some underlying genetic etiology.

When we see someone that has, for example, breast cancer with additional cancers in their family like pancreatic or prostate cancer, that is concerning that there might be some underlying genetic cause, because these cancers can be related from a genetic point of view.

So, families that have hereditary cancer syndromes may show all of these features. They may show some of these red flags or maybe even just one or two. So, it's important to note that in looking at your own family history, you certainly do not need to meet all of these criteria. But if there's just one red flag in the family, that should make you discuss the concept of genetic testing with your doctor.

So, when we see patients for genetic testing, we draw out something called a pedigree. And a pedigree is a way that we can draw out someone's family history, not only the individuals in the family that have had cancer, but those who haven't had cancer as well. So when we make pedigrees, circles are for women and squares are for men. So, the family on the left is highly concerning for a hereditary cause for their cancer. This is a woman who was diagnosed with breast cancer at 43. She has a sister who had breast cancer at 50, mother who had ovarian cancer at 47 and a maternal grandmother who had breast cancer at 42. In this family, we're seeing several affected relatives in a single lineage. So grandmother, mother and two daughters. We're seeing very young cancer in this family. And we're seeing cancers that can be related from a genetic point of view, breast and ovarian cancer.

In contrast, when we look at the family on the right, this is a woman who was diagnosed with breast cancer at 75. She doesn't have any family history of cancer. So there are no affected relatives. Typically, in sporadic cancers, we tend to see these cancers at later ages, and we don't see any clear pattern of inheritance in this family. So when we look at these two families, the family on the left is much more concerning for a possible underlying genetic cause, and the family on the right is less concerning.

One of the most common myths or misconceptions that we hear often in our office is that the patient has been told or they were under the impression that only the maternal family history is relevant. Now when we think about genetics, both the maternal family history and the paternal family history are equally important when we are assessing cancer risk. So both mom's side and dad's side are important. And that's because the genes that we are testing are passed along in families in what we call an autosomal dominant manner. Autosomal simply means that gender does not matter. So we inherit these genes from our father and our mother, and we pass them on to sons and daughters. So, gender is completely irrelevant. Many times, I'll have patients in my office that might have a family history of cancer on their father's side, and for years they were told that it's not important because these genes are only passed on through mom, and that could not be farther from the truth. We know that our father's family history is equally as important as our mother's.

Another common misconception that I'll hear is that the most important feature is the number of individuals with cancer in a family. And the truth is, that's not quite the case. We look at not only the number of individuals with cancer, but the ages at which the family members were diagnosed is sometimes even more important than the number of individuals. And also, we take into account the number of unaffected relatives as well.

So, I'll show you an example. In Family 1, we have a granddaughter who developed breast cancer at

age 83 and her grandmother who developed breast cancer at 77. In Family 2, we have a granddaughter who developed breast cancer at 37 and her grandmother who developed breast cancer at 42. Clearly, Family 2 is much more concerning for a possible underlying genetic cause for the cancer, even though both of these families have the same amount of affected women. So, they both have two women that have had breast cancer, but just based on the ages of diagnosis, Family 2 is much more concerning.

Additionally, as I had mentioned, we also think about not only affected relatives in a family, but unaffected relatives as well. So in Family 1, this individual is one of eight girls, and she's the only one that had cancer. If the cancer in Family 1 was hereditary, we would expect to be seeing a lot more cancer among some of these women. When we look at Family 2, there aren't a lot of unaffected females especially on dad's side of the family. So this woman does not have any sisters. Presumably this mutation would have been passed on from her father as opposed to her mother. So there aren't a lot of unaffected females in Family 2. So overall, even though both of these families have the same amount of breast cancer in the family, we're much more concerned that Family 2 could have some hereditary cause.

So, in the genetic counseling community, we rely on national guidelines to help us determine who qualifies for genetic testing and who doesn't quite meet criteria. We use what are called NCCN guidelines. NCCN stands for the National Comprehensive Cancer Network. And we use these guidelines to help determine who meets criteria for genetic testing. Now what's important to note is that NCCN guidelines change over time. At least a few times a year, new guidelines come out. And it's important for us to stay on top of these guidelines so we know exactly who should be referred and who might not need genetic testing. Overall, as a general trend, our guidelines get more and more expansive and inclusive over time. So in general, we're able to offer testing to more and more individuals as our guidelines expand over time.

