***Understanding BRCA Genes: What You Need to Know About Hereditary Breast Cancer***

**Speaker 1** 00:03

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**Dr. Bill Evans** 00:20

Welcome to the cancer assist podcast. I'm your host, Dr Bill Evans, professor emeritus at McMaster University, and we're talking to you from Hamilton, Ontario, Canada. And I mentioned our location today because we've got viewers now in Germany, United States, Hong Kong, round the globe. It's amazing the reach of this podcast now, and probably a lot of you listening don't know where Hamilton is, so I just ask you to get out a map and look for the Great Lakes. Identify Lake Ontario, and you'll find Hamilton at the western end of Lake Ontario. So wherever you're listening, we welcome you to the show. And the focus of today's podcast is on genetic abnormalities in breast cancer, and specifically the genes. We call them BRCA one and BRCA two, or bracket one, bracket two. And I'm joined by an expert this morning that's absolutely the right person to talk about it. But before I introduce her, I did want to make a few comments about the cancer assist podcast, which is brought to you from or by the cancer Assistance Program here in Hamilton. Now cap is a charity that provides a variety of free services to cancer patients that are cared for at the juravinsky Cancer Center. And these services include nutritional supports, urinary incontinence supplies, wigs and other hair coverings, mastectomy bras, and importantly, free transportation to and from the cancer center for treatments and follow up appointments, as well as to other medical appointments. One of the very special things that cap does, though, is it loans medical equipment to patients, again free of charge, and things like wheelchairs, ambulators, rollators, commode chairs, canes, all sorts of equipment that can make a patient's life a little easier and safer in their home and allow them to be more active. So caps services are made possible by generous donations from the public and from special events. And I want to give you give a big shout I should say to the Hutton family trust for their continued support of the cancer assist podcast. So now let me introduce our guests for today, Dr Andrea Eisen is, as I said, the perfect person to talk about BRCA genes, and she has her, got her MD, and did her residency at the University of Toronto, and then, importantly, did a two year fellowship in clinical cancer genetics at the University of Pennsylvania, and then followed that by a master's degree in health research methodology at McMaster University Of course, and then she was on staff at the Hamilton Cancer Center for a number of years, but then left us and went off to Toronto, where she's been working at Sunnybrook Cancer Center, and up to the present, Although she's coming back to Hamilton as the Buffett Taylor chair in breast cancer research. Andrea, welcome back. Thank you very much. It's great to be back in Hamilton now. I've wanted to do a podcast on this topic for quite a while. We've had a lot of requests, actually, to from women who want us to discuss these genes, the braca one and braca two genes, and so let's start with in a normal person, what do these genes do? Why do we have them? Yeah,

**Speaker 2** 03:26

thanks. BRCA went in to help maintain the integrity of DNA. So they help repair damaged in DNA that occurs, really in all of us, all of the time, and our bodies are very effective at making those changes when we inherit a copy that's defective from either parent, we're kind of set up for an increased cancer risk, because if the other normal, healthy copy gets damaged through these typical DNA damaging activities that happen through, you know, exposure to sunlight or smoking or any other of a number of things, and we have then two defective copies. We then are more susceptible to different cancers and for BRCA one and two. For women, the major cancer risks are for breast cancer and for ovarian cancer, but men can inherit BRCA one and two mutations as well, and they may be at increased risk of prostate cancer, male breast cancer and pancreatic cancer as well.

**Dr. Bill Evans** 04:24

So if you inherit the gene, you don't necessarily get cancer. You have to have the other copy the because we all have two copies of these genes, it has to be damaged in the course of your lifetime.

**Speaker 2** 04:36

Somehow, that's correct. So not that's that's really important, because when the genes were first identified, of course, in order to find the gene, they picked families that had very, very striking family histories. So typically, at least four cases of breast cancer in multiple generations, a very early onset of diagnosis. And so when you pick the families with the strongest presentation or the strongest suspicion of hereditary cancer. Higher than the risks look really high. So at the very onset, we used to tell women that the risk of having breast cancer, for example, if you inherit a BRCA one mutation, is 87% and we now know that when you start to test more broadly and look at families that you know aren't as striking as that, that the risk is closer to 60% so still pretty high. It's pretty high, but not inevitable.

