Rounding@IOWA: Modifiable Risk Factors for Breast Cancer (2/10/2026)

[Upbeat theme music plays]

Dr. Clancy: Welcome to Rounding@IOWA, a continuing medical education podcast developed by and for healthcare teams. I'm your host, Dr. Gerry Clancy, Senior Associate Dean of External Affairs for the Carver College of Medicine, here at the University of Iowa. Today we will learn about modifiable risk factors for breast cancer. Our objectives include, first, we want participants to have a solid understanding of risk factors for breast cancer. Second, we hope our participants can cite those risk factors for breast cancer that are modifiable. And then third, we hope our participants can guide their patients to lower their risk of breast cancer, particularly in areas that they can control. We have the great advantage today to host two guest experts to help us sort through a complex set of risk factors and screening options for breast cancer. Dr. Katherine Huber-Keener is a Clinical Associate Professor of Obstetrics and Gynecology here at the University of Iowa. She is the past Director of the Cancer Survivorship Program at the University of Iowa Holden Comprehensive Cancer Center. She earned a PhD in Pharmacology and MD degree from Pennsylvania State University. She then completed residency in Obstetrics and Gynecology at the University of Iowa. and then followed up with a fellowship in cancer genetics and breast health fellowship at the University of Michigan. Dr. Nicole Fleege is a Clinical Assistant Professor of Internal Medicine in the Division of Hematology, Oncology, and Blood and Bone Marrow Transplantation. She completed her M.D. degree at the University of Iowa Carver College of Medicine. She went on to residency in internal medicine at the University of Iowa. She was then chief resident in internal medicine here at the University of Iowa, and she then completed a fellowship in hematology and oncology at the University of Michigan. Dr. Fleege and Dr. Huber Keener, thanks for being on Rounding@IOWA.

Dr. Huber-Keener: Well, thank you so much for having us today.

Dr. Fleege: We're excited to be here.

Dr. Clancy: Great. Well, I just provided our listeners a brief official description of your educational backgrounds and your current titles. Could you tell us what drew you to this work in the first place? And let's start with Dr. Fleege.

Dr. Fleege: I think I was first drawn to oncology when my dad was diagnosed with lung cancer when I was 16. He passed away when I was 17, so that made me less interested. But throughout my internal medicine training, I found myself just being called to continue that work. And so ultimately, when I went through fellowship, I realized that pursuing lung cancer would be too hard for me, given what happened with my dad. And since I liked

women's health and enjoy taking care of women, I found that being a breast oncologist combined all of the areas I was passionate about into one specialty.

Dr. Clancy: Katie, how about you? What drew you to this work?

Dr. Huber-Keener: Yeah, well, I've always had an interest in genetics, and genetics has to do both with risk factors for cancer and then also how cancer develops. When I was in medical school, actually my second year of medical school, I was diagnosed with a cancer. And then when I was in my PhD, my father was diagnosed with metastatic melanoma. And that for me, just like Nicole, kind of cemented that cancer was going to be something that I wanted to work on, and did my PhD in kind of cancer genetics and pharmacology. And then found my way through OBGYN and doing some breast surgery, that it was a combined field that I wanted to participate in.

Dr. Clancy: We're very glad that you came to this work. What does a work week look like for you? And let's start with Katie.

Dr. Huber-Keener: Well, mine is unique in being in both OBGYN and then I do a full day of clinic in the cancer center, taking care of women who are at higher risk for any of the female cancers, including breast cancer and then breast cancer survivors. And then I still do risk reducing kind of GYN surgeries, including hysterectomies and removing ovaries and things like that. And then I do a lot of work in the resident clinics and some of our procedure clinics as well. So it kind of varies from week to week.

Dr. Clancy: Nicole, how about you? What does a work week look like?

Dr. Fleege: I guess my week is a little bit more standard. [laughter] I am currently 50% research and 50% clinical. In the next year, this will be increasing to 75% research, but I am currently in clinic all day on Monday, and then I see patients during a half day on Wednesday. The rest of the time, if I'm not rounding on our inpatient service, I am doing research.

Dr. Clancy: All right, before we talk about modifiable risk factors for breast cancer, let's talk about where we are regarding breast cancer coming out of the pandemic. What are the trends for breast cancer and where does it rank among women as far as causes of breast cancer? I'll open up to both of you or whoever wants to answer first.

Dr. Fleege: Yes, so I think I can take this one. You know, over the last decade, we've seen a slow rise in the incidence of breast cancer in the United States, about 1% per year. Although there are certain groups where it's risen slightly higher, and I think most concerning is for women under the age of 50. In terms of ranking among women, it remains

the leading cause of cancer incidence in women. And then it's the second leading cause of mortality, second to lung cancer.