I recognize fully that this is a very busy slide, and I certainly don't expect you to read through it. I just wanted to highlight a few of the main points in terms of thinking about women that have had breast or ovarian cancer and who meets criteria for genetic testing.

First of all, when we think about breast cancer, any woman who's diagnosed at age 45 or younger automatically qualifies for genetic testing. So regardless of her family history, even if she has no cancer in her family, if she's diagnosed at 45 or younger, she automatically meets criteria for genetic testing. Any woman with ovarian cancer at any age would qualify for genetic testing. So even if they have no family history, regardless of if they were diagnosed at age 35 or 95, they should be offered genetic testing.

Similarly, individuals with pancreatic cancer at any age also qualify for genetic testing regardless of their family history or age of diagnosis. Any woman that has metastatic breast cancer. So breast cancer that started in the breast and spread to a different part of the body like the bone or the liver or the brain. Any woman that has metastatic breast cancer qualifies for genetic testing, and the reason is that if her tests were to come back positive for specific mutations, she may be a candidate for certain medications that can be targeted to hopefully prolong life.

Any woman that has triple negative breast cancer also qualifies for genetic testing. So again, triple negative breast cancer means estrogen receptor negative, progesterone receptor negative and HER2/neu-negative breast cancer. And I actually want to highlight this criteria only because this is

an example of how our guidelines changed over time. So, this is the latest version of the NCCN guidelines. All of our prior versions included the criteria, triple negative breast cancer for women that were diagnosed at 60 or younger. So, if a woman with triple negative breast cancer did not have any family history of cancer, she would only qualify for genetic testing in the past if she was diagnosed at age 60 or younger. Now, in our most recent guidelines, that has changed and broadened, and now any woman with triple negative breast cancer at any age would qualify for genetic testing.

So, what that means is that if you have a history, for example, of triple negative breast cancer at age 63 and you have no family history of cancer, perhaps in the past, you might have been told that you didn't qualify for genetic testing because you didn't quite meet that age 60 or younger cutoff. Now you would meet criteria. So it's important to continue to have these conversations with your physicians. If you've been told in the past that you're not a candidate for genetic testing, it's very possible that with our new, more inclusive guidelines, that you may qualify.

Any male with breast cancer automatically qualifies for genetic testing regardless of age of diagnosis. And any woman or male who is Ashkenazi Jewish and has breast cancer, or a family history of cancer for that matter, would qualify for genetic testing. So these are some of the criteria that we use to determine who would be an appropriate candidate for genetic testing and who perhaps doesn't quite meet criteria.

Okay. So we spent a good amount of time talking about what makes us concerned or who should be referred for genetic testing. The question is, now what? Ideally, we'd like you to find a genetic counselor. Now most individuals have not met with genetic counselors before. So I just wanted to take a moment to explain exactly what happens at a genetic counseling appointment.

First of all, in terms of time, we do have a lot more time to spend with patients than many physicians. So, we're able to really go through a detailed review of a patient's medical history, their family history. And it's a family history that is focused specifically on cancer in the family. So we go through who in the family has had cancer, what types of cancers did they have, ages of diagnosis. And we go through the genetic testing options. What is the purpose of the genetic test? What are the risks and the benefits of genetic testing?

We take the time to address any concern that a patient might have about the genetic testing process. So for example, some patients are concerned about cost or insurance coverage. Some patients are concerned about do they want to know this information. What might they do if it comes back positive? Some patients are concerned about not only themselves, but their children. So we try to address all of these concerns as best we can before the testing is done so patients have some level of comfort when they decide to go ahead with genetic testing that they feel that all of their concerns have been addressed.

If a patient was just to proceed with genetic testing, we draw the blood at the end of the appointment. In some facilities they collect saliva. Genetic testing can be done through blood or saliva. And the results usually take a few weeks to come back, at which time we would have a thorough discussion of the results, what the results showed, what are the recommendations based on the results, what the results mean not only for the patient, but for their family as well.

So, all in all, genetic counseling is a very thorough review of someone's history. We can provide a

risk assessment for how concerned we are that the test might come back positive. We go through exactly what options may be discussed if the results are positive. And then of course, once the results are back, we're there to help guide patients through those sometimes very confusing results.

