

Speaker 1:

Welcome to the Cancer Aware Podcast, where we'll discuss cancer prevention, treatments, the latest in research, and important news around cancer, brought to you by the University of Michigan Health Rogel Cancer Center.

Today we're here with the MiGHT Study co-principal investigators, Dr. Elena Stoffel, director of the Rogel Cancer Center's Cancer Genetic Clinic, and breast oncologist, Dr. Jennifer Griggs.

Elena, can you talk to us about the importance of genetics and family history with regard to an individual's risk for developing cancer?

Dr. Elena Stoffel:

That's a great question, and I think it's important to recognize that most cancers that develop develop by chance, that there is something that just goes wrong in a cell, but a certain percentage of cancers arise because there was an inherited factor that served as, so to speak, a first strike. And it's really important to be able to identify cancers that arise as a result of genetic inherited factors because this has implications for not only treatment of the cancer, but also opportunities to prevent cancers or detect them early in cancer patients, as well as their family members.

Speaker 1:

So what kind of cancers are identified via an inherited risk from genetics?

Dr. Elena Stoffel:

So work that was done through the University of Michigan MI-ONCOSEQ program actually identified that approximately one in every 10 cancers of across various different cancer types can be associated with an inherited risk factor. When we think about common cancers with regard to colorectal cancer, it's about one in every 10 colorectal cancers. But when you look at colorectal cancers diagnosed in young people under the age of 50, it's about one in every five. In pancreatic cancers, it's about between one in every 10 and one in every 20. In ovarian cancers, it's one in every five as well.

Speaker 1:

So Jennifer, we're talking about genetics and we're talking about different inherited genes that people have relating to cancers. Can you tell us about the MiGHT Study?

Dr. Jennifer Griggs:

The MiGHT Study has two main parts. The first part is designed to increase the quality of the family history that physicians receive from their patients. So one could also say it's the quality of the family history that patients give to their physicians. It's really important to provide a complete family history, and this is first degree family members like parents, children, and siblings, but also second and third degree family members as well. And we found that across the state of Michigan and nationally, fewer than a third of patients have a complete family history documented in their medical record. That missing information in nearly 70% of people with cancer means that we are most likely missing many patients who could be identified as having an inherited susceptibility to breast and other really important cancers, and we're learning more and more about cancers that are associated with these mutations.

So it's a typical thing for a physician with somebody who has breast cancer to say, for example, there's no family history of breast or ovarian cancer, but there's so many other cancers that can be informative. In the case of breast cancer, we need to know if somebody has a family history of gastric cancer,

pancreas, prostate cancer, not just ovarian, endometrial. So there are many cancers for which we might not ask, and if the patient doesn't know, it's basically incomplete information and that information is needed for us to take the best care of our patients and their families.

So the first part of the MiGHT Study is designed to help support practices who care for people with cancer and to the patients to provide a complete family history. The second part of the study is to take people who are eligible, who have a higher than average chance of having an inherited susceptibility to cancer, and helping them get and complete genetic testing. So not everybody needs genetic testing with a family history, but there are ways we can identify those people who do. And there are some people who don't get referred, some people who are referred but don't follow through, some people who see a counselor but don't get the testing, and those are steps that we are trying to address in the project. There's places where things can break down and we're trying to backfill all those needs so that every patient can get the absolute best care. And in this case, it's not just our patients, but it's also their families.

Dr. Elena Stoffel:

So just to give an example of how we designed the MiGHT Study, in gastroenterology, I'm a gastroenterologist so I can talk about how patients who come in for colon cancer screening typically are there because they are worried about their risk for colorectal cancer. As part of the MiGHT Study, individuals who are coming for doctor's appointments in various different settings are getting a family history survey that they can fill out and they can bring that information to their doctor so that at the time that they see their doctor, they show their doctor their family history, and hopefully their doctor will be able to look at that family history and say, "You know what? There's more cancer than I expect to see by chance, maybe you meet criteria for genetic evaluation." For example, in the case of colon cancer. About a third of individuals who are diagnosed with colon cancer had a family history of the disease, but 3 to 5% of all colorectal cancers are associated with strongly inherited genetic risk factors.