Dr. Huber-Keener: Yeah, and we say about one in eight women will get breast cancer in their lifetime.

Dr. Fleege: I think the other thing I wanted to point out is that in Iowa, we've gotten, I think we've talked a lot more recently about the rising cancer incidence in our state in particular. We have the second highest cancer incidence and breast cancer is one of the cancer types that's contributing to that rise. And so I think just especially important when we think about our own state.

Dr. Clancy: For the non-specialists, let's talk through some of the important terminology regarding breast cancer. Starting off, can you help differentiate what we mean by invasive or non-invasive breast cancer?

Dr. Fleege: I think I'd love to talk about this in the way I talk to my patients when we first meet in clinic. And so I start by talking about what breast tissue is comprised of. So we know that breast tissue is made up of lobules and ducts. Lobules are the small sacs that produce milk, and then ducts are the thin tubes that bring that milk to the nipple. We know that abnormal cells can start in either of those locations. And so when the cells are contained within the wall of the lobules or the ducts, we consider that non-invasive disease, or carcinoma in situ. It's when those abnormal cells invade beyond the walls of the ducts or the lobules and into the surrounding breast tissue that we talk about invasive breast cancer. And in general, when we use the phrase breast cancer, we're really talking about invasive disease.

Dr. Huber-Keener: But historically, when we look at data, it does include our DCIS, or ductal carcinoma in situ. So that's why those women get characterized in the breast cancer category, which I think causes a lot of confusion for people.

Dr. Clancy: So within the non-invasive breast cancer types, again, can you help differentiate what are there subtypes of non-invasive as well?

Dr. Fleege: Yeah, I think Dr. Huber-Keener just mentioned really one of the main types we think of, which is DCIS, or ductal carcinoma in situ. It comprises, you know, more than 80% of in situ cases. And again, that's when those abnormal or malignant cells have started within the ducts but not yet invaded into the surrounding breast tissue, so we consider that a precursor to invasive breast cancer.

Dr. Clancy: Got it. And so when we start talking about invasive breast cancer, are there subtypes of that as well?

Dr. Fleege: Similar to what I previously said, the most common type of invasive breast cancer is invasive ductal cancer or invasive ductal carcinoma, which makes up about three quarters of new breast cancer cases. Less commonly, we see invasive lobular carcinoma, so when those abnormal cells are in the lobules of breast tissue and invaded into the surrounding tissue. And then finally, the smallest portion are these special cases or special subtypes that we think of less commonly like cribriform or invasive mucinous carcinoma, but certainly seen much less frequently than invasive ductal carcinoma.

Dr. Clancy: So again, for the non-specialist, can you bring us up to speed on the classification of breast cancer by estrogen and progesterone and HER2 receptor expression types? Again, that's something I'm not regularly involved with, but would love to kind of hear the current terminology and how we use those terms.

Dr. Fleege: This is like the most talking I'll do, but in medical oncology, you know—I'm a medical breast oncologist—and so figuring out receptor subtype is one of the mainstays that guides treatment for this type of breast cancer. And so I always tell patients, we look at three things on the surface of breast cancer cells or within breast cancer cells. Two are receptors. So we look for estrogen and progesterone receptors. Patients might hear that also called the hormone receptors. And then we look for a protein called HER2. And so I like to point out that HER2 is actually a protein that's normally found in cells, and so when we're talking about it in breast cancer, we're actually saying, is it overexpressed in someone's breast cancer cells. And so those make up our different subtypes of breast cancer. So if you have expression of estrogen and progesterone receptors, we call that hormone receptor-positive breast cancer. If you have overexpression of HER2, we call that a HER2-positive breast cancer. If you have all three, we call that a triple-positive breast cancer. And then if none are present or if there's not overexpression of HER2, then that's considered a triple-negative breast cancer. It's so important because treatment is guided by what type of subtype you have. So for example, if you have a hormone receptor-positive breast cancer, we're going to target those cancer cells with anti-estrogen treatment. On the other hand, if your breast cancer cells overexpress HER2, we've now developed drugs that can find that HER2 overexpression as a way to find the cancer cell and then use that to treat the cancer. And so, so much of our treatment these days, which is one of the reasons I'm so interested in oncology, is that it's guided by what type of expression we see in those cells.

Dr. Clancy: Great, great answers. I see why you both are teachers as well. Let's begin our discussions then on risk factors. What are some of the non-modifiable risk factors, starting with gender and age?