So, genetics is a topic that we often find in media. I'm sure as you're watching the news or reading the newspaper, you'll often see genetics pop up. And perhaps no story was more influential than Angelina Jolie's story back in 2013. In 2013, she published her story. Based on her family history of breast and ovarian cancer, she underwent genetic testing and was found to carry a mutation in the BRCA1 gene. And she put out her story that she opted to undergo a double mastectomy, and a couple of years later, removal of her ovaries in order to reduce her cancer risks for the future.

After this story came out, in the genetic counseling field, certainly in our office, we all witnessed something called the Angelina effect where we were being inundated with phone calls from patients that perhaps were now able to work up the courage to start the process of genetic testing, something that they may have been thinking about for a while. So the Angelina effect was a very positive effect in our field. And anytime stories like this come out in the media, we always see a trickle-down effect in our office.

One question that we get asked pretty commonly is who is the best person to test in a family. And the way that I answer that question is through a pretty simple analogy. So, if we have a red apple tree that's growing these delicious, juicy looking red apples, and all of a sudden, one day we look at that tree and we see that there's a yellow apple that grew on that tree. If we're trying to figure out why that yellow apple turned yellow instead of red, wouldn't it be best to test the yellow apple instead of testing all of the red apples on the tree? So similarly, when we're looking to figure out if cancer is hereditary in a family, ideally, we want to start by testing the person in the family that has had cancer prior to testing unaffected relatives.

Now we understand that that's not always possible. In some families, the affected family members unfortunately have passed away. In some families, the affected family member may not want to undergo genetic testing. They may not want this information. In some families, the affected relatives are in a different country where it's more difficult to access genetic testing. So certainly, we do see many patients in our office that are coming because of their family history of cancer. But if we have our way, ideally, we want to start by testing someone in the family that has had cancer themselves prior to testing unaffected relatives. And that's the most informative way to go about genetic testing in a family.

So, this is an example of a patient that came in for genetic testing based on her personal and family history of cancer. So again, circles are for women and squares are for men. This is a 69-year-old woman who was diagnosed with breast cancer at age 48. She has two sisters in their 60s who are healthy. A&W stands for alive and well. She has a son who's 37 and a daughter who's 42, both in good health. Nieces and a nephew who are all healthy. Her mother died of breast cancer at age 64, diagnosed two years prior. She has a maternal grandmother who had pancreatic cancer and died of the disease at age 53. Maternal uncle who had prostate cancer and died shortly after at age 72. And a maternal first cousin who was currently battling pancreatic cancer.

So, when we look at this family history, thinking back to the red flags that we had discussed before, certainly this family history is highly concerning for a possible underlying genetic cause for the

cancer. We're seeing multiple cases of cancer in three generations in this family. We're seeing cancer at young ages. We're seeing the same types of cancers repeating themselves in a family. So the way that we counseled this patient is that her family history is extremely concerning, and we wouldn't be surprised if her test came back positive.

Lo and behold, it turns out that she was found to carry a mutation in a gene called BRCA2. Now you might have heard about the BRCA1 and BRCA2 genes. Mutations in these genes increase the risk for certain cancers over a woman or a man's lifetime. So BRCA1 and BRCA2 both increase the risk for both breast and ovarian cancer. BRCA2 increases the risk for pancreatic cancer a little bit higher than with BRCA1. You can also see an elevated risk for other cancers like prostate cancer, melanoma, as well as male breast cancer. So now that we know that this woman carries a BRCA2 mutation, we're able to discuss with her some general concepts about cancer risk reduction and increased surveillance for the future.

So, the discussion that we had with this patient was regarding increased breast surveillance. So watching her even more closely than we already have been doing in the past. Preventative surgery. So for example, a surgery to remove her ovaries and considering surgery to remove her healthy breast tissue as well. We discussed with her pancreatic cancer screening, given her strong family history of pancreatic cancer, as well as making sure that she is on top of her skin cancer screening because of that risk for melanoma.

Sometimes patients will say, if I've already had cancer, what is the purpose of doing the genetic testing? How will it impact me moving forward? And the idea is that looking forward, we still want to do what we can to prevent any additional cancers from developing. So even though she's already had cancer in the past, now that we know this information, the question becomes, what should we be doing moving forward to hopefully prevent any new cancers from developing? How can we use this information to hopefully prevent more cancer in the family?