For instance, Lynch syndrome, which is a genetic hereditary cancer syndrome associated with high risk for colorectal and gynecologic cancers, is present in about one in every 279 people in the general population. So if a person is coming in to have their colonoscopy because of their family history of colon cancer, it would be really important to know if that family history is significant enough to meet criteria for genetic testing for Lynch syndrome. Because in Lynch syndrome we do colonoscopies really frequently, so every one to two years, starting as early as age 20 to 25, which is really different from a recommendation that would be made to just someone with one family member with colon cancer.

Speaker 1:

So you talked about coming into the doctor visit with the family history all filled out, so is that a separate form or separate tool that they would be utilizing compared to say, now when I go for my annual physical I have to go through and review and put it in the portal and so forth? So is that a separate and is that part of the MiGHT Study of people getting a separate family history form to start the process, or is it already existing in practices?

Dr. Elena Stoffel:

As part of the MiGHT Study, we actually developed a comprehensive family history form that individuals fill out themselves, and this is actually mimicked on what genetic counselors do to elicit a three generation family history. And it involves asking about cancer diagnoses in first and second degree relatives, as well as the types of cancer and the ages of diagnosis. And this is sufficient to create a family tree that is very easy for medical providers to look at, to recognize patterns of hereditary cancers, and it

also elicits information that is used to run some genetic risk models to determine what an individual's risk is of having a genetic susceptibility to cancer.

Speaker 1:

Jennifer, on those forms, if people go through and they mark off their family history, so much you hear about really only breast cancer patients really going through a genetic test or looking at the family history, how does this now impact others to really think about genetics?

Dr. Jennifer Griggs:

You're so right. People with a history of breast cancer, in part due to what we call the Angelina Jolie effect, when she was found to have an inherited susceptibility, she of course was an advocate not just for herself but for others. And so breast cancer leads the way in terms of the proportion of people who are eligible getting tested. There are still gaps though, not everybody with breast cancer who could get tested is getting tested. So although breast cancer is by far, in a way, better than the other cancers, there's still a tremendous gap, particularly for historically marginalized people. So Black people, Indigenous people, people who are Hispanic, and people with less means are not having a good family history taken and also are not accessing the services that they should have access to.

In terms of other cancers, there's a tremendous gap. Colorectal cancer is the one that comes to mind. We see so many people who are eligible for testing not getting it. In addition, people with endometrial cancer, pancreas cancer, and prostate cancer, all of whom benefit not only from detection of a mutation and counseling of family members, as well as prevention of other cancers in their case, but treatment of the cancer they have. So in the past, there was nothing we could do other than surgery or close follow-up. Now we actually direct treatment based on whether or not somebody has a gene that gave rise or contributed at least in part to their cancer. So to me, even one person not having tested, been tested who could have, is a tremendous loss. I'd say given the importance of colorectal cancer, the prevalence in the population, what we're seeing in terms of the rise of colorectal cancer in young people, this is the biggest gap.

But for all those other cancers, I think this is an important issue. I'd love to give a story about a patient who had lung cancer where the oncologist, normally we surveyed oncologists in Michigan, they don't consider the family history as important in lung cancer. As an aside, I do think we are going to find genes that increase the risk for lung cancer, but we know there are other factors that give rise to lung cancer. This oncologist, her practice was participating in the MiGHT Study, saw her patient's family history, and because of the family history, identified that this patient was eligible for counseling and testing for Lynch syndrome, which is important in terms of not just colon cancer, but also endometrial breast and other cancers. So when we say everybody should have a family history regardless of the diagnosis, we really mean it. Even if this patient succumbed to their lung cancer, their family members can be tested. We can save lives by taking a good family history.

Dr. Elena Stoffel:

And I think just to reinforce that, when we look at who gets genetic testing in the state of Michigan, over 80% of individuals who are having genetic testing are presenting because of a personal or family history of breast cancer. And to just reinforce what Jennifer said, we know that there are a lot of other people out there with cancer diagnoses or with family histories of cancer that meet criteria for genetic testing, maybe not for hereditary breast cancer, but for some of these other conditions that have huge implications for the care of their family members. And our hope is that we can actually expand access to genetic testing by educating providers about who needs genetic testing, and actually empowering

individuals to talk to their doctors and also to seek out where to get genetic testing. And we are so excited to have partnered with the Michigan Department of Health and Human Services who has a cancer genetics hotline that is both for individuals as well as for providers who have questions about how to access genetic testing resources in their communities.