**Dr. Bill Evans** 05:23

And you mentioned a couple of things that can potentially damage your genes over your lifetime, like exposure to radiation. And you mentioned smoking. Is there a higher risk if you have one copy that's abnormal and you smoke? Is that increase your risk

**Speaker 2** 05:39

having breast cancer, yeah? So no in BRCA one and BRCA two, we don't think that smoking is a strong risk factor for cancer. I really mentioned that as an example of exposure that we have

**Dr. Bill Evans** 05:50

that things like DNA. Yeah, right. So what do you think the major things are that are causing us to women to lose the function of that particular normal gene and allows the other one to lead to a cancer development.

**Speaker 2** 06:03

Yeah, that's a very important area of research, like, how can we define, how can we predict if you have this mutation, are you going to be one of the 60% who develop breast cancer or not? And there are other factors that are associated with an increased risk, like the degree of family history and some of the usual breast cancer risk factors, like parity, when you have your children and how many you have, whether you use oral contraceptives or not, can influence the risk of ovarian cancer. So there's lots of environmental and reproductive and hormonal risk factors that are associated with it,

**Dr. Bill Evans** 06:39

okay, and are there conditions where both genes are abnormal? Both have BRC one or two? It's

**Speaker 2** 06:48

very rare that an individual inherits two copies from you know, as a hereditary predisposition. We see that sometimes in populations where there's an increased prevalence of mutations. And the most common one that we have in North America is the Ashkenazi Jewish population. So these are individuals who are from Eastern Europe, essentially. And because about one to 2% of the population carries a mutation in BRCA one or BRCA two, and there are specific mutations called founder mutations, which we can talk about because it's so common, then it's it's not unheard of for an individual to inherit one copy from either parent, but we still don't see that as much as we might expect to. So we think that some of those events, when they occur in a fetus, for example, they're not viable. It doesn't result in a lot of pregnancy.

**Dr. Bill Evans** 07:44

Now, you mentioned Ashkenazi Jews, and something I learned in medical school, but I don't really know how to identify that population, but I think that European origin for Jewish people is pretty common. I read somewhere about 50% of the Jewish population would be called Ashkenazi Jews. Is that

**Speaker 2** 08:02

correct? Yes. And in North America, that's the most common origin story for the Jewish population. But in you know, there's very large Jewish communities from Africa, from the Arab countries, etc, and we refer to those as Sephardic Jews. We just don't have as great a population of those in for example, Hamilton or Toronto or Canada.

**Dr. Bill Evans** 08:23

Are there other population groups we should be thinking of as well?

**Speaker 2** 08:28

There are other populations where we see specific mutations. So these are called founder mutations. And we think that founder mutations, what that means is, you know, BRCA one and BRCA two are very large genes, but in some populations we see one or two or three kind of unique mutations. So in the Jewish population, we see three mutations, two in BRCA, one and one in BRCA, two and one of the two that we see in BRCA, one is more of a like an Eastern European mutation that we see in non Jews as well. But there are other populations where we see these kind of unique mutations. So in Iceland, for example, most of the hereditary, or if not all of the hereditary breast cancer comes from a single mutation. In BRCA two there are French Canadian founder mutations. You know, there are any time when there's been a population that has been kind of isolated, either geographically or culturally, and there's sometimes been a contraction of the population historically. That's when you can be set up for this kind of founder mutation. Now,

**Dr. Bill Evans** 09:32

when we talk about mutations, maybe some of the people listening need to understand that a little better and also to appreciate that when we talk about BRCA, one mutation, it isn't one entity. There's a whole lot of different abnormalities in that gene, and some of them, some of these variants, aren't considered to place you at risk, and others are categorized as ones that are predisposing to malignancies. Yeah,