So now that we know that this patient has a BRCA2 mutation, we had a discussion about how to relay this information to her relatives, specifically her children, her siblings. Now that we know that she has a mutation, we know that this is something that is inherited through her family. We assume that it came from her mom, although we don't know for sure. But now we know that each of her sisters and each of her children have a 50% chance to have that same mutation.

So, the next person in the family that underwent testing was her daughter, and her daughter tested positive for the mutation as well. Having witnessed her mother and grandmother encounter a diagnosis of breast cancer, the daughter decided to undergo a preventative surgery, a bilateral mastectomy. And it turns out that when her tissue was sent to pathology, they actually found that there was a very early-stage breast cancer in that specimen. So, she was quite relieved that she had made the decision to have the surgery that she did. She also plans to have her ovaries removed in the near future as well.

The patient's son and both of the patient's sisters ended up testing negative. And this actually shows why it's always best to test an affected relative first. By testing the affected relative, we were able to identify exactly what it is that's causing a lot of the cancer in her family and were able to then test other family members to see if they have that same genetic risk or not.

In thinking about this patient and all of the information that she had to relay to her family, I wanted

to discuss how one mentions or discusses a positive result with their children. And this is something that we review with patients who test positive because they are concerned not only for themselves, but for their family as well. So in thinking about having these conversations with offspring, there are many points to consider, one of which of course is age of offspring. Certainly, the conversations that you'd be having with a 5-year-old are very different than the conversations that you'd be having with an 18-year-old or a 35-year old. So, obviously we have to tailor those conversations based on age and level of understanding.

We also want to take into account their experience with cancer in the family. So, if they've witnessed multiple relatives that have been diagnosed with cancer and died from their disease, their perception about this genetic risk can be quite scary. Whereas some individuals don't have a lot of cancer in their family and their perception is sometimes quite different.

Also, we want to consider the setting, the location, the timing of how and when to discuss, where to discuss this with offspring. And that really comes down to where do you communicate best with your family. For some individuals, that's in the car driving home from school. For some individuals, that's at bedtime. For some people, that's at family dinner. Or maybe some people have family members that live all over, so they prefer to just send out a mass email or text message. And there really is no right or wrong answer, but these are just some points that we consider when having that discussion with patients about how they can best relay this information to their family.

You always want to make sure that you're presenting the facts. And the only way that you can do that is by making sure that you have a good understanding of your results first before you try to explain it to family members. So we do strongly recommend meeting with a genetic counselor or an otherwise qualified healthcare professional so you can make sure that you have a really good understanding of what your results mean, what are the next steps based on this result before you go and relay that to family members.

And just like anything, we recommend practicing. So sometimes when I have patients that test positive, they'll kind of go through a script of how they might discuss this with their children. Sometimes I'll role play with them, and we're happy to do that. Obviously, each patient knows their own family best, but these are just some points to consider, some things that we think about when having that discussion with patients.

So, we had mentioned the BRCA2 gene, which is the gene in which that prior patient had tested positive for. But when we think about breast cancer in general and ovarian cancer as well, again, about 10% of these cancers are hereditary. And BRCA1 and BRCA2, while these are the most well-known genes, they are not the only genes that can increase the risk for breast and ovarian cancer. We now know that there are many other genes as well that can increase the risk for breast and ovarian cancer. And with that knowledge, our process of genetic testing has actually evolved a lot in the last number of years in that it's very rare now for us to test just BRCA1 and 2. The vast majority of cases, if not all of our cases, we're ordering something called a multi-gene panel.

So multi-gene panel is a genetic test that looks at many different genes related to cancer risk all on the same test. So instead of testing just two genes, BRCA1 and BRCA2, we're now able to test a whole panel of genes. And these panels can range anywhere from 25 genes, 35 genes, 47, 83. It just gets more expansive over time. But our genetic tests nowadays look at many genes at once as opposed to just a few.

Of note, it's the same cost and the same turnaround time. So there's really no downside there when we think about doing these multi-gene panel tests. And the benefit of these tests is a higher yield. So the more genes that we analyze, the higher the chance is that we may find a mutation, if there is one present in your family.

There are limitations or downsides. One is that there is an increased potential for what we call variants of unknown significance. And I'll go into this in more detail in just a bit, but variants of uncertain significance are variations within genes that we don't really know what they mean at this time. So it is essentially an uncertain result. The more you look, the more you find, and we don't always fully understand everything that we're finding.