Dr. Jennifer Griggs:

I'd also love to add that in cancer we see so many advances in the treatment of people with stage four advanced cancer. This is a prevention methodology. By taking a family history, we're preventing cancer. And in medicine we're very reactive. We tend to take people who are sick and try to scoop them up and make them well, and a lot of our treatments in cancer actually make people sick before they make them well. We're trying to prevent recurrence or prevent death from cancer. There are very few things we can do in oncology to prevent cancer. We know HPV vaccines are important, early detection with colonoscopy, mammography, cervical exam, pap smears, but this is actually not just early detection, but prevention of cancer. And I don't think we can stress enough how much oncologists would like to be put out of business, and this is one step toward that.

Speaker 1:

Who should consider genetic testing in general? I know we've discussed a little bit about who, but who realistically should be, and does that differ from those that should be interested in the MiGHT Study?

Dr. Elena Stoffel:

When we think about who would benefit from genetic testing, it very much depends on the individual's own cancer history as well as their family history of cancer. In the early days when genetic testing was very expensive, there were some very, very strict criteria for who met criteria for genetic testing. Now that we've realized that these genetic diagnoses are relatively common, as I mentioned Lynch syndrome affects one in every 279 people walking down the street, and hereditary breast ovarian cancer syndrome, gene alterations are carried by about one in every 300 people walking down the street. When you look at Michigan Stadium on a Saturday, there's a lot of people there who have genetic susceptibility to cancer that don't know it yet. And so there are a number of different criteria for genetic testing. We could go on all day, but basically the hallmarks are if there are very young cancers diagnosed in the family, so particularly young cancers, I'm talking breast cancer under the age of 60, I'm talking colon cancer under the age of 50, uterine cancer under the age of 50, prostate cancer under the age of 50.

Likewise, if there are multiple people in the family affected by the same type of cancer, or by related cancers that go together. So for example, breasts and ovarian cancer, colon and uterine cancer, prostate and pancreatic cancer, those also raise red flags. And I think it's really important for individuals to talk to their medical provider about their family history and to ask specifically, "Does my family history raise concern for the possibility of a hereditary cancer syndrome?" Because now that genetic testing is much more readily available and the costs have come down, the opportunity is there for people to talk to their doctors about genetic testing and if genetic testing is indicated, this is often available, covered by insurance for people who meet specific criteria. And also, it's really important to know that this is there and available. And that's what the MiGHT Study is trying to do, get the word out and help individuals who would benefit from testing, find out how they can get testing done.

Speaker 1:

Jennifer, as a quick follow up to that, you had mentioned previously about making sure different ethnic groups, Indigenous, African-Americans, I'm going to assume Mina as well, could really benefit from this. How do you approach reaching those communities when, in many cases, they sometimes also have a lack of trust of healthcare and them wanting to understand that this could benefit them?

Dr. Jennifer Griggs:

Trust is a big factor in terms of who gets any healthcare. And when we're talking about collecting information for genetics, people who have been historically oppressed, historically marginalized people who don't have access to high quality information support, this is going to be a major driver of those disparities, in addition to economic disparities as well. Not that these tests costs what they do, but even perceived cost we know decreases uptake of genetic testing. So it's multifactorial, which means that multifactorial, multifaceted interventions will be required. One of the most important things is that people receive care from people who look like them, and we know that increasing the diversity of our workforce is going to be a key way in terms of minimizing disparities across the board regardless of what they're due to. So making sure that people delivering care look like their population and are familiar with the culture.

So we've done a lot of outreach in other settings regarding cancer care to have other people, I even hate to say bringing people to the table because that puts us in a position of power, and sending those invitations out, but actually making it a place people want to be. So working with communities is the most important thing, I believe, so that they're getting information from people who understand them and can listen to them. I think we have to be careful not to be colorblind. When we're colorblind, we're not actually seeing people for who they are. So cultural humility is a major step that we work on throughout the state with our oncology practices. A lot of question asking, what's important to you? What matters to you? And for most people, that's family and safety, and if we can increase safety and increase the way we leverage people's values and align our values with them, we're going to take great strides in closing those gaps.