**Speaker 2** 09:57

right. Yeah. Thank you. So that there. Is a distinction. So a mutation really just means a change in the sequence of the DNA, and that doesn't really tell us if it's an important change that is associated with a disease or a risk, or it's just a silent change, similar to the difference between having blue eyes or brown eyes. Both of those are highly functional, but they're, you know, they're biologically different. And so we colloquially use the term mutation and mutation carriers, but the correct term is pathogenic variant. So there's a change in the DNA that's associated with the disease. That's what pathogenic means. And so that's what we really mean when we're talking about mutations. You're right. These are both very BRCA one and BRCA two are very large genes, and the way we've approached testing over time has really changed. So when I was first involved in the testing program in 2000 2003 the testing was very focused on a single segment of the gene that carried most of the mutations, and it was really just for BRCA one and BRCA two. Now we test at least 19 different genes that may be associated with hereditary cancer risk, breast cancer risk, and we do full sequencing of all the genes, and there's been a tremendous improvement in the technology and a reduction of in the cost of the testing, and so now it's much more widely applied than it used to be. So but that's another important thing. I wanted to say which BRCA one and BRCA two are still the most important genes for hereditary breast cancer. We find those the most and that we find them in about 5% of women who meet the criteria for testing for mutations, but we also find mutations in the other genes about 5% of the time. So we now have much more elaborate or involved a discussion when we find mutations because the risks are different?

**Dr. Bill Evans** 11:45

Yeah, it sounds like it's become very much more complicated to even understand, if you've got different mutations in different genes, what the level of risk is. And I'm sure that's an area of research to try and be so we can explain to patients in a more accurate way what the risk is and whether something should be done about it. We want to talk about what you can do about it in a minute, but that must be a complicated thing to sort out when there are so many of these different variants. Yeah, exist.

**Speaker 2** 12:12

Yeah. So for BRCA one and BRCA two, we've had the advantage of lots of research over the past 30 years since they were identified. So we're, I think we have a really good understanding of the cancer risks and the the ways to manage those risks. There are several other genes that have been identified that are associated with a similar level of breast cancer risk, one of the more common where one of them is called pal, B, 2p, a, l, b2, that's much less commonly identified, but still has a similar risk of breast cancer, although a lower risk of ovarian cancer, and then the other two more common genes that we find that are associated with less of a cancer risk but still slightly increased are called ATM and check two. And those are really are involve a very nuanced conversation, because the risk may not be rather than a 60% lifetime risk. It's more like a 25% lifetime risk, maybe double the average woman's risk. And so the conversations are a bit more nuanced around those two genes right now.

**Dr. Bill Evans** 13:10

So that leads us to how is testing done, and then who should be tested?

**Speaker 2** 13:16

I'm so glad you asked me that, because this is a very big area of research right now, and I want to try to get the message out about who, who may have been missed for testing. And also, when we identify a mutation in a cancer patient, we're not really seeing other family members coming in for testing who don't have cancer yet that we could really intervene and help prevent cancer with. We see on average, one or two family members per person. That's the pro band the first person to be tested. And we really feel that it's important to increase that number, because finding the information out when you have cancer is important. The treatments may be different, and we have targeted drug therapies now for breast and ovarian cancer, if you have a BRCA one or two mutation, but being able to tell a 30 year old woman that she's at risk and can do things to help prevent getting cancer in the first place is also very important, and we're not capturing those patients as much as we should do.

**Dr. Bill Evans** 14:11

You have an idea of why that is? Yeah, well, I think part of it is ignorance, or is it fear?