Dr. Huber-Keener: Well, certainly the female gender is your number one. I mean, men can get breast cancer, anybody who has breast tissue and men do. So men with gynecomastia or if they have a mutation like a BRCA mutation have those higher risks. And then obviously risk increases with age, although some of our more aggressive breast cancers do happen in our younger patients.

Dr. Fleege: And I think that's a growing area that we want to research is why does it seem that patients are getting diagnosed with breast cancer as they're younger? And so I think that's just a growing body of data in an area that we just need more research in.

Dr. Clancy: How about when menarche starts and how about when menopause starts? Are those influential as far as breast cancer risk?

Dr. Huber-Keener: Definitely. So we say earlier menarche, so younger than age 11, definitely increases risk. And then older menopause, the average age of menopause in the US is about 51, 52. And then certainly the women that are still having menstrual cycles at 55 have a higher risk. We think a lot of that is because that is an active, like the breast tissue proliferates and regress kind of on a monthly basis, depending on what's happening there, and that there's just more chances for mistakes to replicate during that time.

Dr. Clancy: And what do we know about family history for breast cancer and family history for other cancers as well, as far as risk factors for breast cancer?

Dr. Huber-Keener: Yeah, I think most people know that if they have a first-degree relative like their mom or their sister or their daughter that has had a breast cancer, that increases their risk regardless of whether they have a genetic mutation that does that. But then when we think about, when we are looking at and doing genetic cancer risk assessments for these patients, we are looking to see what about also their second and even third-degree relatives. So that goes out to your great aunts and your first cousins. And certainly we think that people have a greater chance of genetic mutation if they have three members on the same side of the family. But the thing that I think is so interesting and so important is it is other cancers in family members that also increase. So most people don't think if their dad and their uncle both had prostate cancer, that they may be at risk for a breast cancer. Same if they had a bunch of men in their family die from aggressive stomach cancers, that there could possibly be a link to breast cancer. And so our best kind of guide for who may be at risk is put together by the NCCN, or National Comprehensive Cancer Network, has a nice kind of guide of who meets criteria to get genetic testing.

Dr. Fleege: I love that Dr. Huber-Keener said that because I agree on the second- and third-degree relatives. I think that of course you think about your mother, but a lot of people aren't thinking about great aunts and that role that it may play. And so I think that's

really important. I'd also point out personal cancer history. So for example, if you've received chest radiation for a prior diagnosis, sometimes people have received that for lymphoma. That could also increase your risk for breast cancer.

Dr. Huber-Keener: Correct. And upper abdominal cancers as well. It can get in—the breast can get in that area.

Dr. Clancy: And we know Iowa is a high radon state. Is radon one of those exposures that—I know it increases it for lung cancer, but is there any association with breast cancer?

Dr. Huber-Keener: I don't know that we have good data on that.

Dr. Fleege: I think that's a good question. Not that I know of.

Dr. Clancy: Yeah, got it. Got it. So, Katie, you mentioned a little bit about mutations and such. So do we have, are we, do we now have specific genetic markers and ways to be able to identify those mutations in really before breast cancer shows up?

Dr. Huber-Keener: Yeah, so we, you know, I think most people are familiar with hereditary breast and ovarian cancer syndrome with the BRCA1 and BRCA2 genes or BRCA [Dr. Huber-Keener pronounces BRCA as "brah-kuh"] 1 and 2 genes. And people know that the breast and ovarian cancer go together. And so there are many people who have those family histories, if that gene is known, or they have those family histories that get genetic testing. But interestingly, the most common mutation or gene that we have a mutation in the state of Iowa for breast cancer is actually the CHEK2 gene, which most of our patients and even most of our providers are like, I've never even heard of that gene. Some of our really high-risk breast cancer genes also include things for TP53, which is Li-Fraumeni syndrome, STK11, which is Peutz-Jeghers syndrome, the one with a bunch of polyps. You would never think that breast cancer is kind of related to that. CDH1, which is hereditary diffuse gastric cancer syndrome. And so there are all these different genes, and there's many that are in a moderate risk category as well. And it's one of the reasons why we say that everybody should have some type of risk assessment by age 25, because BRCA actually starts their breast cancer screening at that age.

Dr. Clancy: We're still on the less modifiable category. How about density of breast tissue as a risk factor?

Dr. Huber-Keener: Yeah, so we definitely know that breast density or how white your breast appears on mammogram plays a role. Some of it is kind of in flux of exactly how much. I think a lot will say for extremely dense breast tissue, which about 10% of women at the age of 40 will have, that they have a 1.8 odds ratio of having, of getting breast cancer. So I like to say not only does dense or really white breast tissue make it harder to see a

breast cancer on imaging, but it also means that you have more of the milk tissue, as Dr. Fleege was talking about, milk ducts and lobules that could become a breast cancer. So breast density is one of those things that is now required federally to be on all mammogram reports.