Speaker 1:

With this partnership of the MiGHT Study being through the state and through the Michigan Department of Health and Human Services, does that help in being able to reach some of those communities through the study?

Dr. Jennifer Griggs:

Our hope is that it does. I think it remains to be seen. I think this is a wicked problem that people are working really hard to address.

Speaker 1:

To follow up, since we're talking about communities and we're talking about family and understanding, when it comes to the main part of the MiGHT Study, that family history, that family audit, if you will, how do you go about talking to patients to really take the time to go through and get that information? Sometimes people don't like to talk to other family members because they don't want to necessarily know, or they're closed off. How do you tell them good tools to help them be able to talk to their family, to be able to put that history down?

Dr. Elena Stoffel:

I think it's really important to let individuals know that talking about family history is really important, and I know that the Michigan Department of Health Human Services has issued a proclamation that November is Family History Month specifically because we want to encourage people to talk with their family members from multiple generations about the health of the family because this information can really, really be useful for providing care. The Family Health History Survey that we developed for the MiGHT Study, we went through multiple iterations with multiple different focus groups to make sure that individuals thought that it was easy to complete and that it asked questions in a way that made sense. And we're really proud to be able to say that we've had individuals complete this family health history tool in multiple different settings from multiple different communities and have had success in hearing the feedback, "Hey, in filling out this family history tool, I got information from my mother that I had never heard before, and I brought this information to my doctor and my doctor recommended genetic testing."

And I think that when somebody asks, "Do you have any family history of cancer?" The automatic answer is no, or yes, and then you give one example, and then typically the healthcare provider will move on to the next question. But I think this family health history tool allows you to go through each generation and identify whether there were any cancers in each generation that basically builds that full family tree. And it's really only by looking at that full family tree that we can say, are there any cancers here that are unusual or that affected young people? Or do we see the same type of cancer repeated multiple times? And those are the prompts for additional conversations about cancer risk and genetic testing. Because sometimes even if the family history doesn't meet criteria for genetic testing, it allows for the opportunity to talk about, what other cancer screenings are necessary now? And for instance, is it better to start your breast cancer screening earlier because of the family history of cancer, with or without a genetic test recommended?

Dr. Jennifer Griggs:

I would like to address the estrangement. So we know a lot of people are estranged from their family members, and one could consider the family history as a lever for repair. So I know of families where there was estrangement and the purpose became prevention in the family and in the offspring, and so siblings actually have come together to share information because they care about their kids. So you might be really mad at your brother, but you care about your nieces and nephews. So one could consider the family history as a lever or a way to bring family members who are disparate together, even if it's just for that purpose. So we'd love to have people consider this as a gift to other people in the family. Again, you might want to not think about the one person from whom you're estranged, but all the people in their orbit, so I think it's an opportunity for some repair.

Speaker 1:

So about estrangement, how does a person who maybe doesn't know their family, so they were adopted or may be a refugee, or something where they don't have that connection to, how do they go about piecing together a family history, if possible?

Dr. Jennifer Griggs:

That's such an important question, and it relates to inclusion, which is one of our key tenets when we talk about justice. The tool's been designed so people can fill it out according to the family members they know. But I had a patient who had triple negative breast cancer and was adopted and found her birth mother. Her birth mother had a mutation and so did her birth mother's other daughter. Now they're in pictures together on social media, so she's reunited and all three have taken measures to

decrease their risk of breast and ovarian cancer. So miracles can happen, I view that as a miracle, one person very committed to finding things out. She knew she had a mutation, she had a gut feeling, and went to the work of finding her birth mother. I'm sure Dr. Stoffel has something to add.