**Speaker 2** 14:17

There's a number of things that have been suggested. One is, we identify the mutation in cancer patients at a very kind of vulnerable time, right? They've just been diagnosed. Often, they're dealing with all the treatment, side effects, managing, managing all of that. And so it may not be the best time to say, you know, hey, please send this letter to 30 of your relatives, right? It's hard, and we don't have the ability to do direct contact tracing right now in Ontario, for some some diseases, like if you think of public health, if you're diagnosed with an important disease for that has public health implications, there's contact tracing right a nurse from the Public Health Department will ask you for your contacts. Will contact your family members. We don't have that ability right now. For these cancer risk genes, and people have looked at that, at the success of doing that, and there's some interesting stories from the United States where they've shown that it's promising, but really they get by doing that method. Mostly, so far, they've brought in, like, very closely related people, and that's I'm not sure you know, most people tell their sister or their children, right? So contact tracing is promising, but maybe not the next step for us. I think also it's geographic. You know, people live scattered and often, you know, we're very multicultural. It's not, it's not uncommon for me to counsel someone whose entire family lives in China or in India or another country, so that's challenging as well. And then I think, yeah, it's just prioritizing it, and it's uncomfortable. Some people don't, aren't close to their other relatives, you know? And it's so it's a message, different reasons. Yes, a lot of different reasons. But in terms of how you get tested, currently, the most common way is to have a blood test. So if you meet certain criteria in Ontario, and there are several, and I'll kind of try to prioritize them and group them together to make it more simple, if you meet the criteria for testing, you give a blood test, and we get the result within weeks to a couple of months, depending on the priority. There are other ways to do genetic testing. Often, you can do what's called a spit kit. So you spit saliva into a tube, and that has the advantage that you don't have to go to a lab. You do a spit kit at home, and then, you know, bring it in. It used to be in the past that your genetic testing had to be done at the cancer center, and that was a positive development in covid, there's been partnerships now developed with the local labs, like Life Labs, etc, and you can bring a requisition there and have the test done there and sent in. So it's much more accessible. Also, genetic test counseling is often done virtually. So for example, patients who are family members of someone who has a mutation, they can have a virtual consult, get the requisition sent to them, and go to their local labs. They don't have to drive into Hamilton, for example, to meet a genetic counselor in person anymore. So it's a DNA test that's done on a blood sample or a saliva sample, typically.

**Dr. Bill Evans** 17:15

And did we cover all the who should be testing? No,

**Speaker 2** 17:18

thank you. We didn't. So currently, there are many different criteria, and I'll just give you the highlights. The features of hereditary breast cancer are multiple generations affected. And I want to point out something bill that many people don't realize they can also inherit this risk on the father's side as well. They've been told, or they understand, that they can only inherit this risk from the maternal side, and these genes are not inherited that way. You can equally get it from your father's side or your mother's side. It's an important point. Yeah, it's just that the family history on the father's side might not be as obvious. You know, it's obviously not your mother who has it. It's might be an aunt or a cousin. So if you have a strong family history, and that's typically multiple relatives with breast cancer or ovarian cancer, and typically at a young age. And we sort of use 50 as a cut off, or if you personally have breast cancer diagnosed at 45 or younger, okay? And it used to be 35 and a few years ago was increased to 45 and I want to mention that because there are lots of women out there who are diagnosed between 35 and 45 and may not be connected with the cancer program anymore, and so if they have a history of breast cancer diagnosed at 42 they should talk to their family doctor about being referred back for genetic testing if they haven't done that. So that's new information. Yes, that's new information, and that number may be changing soon to 50, but really that's yes, but for now, it's 45 if you're Ashkenazi Jewish ancestry and have any history of breast cancer, then that you're potentially eligible for testing if there's a history of breast or ovarian cancer, I should have mentioned before. And also, there's another subset of patients too that we recognize, which is women with triple negative breast cancer. So those are women whose tumors do not express estrogen receptors, progesterone receptors, or her two new marker, and we recognize that that's a very common expression of breast cancer in people who have BRCA one mutations. So if you've been diagnosed with triple negative breast cancer at age 60 or younger, then you're also eligible for genetic testing. So it could be your personal history, your ancestry, or a strong family history that makes you eligible.

**Dr. Bill Evans** 19:25

What if you is a family history of other cancers, like ovarian cancer, pancreatic cancer, would that also Yes?

**Speaker 2** 19:30

Ovary signal, yes. So ovary and breast are the most important, but if there's at least one of those and some prostate cancer as well, or pancreas and melanoma may be increased as well. Those are not considered as strongly in making the testing decision.