Dr. Clancy: Got it.

Dr. Fleege: And I think. We're talking more about breast density too. And as Dr. Huber-Keener mentioned, not only for the risks of what is within the breast tissue, but also making it harder to detect a small breast cancer earlier. And so I think that's becoming much more of a conversation of how breast density impacts both, you know, screening and need for future breast cancer risk screening.

Dr. Clancy: So it appears to me one of our factors that's hard to modify is how long you're exposed to hormones, and another is how much tissue you actually have that could be at risk as well. So not much you can really do about that other than be on guard to a greater extent, obviously. Let's move over to modifiable risk factors for breast cancer. And if you can on some of these modifiable ones, maybe at least put at least your theory why these are modifiable and what we can do about it. So let's start with physical activity and body weight. Are those risk factors and do you have a sense of why?

Dr. Huber-Keener: So a lot of our data, especially for physical activity, has to come from big observational kind of studies. And those are studies that look at your upper quartile of people who are doing the most exercise to the people doing the least, the most sedentary patients. And there's a significant difference in cancer risk for the people in the lowest quartile compared to the upper quartile. Our recommendations currently are doing at least 150 minutes of moderate exercise per week, the same as the American Heart Association. But even doing more exercise has been shown to decrease the risk for cancer even more. In terms of weight, now we use BMI, which is not perfect for obesity, right? People with a lot more muscle have higher BMIs and not necessarily that, but we do think it is the adipose tissue itself. As I always say, adipose tissue produces both estrogen, like right, it gets, your male or androgens actually get broken down into estrogen, and then also inflammation, two things that don't cause breast cancer, but can stimulate breast cancer cells to grow. that are there. And so for every, when we look at BMI, it's actually for every five points of BMI that you go up, your risk significantly increases. And when we do risk calculations, BMI becomes a big factor in that.

Dr. Fleege: And I think one of the things that's confusing is when I talk with patients, they say, you know, I've been through menopause, my ovaries aren't making estrogen anymore. So how, why, you know, why am I at risk for a hormone positive breast cancer? And so I

think we forget that a lot, you know, estrogen can still be produced in the tissue from adipose cells, as Dr. Huber-Keener mentioned, even when we've been through menopause. And so I explain targeting that as one of our treatment mechanisms, and it makes sense why weight loss in the setting of obesity can also help.

Dr. Clancy: And we're learning more and more about diet and inflammation and such. And as I mentioned before we started, you know, my mother was a breast cancer survivor and was part of the diet studies back then. So what do we know about, is there a diet that is better and a diet that is worse for breast cancer?

Dr. Huber-Keener: Yeah, so I mean, maybe back even when she had breast cancer the big thing was to tell people to avoid soy products, things that could appear to look like estrogen to the breast tissue, which is really not panned out in our larger studies. What has panned out are anti-inflammatory types of diets. So Mediterranean is our classic one, and patients seem to know, at least when you talk about it, what that is. And then true plant-based diets also have good, getting more of your protein sources actually from a plant-based diet. And then some of our newer research will also look into, we're really big now into trying to get people to eat more whole foods. So I go by like trying to get patients to do an 80-20, less of that ultra, ultra processed food, because we don't know what's increasing our cancer rates. And that probably does play a role for some of these young cancers that are happening.

Dr. Fleege: I think it's always a balance. I get this question a lot. Like if I just had never eaten sugar, would this not have happened? And I think that is not the right path. Often I do recommend if someone wants to follow a specific diet, a Mediterranean diet is reasonable. But some of our newer fads like intermittent fasting, keto, like as we go through the trends of what people are doing from a diet standpoint, that comes to our clinic. Is that what I should be doing to prevent breast cancer or treat breast cancer? And I think for most of these trends when it comes to eating, we don't have the data to support that. So I completely agree with what Dr. Huber-Keener recommends as well.

Dr. Clancy: Great. So when we think of tobacco exposure and smoking exposure, mouth, throat, tongue, lung cancers come to mind. But where does smoking come in as far as breast cancer risk?

Dr. Huber-Keener: It’s another one of those, we certainly know that it can increase the risk for breast cancer, but it's all from observational data. And we can do alcohol by itself because there's plenty of people who drink alcohol who don't smoke. There are not as many people who smoke that don't drink alcohol. And so getting that data on smoking specifically is difficult. We do think that the more and the longer that you smoke, the more

increased risk, not like a lung cancer, but it does increase, and that the risk never goes down to 0, like back to baseline if you stop smoking, but cessation certainly improves the risk from where you were before.