Dr. Elena Stoffel:

I think that so much of the cancer screening that we recommend is based on family history, and so for individuals who were adopted and don't have that biological family history, genetic testing can also be appropriate and can be a way to identify whether there's any particular genetic alterations that would prompt earlier screening. For instance, if somebody were found to have a diagnosis of Lynch syndrome, we would start colonoscopies between the ages of 20 and 25. And so I think that as genetic testing has become more readily available, there are more opportunities to have testing. And I think it's important to emphasize that many medical professionals still believe that genetic testing is hugely expensive and very difficult to do. But the reality is that innovations in sequencing technologies and the fact that there are multiple avenues for genetic testing has really made this testing come down in cost.

And there are different ways to access genetic testing. For instance, many individuals come to our cancer genetics clinic to meet with a genetic counselor and undergo an evaluation that includes germline genetic testing, but there are other alternative methods for care delivery. We have a lot more telehealth since the pandemic now, so individuals from the comfort of their home can meet with a genetic counselor. But there are also genetic testing laboratories that are clinical laboratories that actually offer testing directly to patients, where patients can actually order the testing themselves and receive a genetic test result and if that result is positive, there are instructions as to what to do for follow-up care. One of the things we're interested in looking at is that traditionally, the people who came to get genetic testing were people who lived near genetics clinics. But now that we have all of these other methods for care delivery, our hope is that people who are not able to travel to genetics clinics will still have the opportunity to get tested.

Speaker 1:

So this final question, now that someone has filled out their family history, they've talked to their doctor, it's appropriate for them to have genetic testing, comes back that they have a mutation. What is next for that MiGHT Study participant that goes through that process and then finds out that they do have inherited risk of cancer?

Dr. Elena Stoffel:

So it depends on what gene the alteration is in. Many of the genes included in clinical genetic testing panels have what we call actionability, which means that there are particular recommendations that we make for the patient's own treatment based on the result of the gene alteration. So for example, going back to that individual with Lynch syndrome, if they have a Lynch syndrome gene alteration, we basically make recommendations for colonoscopy, upper endoscopy. And for women, there's an increased risk for gynecologic cancer, so we also plan strategy for gynecologic cancer risk reduction. For individuals who have a family history of breast cancer, if there is a BRCA1 alteration that's identified, then similarly we make recommendations for cancer screening, for breast cancer screening that's enhanced and starting at younger ages, we have conversations about medical and surgical options for cancer risk reduction for breast and gynecological cancers.

So our feeling is that this testing gives you information that you can act on, but we also recommend that an individual who has a genetic diagnosis communicate that information to their family members. Because one of the things we are finding as part of the MiGHT Study is there are individuals whose

family has been identified as having a genetic diagnosis, but they themselves have not undergone genetic testing for a variety of reasons, including worry about what to do with this information, as well as sometimes logistics of just not knowing where and how to get tested. So this information is information that can help with the management of individuals with or without cancer, and also families that have been affected with cancer.

Speaker 1:

I really appreciate the time, Jennifer and Elena. As we wrap up, what's the biggest, most important message around both genetics and the MiGHT Study that people should know?

Dr. Jennifer Griggs:

I think for me, the biggest thing is that this is an opportunity to prevent cancer, and to detect it early before one needs an oncologist, or where one can have an oncologist for a very short amount of time. We can decrease the need for chemotherapy, we can decrease mortality from cancer, and this is an opportunity, the gap of which we need to close urgently

Dr. Elena Stoffel:

And my take home is talk to your doctor about your family history of cancer and ask is there anything about your family history of cancer that brings up the question of, are there specific cancer screenings that you should be getting now? And, does your family history meet criteria for genetic testing? Because I think that by talking to your family members about their health and talking to your doctor about the health of your family, knowledge is power, and this can really make a difference.

Speaker 1:

If someone is interested in learning more about MiGHT Study or genetics in particular and their family, how do they get started with that?

Dr. Elena Stoffel:

We would invite anyone who's interested in the MiGHT Study to go to register.mightstudy.net where you can see some information about what the study is all about, and also find a link to the family health history form. We also would encourage you to access the Michigan Department of Health Human Services Cancer Genetics Hotline.

Speaker 1:

Thank you again. I appreciate the time.

Dr. Jennifer Griggs:

Thank you.

Dr. Elena Stoffel:

Thanks a lot.

Speaker 1:

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