**Dr. Bill Evans** 19:45

Okay, so we've covered the who and how, and then you can ask, why? Because, why be tested and what can be done about it. And really, the whole idea is to try to detect people are at risk, and then have a conversation about. The level of risk, right? And then make suggestions as to what options are available to those individuals. Yeah.

**Speaker 2** 20:07

So I divide this conversation up into, am I talking to a person who has current breast cancer or potentially ovarian cancer, and how, what are the implications for them? And then, what are the implications for family members. So if we focus first on the breast cancer patient, for example, if we're able to identify that there's a mutation very early in the diagnostic period, so you find out you have breast cancer and you have a genetic test, we really can help inform the surgical decision making, because with BRCA one and BRCA two and some of the other cancer genes, you are at high risk of getting a first cancer, but also a very high risk of getting a cancer in the opposite breast. And so for some women who have a more favorable prognosis and who have cancer in one breast, it may make sense to do surgery to remove both breasts at the time of diagnosis. And I have to say, some people feel this is a bit antithetical to how cancer treatment has evolved, because for many years, we've worked towards doing less surgery right in women who have breast cancer, and we know that lumpectomy and radiation for the average woman is just as good as having a mastectomy. So it's only in these women with very high risk of getting a second cancer in the other breast that we sometimes we make that recommendation. Also, there are now targeted treatments in breast cancer for women who have BRCA one or two mutations, and there's a drug called olaparib. The brand name is limparza, and this has been shown in a large randomized trial that we participated in in Canada as well, that if you take that drug for one year after you finished all your other cancer treatments, and you have high risk of recurrence, then your survival improves by four or 5% at six years. So it really is an important addition to the to the treatment regimen, but we can only do it if we know the person has a mutation, so that's another reason to be tested. The third is, if you have breast cancer and you've finished all your treatment, we really wouldn't want to see you get ovarian cancer, so we recommend interventions for that. And right now for ovarian cancer, we don't have an effective screening test, so the major recommendation is to have your tubes, fallopian tubes, and ovaries removed. Typically that would be after all the breast cancer treatments completed. So those are for the options for women with breast cancer. And then there's the whole family piece. Or sometimes we see women who have come in as the first person to be tested because of their strong family history, perhaps their relatives are deceased or can't be reached, or are not available for testing. And so then we're really talking about preventive options. So for women who have this very high risk of developing breast cancer, the options include doing a preventive surgery, such as bilateral mastectomy, removing both breasts. Typically, this can be done with immediate reconstruction. It's a planned operation, and the plastic surgeon and the surgeon work together, and that surgery has been shown to reduce the risk of developing breast cancer by over 90% but clearly that's a pretty intensive intervention. It's not for everybody. For women who opt not to do that, we have heightened screening. So the Ontario breast screening program has a separate program called the screening program for women at high risk, and this includes both a mammogram every year starting at age 30, and an MRI every year starting at age 30, and it goes to age 69 so that's intensive screening program that's not available unless you have a mutation, or at very high risk of a mutation, or we can't find the mutation, but your family history is very strong and you have a high risk. So those are the main we might talk about taking a medication to reduce breast cancer risk in these women, and we always try to counsel about other healthy lifestyle options. So maintaining a healthy body weight, exercising regularly, there's more and more evidence that alcohol is a risk factor for breast cancer now, so counseling around that, and of course, not smoking. It's not smoking, even though that's not necessarily related to BRCA one or two. I do see patients who are very worried about their breast cancer risk, but they also are smokers, so we use that opportunity to discuss that as well for ovarian cancer prevention, as I said before, really the main intervention is removing the ovaries, and the question of that is really the timing. We obviously want to do it after someone's finished having children, and not too early, because ovaries help maintain health in a lot of other ways.

**Dr. Bill Evans** 24:38

You've given us a huge amount of information over a short period of time, so I think we need a break to process this, and we'll be right back to talk to Dr Andrea Eisen about breast cancer and genetic predisposition and the management of it.