Along those same lines, sometimes we find a mutation in a moderate risk gene or a gene that maybe only slightly increases the risk for cancer. And sometimes with these newer genes, our cancer risk estimates are still to be determined. So we're still learning about these genes as we go. And therefore, our medical management options are still in works. They're still being established. So while we are learning more and more about all of these genes as we test more individuals, there is certainly more of a potential for some uncertainty when you go ahead with such a large genetic test.

Additionally, of note, there is a potential to identify mutations that confer risk for an unexpected cancer in the family. So for example, if I'm seeing a patient that is coming because of a family history of breast cancer, sometimes we find a mutation in a gene not associated with breast cancer risk, but maybe colon or pancreatic cancer risk. So, while that information is still clinically relevant and still useful in terms of making decisions about cancer screening moving forward, sometimes the results do come back a little bit unexpected. And these are all things that we discuss with patients beforehand, so they know what they're getting into before they actually commit to genetic testing.

So, in thinking about these panel tests, there was a story that came out in the New York Times just a couple of months ago, so still quite timely. And the story described several women who tested positive for a gene called PALB2. Now, some of these individuals had relatives that might have had BRCA1 and BRCA2 testing in the past with negative results, and now on these panel tests are being found to have a mutation in a newer gene called PALB2. PALB2 is a gene that, similar to BRCA, increases the risk for breast cancer. It's not quite as high of a risk, but still a very elevated risk for breast cancer. We also see an increased risk in individuals that have a PALB2 mutation for pancreatic and possibly other cancers like prostate and ovarian.

So, the general take-home message from this article was that any individual who had genetic testing more than a few years ago, certainly prior to 2014 before we were offering these panels, many of these individuals now may benefit from updated genetic testing. I see many patients in my office on I'd say a weekly basis that might have had genetic testing in the past and they're now coming back to do more testing just because our testing now is so much more advanced than what it once was. And our recommendations, our knowledge for each gene certainly changes and evolves over time.

So, whenever we do genetic testing, the result can come back in three ways. The results can come back positive, meaning they have found a mutation, and that is something that most often is inherited from generation to generation in the family. Results can come back negative, which

means they did not find any mutations. And then the third possible result, as I had alluded to before, is called a variant of uncertain significance, or a VUS. A variant of uncertain significance means that sometimes we see variations within genes that we don't really know what they mean at this time. We're not sure if that's something that causes an elevated risk for cancer or not. What's important to note is that variants of uncertain significance are not to be used to make decisions about medical management. So we do not consider them to be what we call clinically actionable. The only result that might potentially change someone's management is if the test comes back positive. So if it comes back negative or maybe with one or two variants of uncertain significance, we wouldn't do anything differently based on that result.

So just to review some of the main reasons why people might opt to undergo genetic testing. One would be to better understand why they developed or how they developed a particular type of cancer. To better understand their risk to develop cancer again in the future. Sometimes testing positive can have treatment implications. And additionally, some people undergo genetic testing not only for themselves, but for their family to understand if their relatives may be at higher risk to develop cancer.

So just a quick check-in with all of you, Q&A. Who can genetic counseling and testing help? A) a patient with a new diagnosis of breast cancer; B) a cancer survivor; C) healthy family members; or D) all of the above. And I hope by now everyone's able to answer D) all of the above. So, we see patients in all of these scenarios.

One important point to take home for all of you is how to take your family history. What kinds of questions do you want to ask your relatives in order to determine if you might be a good candidate for genetic testing. So, you'd want to make sure you ask your relatives their ages of diagnosis as well as their primary site of cancer, what type of cancer did they have? And sometimes when cancer spreads from one part of the body to the other, there's some miscommunication about what types of cancers relatives had. But we always want to know the primary site or where did cancer originate in that relative.

And I'll give you an example of why that's important. This is a patient who was diagnosed with breast cancer at age 54 and she's now 62. She came because of her family history. So she had mentioned that her mother had some type of stomach or abdominal cancer. Wasn't exactly sure what it was. So we wrote down stomach, although she really didn't know. Grandmother had what she thought was liver cancer. And then she had a maternal uncle that died very quickly after his diagnosis. All she knew is that he was jaundiced at the end of his life. When we look at this family history from a genetics point of view, it's actually not very concerning for an underlying genetic cause. It's hard to find a gene that would link all of the cancers in the family. Because she was so vague about some of the information as it pertained to the relatives' diagnosis, we asked her to go home and try to collect a little bit more information, maybe speak to some relatives that might know more definitively about what types of cancers were in her family.