**Speaker 1** 24:52

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**Dr. Bill Evans** 25:35

We're back with Dr Andrew Eisen talking about breast cancer and BRC and BRCA, one and two genes. We did have a question at the break a bit about risk and related to number of pregnancies and use of oral contraceptives. Could we just go back and talk about that a little bit

**Speaker 2** 25:51

more? Yeah, for sure. So this has been observed not only in BRCA, one and two carriers, but in the general population as well. That for example, for ovarian cancer, risk taking oral contraceptives for at least several years does significantly reduce the risk of developing ovarian cancer. Probably because you're suppressing those monthly cycles of ovulation and the stimulation that happens in the ovary, there may be a very slight increase in the breast cancer risk. So this is what, this is the tension, if you will. And BRCA carriers, okay, but I might reduce my ovarian cancer risk, but what about my breast cancer risk? But that risk tends to be mostly while you're taking the medication, and may go, you know, may reduce afterwards, and is not as strong as the the suppression of the ovarian cancer risk. Having said that, I don't recommend that women you know who weren't otherwise going to do it necessarily take oral contraceptives, but it's kind of reassuring that if that's a choice that they they made, that them that might help reduce their risk. And it does come up when counseling really young women who might be considering different options.

**Dr. Bill Evans** 26:56

That covers that I had a question though about testing on on breast cancer tumors, for for genetic abnormalities, and can you find BRCA one in a tumor, but not in the germ cell line? Okay, that

**Speaker 2** 27:11

is actually a really important question. Thank you for bringing that up. So for ovarian cancer in Ontario now and in many other places in the world, when you are diagnosed with ovarian cancer, the tumor is automatically tested for BRCA one and two mutations, and that's because the medication that I mentioned, olaparib, is very important in the treatment of ovarian cancer, or BRCA one and two related ovarian cancer, and it works if there's a mutation only present in the tumor that might have developed, or if you have an inherited mutation, it's rare that we find a mutation in the tumor that's not in the germ line, but we do in a small percentage of patients, and that's in ovarian cancer. We also do tumor testing and in other sites, like prostate cancer, for breast cancer, testing the tumor is not the first step. The drug is only approved in women who have germline mutations. But that's important question. There was a small study that showed that in women who have advanced breast cancer, if they happened to be tested and had a tumor mutation and not a germline mutation, they also benefited from Yeah, the treatment, yeah. It's just not part of the algorithm right now to do the the tumor testing for breast cancer, but it made a huge difference in ovarian cancer when that was brought in, because, for a number of reasons, ovarian cancer patients weren't often getting referred for genetic testing. Often they're very you know, patients with ovarian cancer are often very sick when they are present at diagnosis, and we were missing some, but now, essentially, they have universal testing. It's done on the tumors, and so we have a lot more ovarian cancer patients being tested now. And maybe if we did it in breast cancer, we'd have the same phenomenon. We wouldn't, we wouldn't miss some.

**Dr. Bill Evans** 29:00

And you mentioned when, when you were talking about the prophylactic surgery to avoid ovarian cancer, you also take out the fallopian tube. So one of the things that surprised me in my reading is that ovarian cancer can arise from the Fallopian Yes, I just never knew that. Yeah, that's actually

**Speaker 2** 29:16

the new thinking that ovarian cancer may originate in the fallopian tube. And so there is a procedure that's being studied right now, which is to do a removal of the tubes, called a salpingectomy first. And younger women, say, who we don't want to put in, take out the tubes. Just take out the tubes as a first step, and leave the and leave the ovaries in until, say, menopause, and then go in and take out the ovaries. This is a promising strategy, but certainly not the standard right now. We're waiting. There's several large international studies ongoing right now to look at that. There are times where that's done kind of opportunistically. So women opt for used to be tubal ligation for contraception, and now people are taking out the tubes because of that. That theory. Yeah,

**Dr. Bill Evans** 30:01

okay, no, we haven't talked about men. And so if you're a man with breast cancer, similar sort of approaches in terms of contralateral mastectomies, etc, etc. For men,

**Speaker 2** 30:14

it's a bit different. So first of all, for BRCA, two, the lifetime risk of breast cancer for a man is an order of magnitude lower. It's about six five to 10% but really about five or 6% and so it's still an uncommon event, but it's certainly one of the clues. And you know what? I realized I didn't mention that before, when I talked about the patient groups who are automatically eligible for testing just based on their history, that includes men with breast cancer, I just focused on the limit. So sorry about that. So we don't do remove the other breast in men with BRCA two mutation in breast cancer, because the contralateral risk isn't that high, but they are at increased risk for an aggressive form of prostate cancer that may be diagnosed a little bit earlier, but is typically high grade and has a worse prognosis. And so the typical recommendation now for men with BRCA two mutations is to start prostate cancer screening at age 40, and there are some research studies ongoing looking at MRI screening for prostate cancer in that population as well, there is an increased risk in pancreas cancer, and it can happen in men and women. And the problem is that we don't have effective screening for pancreatic cancer there are so there were a series of trials, including an important one done in Ontario that didn't show it to be very effective. But the the technology has changed. And so there's a new a new study ongoing to look at two techniques, really, MRI and endoscopic ultrasound, which is when the physician inserts a scope that has a small ultrasound probe on it to get a close look at the pancreas. So there's a, you know, I think it's better if people enroll in their research study to evaluate that, but for very high risk families who are not inclined to do that or can't for whatever reason, we do sometimes offer pancreatic cancer screening, and you have to have a mutation and also a family history to be eligible for that. There may also be an increased risk of melanoma in BRCA, two carriers, and for melanoma, it's really what we should all be doing right sunsets, covering up and education around skin lesions, moles that might change or enlarge or become asymmetrical, etc. So those are, those are really the main interventions. So

**Dr. Bill Evans** 32:41

we've done some podcasts on safe sunsense, and so listeners can go back and find those and get the information about what they should be doing. What I wanted to ask you now is really around the conversations that take place to counsel people. And I just think what we've talked about is complex involves risks and various percentages and so on. And I just, I guess I'm a little perplexed how those conversations would go with the average person, and the ability to absorb that information, use it, and how they make decisions and and what's your observation from that?

**Speaker 2** 33:16

Okay, so Well, fortunately, we have a whole category of healthcare provider called genetic counselors who are highly trained and skilled members of the team who specialize in this. So they deal with this every day, and they are always involved in the care of patients who are found to have mutations. And they provide that information, and then, typically, it's followed up by appointment with a physician, someone like me or one of my other colleagues at the juravinsky Cancer Center who specialize in this area. What's changed, though, is that that typical model where a genetic counselor would see you before your test and give you a lot of counseling around the possible results, and then see you again after the test and really focus on the if you have a change in BRCA, one or two focus on the risks, etc. For that, we can't accommodate the volume of patients that we have for testing with that one on one kind of model. And so what's evolved more recently is a strategy where it's the catchphrase is called mainstream testing, but really it's testing initiated by the oncologist. So if you were seeing a patient in your office who met the criteria for testing, you would say, you know, I think you would benefit from genetic testing. Here's the reasons why. Here's the possible reasons why you might not want to do it. You can go to the lab right now, give your blood test, and then the genetic counselor will follow up with you. If your result is negative, you'll get a minimal intervention from the genetic counselor. But if the result is positive, clearly, you you know, you'll get more intensive counseling. And that has really enabled us to deploy genetic counselors to the small proportion of patients who really need it, but in whom. The number is growing. So instead of spending two hours talking to every patient, they really can focus on the ones who need the genetic counseling. And we're able to do that because there have been research that shows that, in general, that approach is well tolerated and that most people don't have serious psychological adverse reactions from genetic testing, they can do more limited pretest counseling was

**Dr. Bill Evans** 35:23

worry, I think, and maybe it still exists about you have genetic testing, and then your insurer finds out that you have this increased risk and coverage issues. Where are we that can follow that literature?