So, it turns out that her mother's abdominal cancer was actually ovarian cancer. The uncle that had jaundice at the end of his life and died very quickly after his cancer diagnosis actually had pancreatic cancer. And the grandmother that she said had liver cancer actually had breast cancer that metastasized and spread to the liver. Now when we look at this family history, it's actually very concerning for an underlying genetic cause, and she certainly would be a good candidate for genetic testing based on this information. So we always want to pinpoint as best we can exactly

what types of cancers were in the family. If you're able to obtain medical records, that's even better.

Sometimes people aren't able to find out exactly what types of cancers were in the family, but if we ask certain questions to relatives, it might give us clues as to what types of cancers their relatives had. So, maybe if they can find out how was the relative treated or what symptoms did they have that led to the diagnosis of cancer. And then another important question to ask is if anyone in the family has had genetic testing. So if you have a couple of cousins that might have had breast or ovarian cancer, you might want to pick up the phone and ask them, did you have genetic testing? If so, would they be comfortable sharing their results with you?

One important law that came about was the GINA law. And the GINA law stands Genetic Information Nondiscrimination Act. And this was signed into effect in 2008. Essentially this is a federal law that prohibits one's health insurance company or an employer from using genetic information against someone in any way. Which means that your insurance company, for example, if your tests were to come back positive, they cannot raise your premiums, they cannot charge you more, they cannot view this as a preexisting condition. Your employer, if they were to find out by chance about a positive result, they can't decide not to promote you or they can't fire you based on this information. We do have legal protection there.

There are limitations and exceptions to the GINA law. And again, this is something that we always go through with patients before they decide to go ahead with genetic testing. The most prominent exception, I would say, is that the law does not apply to life insurance, disability and long-term care insurance. So, what that means is that if someone tests positive and then they go and apply for life insurance, for example, it's not to say that they will use this information against that patient when deciding cost, but if they do, we don't really have any legal backing to say that they can't. So again, this is something that we review with patients ahead of time before they decide to go ahead with genetic testing.

I would be remiss if I didn't mention the men. I try to mention this in all of my talks just because it's something that we really need to do a better job regarding raising awareness of. And by we, I mean the medical community. So recent research has shown that men with a family history of cancer are tested at one-tenth the rate of women for BRCA-related indications. And what that means is that if a woman goes to her doctor and says, my mom had ovarian cancer versus a male that says, my mom had ovarian cancer, that woman is much more likely to be referred for genetic testing. And the reality is that, again, these mutations can be passed on through men or women to sons or daughters, so we want to be seeing these men as well.

There are certainly misconceptions among the general population as well as the medical community about implications for males as well as their relatives. So again, even though a male may not develop ovarian cancer over his lifetime, some of the genes that can increase the risk for ovarian cancer in women can cause certain cancers in men. Like male breast cancer, pancreatic, prostate cancer, colon cancer. So this is certainly information that will be important not only for females but for men as well. A lot of it has to do with branding. When we think about hereditary breast and ovarian cancer, we often see it as a woman's issue. We see a lot of pink. And so, I think we have to kind of scale back and think about this not only as a woman's issue, but an issue for men as well. 50% of people on this planet that carry mutations are men. So again, something important not only for women but for men as well.

So, during the height of the pandemic, we were all urged to stay home if possible and flatten the curve. And so many genetic counselors throughout the nation transitioned to counseling their patients via telemedicine because their patients were not comfortable coming into the office, which certainly at the time made sense. So this was a trend that we saw, again, all across the nation. Genetic counselors were counseling their patients from home. And genetic counseling is something that really does lend itself quite well to telemedicine just because there is no physical exam, and there really is no need to be in the same room for the appointment.

So, a lot of patients will ask, well, how can they get the testing done if they're being seen from home? And the reality is that all of the testing labs have pretty much adapted and now can ship kits right to a patient's home. They can collect saliva at home and send it right back to the lab without necessarily needing to come into the office. So the bottom line I just wanted to mention is even if you are still concerned about coming in due to potential risk of exposure, despite high vaccination rates, don't let COVID deter you from making an appointment because certainly you should be able to do this through telemedicine, if that's something that you're interested in.