**Speaker 2** 35:35

Yeah, it's a good question. So for patients who have cancer, that's not really an issue, because their Insurability is really related to their cancer history. You know, if you've had breast cancer, your your ability to get life insurance or critical illness insurance is really tied to that diagnosis. It's more of an issue for people who haven't had cancer, and we do have legislation in Canada that protects against genetic discrimination. So when you apply for insurance, you are not allowed to be asked about a specific mutation in the family. If you tested positive or tested negative, they can't be asked questions about genetic testing. However, you can be asked questions about your family history. And so I feel like all of the legislation is there, and it's important. It's not a complete protection. And so we counsel about that for for patients who don't have cancer

**Dr. Bill Evans** 36:28

unfortunate to see that there's a loophole in the legislation, there something to think about. So you have the Buffett Taylor chair in breast cancer research. I'm sure your research interests go into the management treatment of breast cancer. But what are the research areas in terms of the cancer genetics part of it that are, what are the things that are driving researchers these days in relation to genetic abnormalities in breast cancer? Well,

**Speaker 2** 36:57

as you can imagine, it's hard for a single center with it with a rare disease, to have enough mutation carriers at their own center to answer these important questions. So most of the information on BRCA one and two have come from large international collaborations, so we participate actively with groups in the University of Toronto and elsewhere to recruit all of our gene carriers so that we can ask questions about, what are the risk factors, for example, and what are the features of for example, pal b2, related breast cancer. We're also involved in a study looking at what we call cascade testing. You identify a BRCA, one or two carrier who has breast cancer. How do you make sure you bring in all the family members so that we can help prevent the disease? So we're looking at strategies for that. Are there digital tools that can help? You know, maybe if it's hard to call up all your relatives, you could send out an email that says, go to this portal. You'll get all the information that you need about this. So that's sort of what people are looking at now we're also looking at other possible novel treatments. So this is very early on, but there's a group in Israel that has shown that if you give preventive radiation to the opposite breast in someone who has cancer on one breast and has a BRCA one or two mutation, you actually reduce the risk of cancer in the other breast. And so is that something that could is that feasible in our environment? We're thinking about that kind of research study. So those are some of the areas.

**Dr. Bill Evans** 38:27

Well, you've really shown us a lot about what's going on in this area, and it's I've learned a lot myself. I thought I knew a bit. You've taught me a lot, and hopefully our listeners have gained a great deal from it. What messages would you like to leave to listeners, particularly women who may have recently been diagnosed with breast cancer, or relatives of those who have breast cancer but don't have it themselves?

**Speaker 2** 38:53

Yeah, I think if you've recently been diagnosed with breast cancer and you're wondering about whether you could be a genetic mutation carrier, that you should ask your care providers, your oncology team. It's also a good exercise to ask your family history, because, you know, a lot of not in the not too distant past. It was something that was hidden and not openly discussed. And there are people who come forward, who say, You know what, I just found out, I have all this history on my father's side. So use the opportunity to ask about your family history and ask your providers if you could benefit from testing, if you've had breast cancer in the past and were not offered testing or even thought about that you should be or you were told you weren't eligible. Re ask that question, because the criteria change, as I mentioned, went from 35 and under to now 45 and under, and maybe soon we'll see 50 and under. So that's, I think, an important group that we've most of those patients. Many of those patients will have been discharged back to their primary care provider. They're not in the cancer system anymore. So ask if you you know if you're now eligible. And then finally, if you don't have cancer, but you're worried about your family history, ask also, because the criteria. For being referred for assessment to see if you're eligible are much more broad than those specific categories that I told you about. So we don't want to miss anybody. You're eligible to be referred to a genetic counselor if you have a family history that doesn't even you're not sure if it meets those criteria. Well,

**Dr. Bill Evans** 40:17

that's great advice, and this has been extremely helpful to anybody and everybody listening. I'm sure you're so knowledgeable, and your expertise is fantastic to have in the Ontario system. I know you've been leading the breast group for years in this province and and so active in research in the cancer genetics area. So we're really blessed to have you working with us, and so thank you so much for giving up your time and doing this podcast with us.

**Speaker 2** 40:45

No, it's actually been a real pleasure, and thanks for giving me the opportunity

40:49

to reach people. Thank you. Thanks.

**Speaker 1** 40:53

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