As we wrap up, I wanted to go through some common myths and facts as they pertain to cancer genetics. So one of the most common myths that we hear quite frequently is surrounding the concept of cost and the cost of genetic testing. The reality is that genetic testing used to cost thousands and thousands of dollars, but nowadays, the self-pay cost for genetic testing through very good labs is \$250. So not nothing, but at the same time, much, much cheaper than what it once was. And through insurance, most individuals pay \$100 or less. Along the same lines, a lot of individuals feel that for whatever reason, their insurance won't cover the cost of the genetic testing. And for my patients at least, I find that if they meet medical criteria, then insurance absolutely should cover most of the cost of testing, if not all.

There's a common misconception that blood is more accurate than saliva, and the reality is that both blood and saliva are equally as accurate. We would not test saliva if it wasn't as accurate. So genetic testing really can be done through blood or saliva. Both are fine.

Another common myth is about 23andMe testing. And through 23andMe, you are able to opt in to request BRCA analysis. But what I will say about that is even though some people think that they're getting a pretty comprehensive test, while 23andMe is neat to find out some health risks, I would say, it is certainly not as comprehensive as a clinical grade genetic test that's ordered by a qualified healthcare professional. So, I urge you, if you do have a personal and/or family history of cancer, I do urge you to make an appointment with a genetic counselor or a qualified healthcare provider and not go through the direct-to-consumer testing route.

Another common myth is, well, I had testing in the past. It was negative. Therefore, I really don't need to have genetic testing. As we discussed, our genetic tests are improving constantly. So it's always important if you tested negative in the past, to discuss with your doctors whether or not any additional testing may be available to you at this time because chances are you could probably get an updated test.

And then again, another common myth which we have discussed is I've already had cancer, and therefore I don't need to do genetic testing. And we know that, again, genetic testing ideally should be performed on someone who has had cancer themselves. So they would certainly still be an

appropriate candidate for genetic testing.

So, remember, even though we know a lot about hereditary cancer syndromes, our research is ongoing. As we do more testing, we're learning more, and our guidelines certainly change over time. So, it is important to keep in touch with your physicians and your genetic counselors on a regular basis just to make sure that we're caring for you with the most up-to-date information.

And lastly, I wanted to leave you with a slide on how you can find a genetic counselor near you. The website is www.findgeneticcounselor.com. Pretty easy to remember. And I just wanted to show you what the website looks like. You can click on either finding a genetic counselor in person. So within I'd say a 25 or 30 or 50 mile radius of where you are, if you put in your zip code, but also telehealth. So, if you live in an area where the closest genetic counselor is maybe three hours away, telehealth might benefit you in that situation. So you can click on either in-person or telehealth and hopefully you can find a genetic counselor that suits your needs.

Thank you very much for having me, and if you have any questions, I'm certainly happy to answer any.

Robin Perlmutter: Thank you so much, Nicole.

Caller #1: So, I had a question about the GINA law. So I understand what you said about it, but can the reverse be used? So, for example, if you're thinking about having some kind of prophylactic surgery or extra surveillance and you test negative, can they use that result to deny coverage?

Nicole Boxer: I don't think a negative result could be used to deny coverage. Maybe I'm not understanding the question, but --

Caller #1: So, if somebody was considered high risk and was planning, an example, bilateral prophylactic mastectomy because they're already high risk. And if they were to go for a genetic testing and they were negative, can the insurance -- does that GINA prevent the insurance from using a negative result to say you're not BRCA positive, so why would you have the surgery?

Nicole Boxer: Right. So that's a great question. We can always argue, if there is reason to consider a patient high risk, we have to argue those other risk factors. So sometimes patients have a very strong family history and test negative, and we might think, well, maybe there is some gene in this family that we just don't know about yet. So, a negative result shouldn't bring someone from high risk to no risk. And therefore, it might take a little bit of discussion with an insurance company, but in general, that should not be used as a reason to deny some of these high-risk services. It's a good question, though.

Caller #1: Thank you.

Caller #2: You had shared a slide with us on the NCCN guidelines, the criteria for hereditary cancer testing. And I was examining it closely, trying to figure out, gee, do I qualify? The term "close blood relatives" was used in that often. Can you define what that means?

Nicole Boxer: So, a close blood relative is a first, second or third degree relative. So first degree relatives are your parents and siblings and children. Second are you. relatives who would be aunts, uncles,

grandparents or grandchildren. And third-degree relatives would be, for example, your first cousins, so the children of your aunts and uncles, or your grandparents' siblings, for example.

Caller #2: Okay. So that goes back quite a way.

Nicole Boxer: Correct.

Caller #2: Okay. Thank you.

Caller #3: I was wondering, I was tested 2005, so long time ago, and my BRCA was negative. But I have triple negative breast cancer before in my 30s, and I'm also Jewish. So I was -- but it's 15 years ago. So even if you're 15 years out of diagnosis, would genetic counseling be covered? Would I could still be -- because I was always thinking that because it's so long, I wouldn't be a candidate, but you're making it sound like I could be.

Nicole Boxer: You absolutely would qualify for genetic testing. So you don't need to be at that point in your life right now. So, for example, I might see a 90-year-old woman that had breast cancer when she was 30. She still would qualify for genetic testing just based on her personal history. In general, if you qualified for BRCA testing in the past, in general, you would qualify for a panel test at this time just because our criteria in the past was so much stricter that certainly you would likely meet criteria now if you met criteria in the past.

Caller #3: So, the amount of time from diagnosis doesn't matter. Okay.

Nicole Boxer: Correct.

Caller #3: And from those results that would tell information for like my son, because I don't have a daughter, but I have a son.

Nicole Boxer: Right. Exactly. So, this information theoretically could be relevant for him. So, if someone is found to carry a gene maybe for breast and colon cancer, well, we know that men can develop breast cancer and certainly colon cancer as well. So, this information could be important for male offspring as well.

Caller #3: Okay. Thank you.

Caller #4: Yes. I have a question. I was diagnosed with cancer. in 2009. I believe I had testing in 2010 or 2011. My sister got breast cancer I believe two years ago. And I also have two cousins on my father's side that had breast cancer. My father had cancer of the larynx and his brother had cancer of the lungs. Be it I had testing back, and I believe it's 2010/2011, but since all these cancers, would I be able to get testing again?

Nicole Boxer: Yes. In short, yes. So again, if you qualified for BRCA testing in the past, there's a very strong likelihood that you would qualify for this updated testing now. And we weren't doing panels back then, so chances are you were just tested for BRCA1 and 2. So most doctors would recommend a kind of an updated genetic test at this time.

Caller #4: Okay. Yeah, because like I said, my sister was actually the same degree, but she got it too late, and

then she needed the chemo and the radiation. But I have a history. And my sister did get tested for a lot more things than I did, and she was positive for colon cancer gene or whatever.

Nicole Boxer: Right. So that's an example of sometimes we do genetic testing. In a relative, we do the BRCA testing and it's negative, and then someone else in the family has a more updated test and there's a finding in a different gene. So the question is, the thought is that you probably weren't tested for that gene at the time of your testing initially. So, the question is, do you have that same finding as well? And this is something that this updated panel test would cover.

Caller #4: Okay, good. Well, I was different insurance, and now I'm Medicare, believe it or not. But it should be covered. It's over 10 years since I had that original testing.

Nicole Boxer: I would think it should be.

Caller #4: Okay. Well, thank you very much. It was very interesting, and I learned so much. I got so much knowledge from this webinar.

Nicole Boxer: You're welcome.

Caller #5 Robin, I just wanted to ask, do you need a doctor's referral to go to a genetic counselor?

Nicole Boxer: So that would depend on where you're doing it. I know here, we don't require a referral from a physician. We certainly will take self-referred patients. But some facilities may require a referral, or some insurances may require that their patient get a referral. So it's something that we would need to look at on a case-by-case basis, but in general, you don't need a referral from your doctor, but it is always a good idea to discuss this with your doctor in terms of thinking about the pros and cons of doing more genetic testing. In general, I find that most doctors are in favor of getting as much information as we can about their patient's risk moving forward so we can make the best decisions about their screening. But it's always a good idea to discuss this with your doctors in terms of the consideration to go ahead with genetic testing.

Caller #5: Thank you.

Robin Perlmutter: You did such a great job, Nicole. So comprehensive, so thorough. We can't thank you enough for you taking the time, for your passion, your dedication, your commitment to the cancer community, and to all of you ladies who came out tonight to learn about this very important topic. So I wish you all a great evening, and thank you again for joining us.

Caller #6: Thank you. It was excellent. Thank you, Nicole.

Nicole Boxer: Thank you all for coming. It was my pleasure.