Dr. Clancy: So you mentioned alcohol.

Dr Huber-Keener: Yeah.

Dr. Clancy: And as we try to educate Iowans about what are those many risk factors that puts Iowa out ahead of other states right now as far as cancer risk, we do know that binge drinking in Iowa is pretty high. Do you have a sense of how it relates to breast cancer risk? And even harder question, do you know why? Is there a pathway of pathophysiology that alcohol actually, you can see how it increases risk.

Dr. Huber-Keener: I think that maybe one of the reasons it could increase risk is kind of similar to why we think obesity does, is that through liver metabolism and everything, it can increase estrogen and inflammation kind of in the body for some of those things. And then obviously it's wreaking its own kind of havoc when done on a very regular basis or done in large amounts. Again, a lot of it is observational data. And it used to be that we would say, when we looked at it, zero drinks per week was really safe for women. But when we've parsed out the data, we really do think about zero to three drinks per week on average. It does not seem to substantially increase risk. And I think that's a little bit easier to tell patients, because if I tell them zero alcohol, it's almost like they feel like they can't do that. And then when I talk about, if they're doing 7 drinks or more per week, which we know substantially increases the risk, they feel like it's a little bit easier for them to go from 7 to 3 than 7 to 0.

Dr. Clancy: Sure. So probably the, I imagine this may be one of the hardest questions to parse out, but where do we stand as far as hormone replacement therapies and birth control as adding or subtracting to the risk for breast cancer? Because I know it's been up and down for a while.

Dr. Huber-Keener: Correct. And I mean, certainly the original birth control pills that we had substantially increased the risk of breast cancer. So I even remember at the beginning of medical school and I was in medical school for a long time with an MD PhD. I was certainly taught that birth control pills substantially increase your risk for breast cancer. The ones that almost all of our patients have been exposed to at this point are all considered low risk for breast cancer. It's not that there's zero risk, but when we look at the data, if you look at all women, you have to treat between 7 to 8,000 women to cause one breast cancer from hormonal birth control. There is probably a difference as you get up in age. So I say once you get into your 40s, maybe it's one in a thousand have to be treated to

cause that. So it's not, if I have a patient who wants zero, like to do anything that could increase their risk, maybe it's, you know, that could play a role into that, but it's not gonna be the big deciding factor. And interestingly, progesterone IUDs, which have way less circulating hormone, actually have the same risk. And so I can't say that that's no risk. And then hormone, it depends if it's menopausal hormone therapy versus perimenopausal, we really don't know. Perimenopausal may be very similar to birth control pills, but it's a data free zone, right? We don't have studies that use the bioidentical estradiol, bioidentical micronized progesterone. We just don't have that. When we look at menopausal hormone therapy, you know, the study, the Women's Health Initiative that made—WHI—that made people very worried about breast cancer risk, it did increase breast cancer risk. It was started in women who were older, but we can look at that group that's that 50 to 59, and when they look at the absolute increased risk when people used five years of a type of hormone replacement that we don't use very much, it's conjugated equine estrogen along with a medroxyprogesterone acetate, which is not what we use, that seemed to have the absolute increased risk of 2%. So not the biggest kind of increased risk. And if we say everybody has about a 12 to 13% risk, it does increase it, but not into the high-risk category, which would be 20% or greater. And so then, the longer people do hormone replacement therapy, the greater the risk that there is with it. But there are patients that may qualify that are around there, depending on what their risk tolerance is.

Dr. Clancy: That was a really good answer, by the way. It was really good because I knew it would be hard.

[laughter]

Dr. Huber-Keener: Yeah.

Dr. Clancy: Very much so.

Dr. Fleege: Let the gynecologist answer that one.

[laughter]

Dr. Clancy: And the PhD as well. Yeah.

Dr. Fleege: Well, and I think it's interesting because we just removed the black box warning, right? From hormone replacement therapy.

Dr. Huber-Keener: Yes, that was, we were, because I was like, it's not that there's zero risk, but the black box was really prevented a lot of people and a lot of insurances from actually covering it. And it's only in the last two years that we've gotten better insurance coverage.

Dr. Clancy: Right.

Dr. Fleege: Yeah.

Dr. Clancy: So for both of you, when we're working with a patient who has breast cancer and has been treated for it, are there things you pay particular attention to as far as preventing recurrence for the individual who's already had breast cancer?

Dr. Fleege: That's a great question. I think for someone who's already had breast cancer, part of what I recommend depends on the type of breast cancer. So I think a lot of the modifiable factors for someone with hormone receptor-positive breast cancer are related to trying to reduce exposure to hormones. All within a balance, though. I think sometimes it's easy to come on here and talk about avoid, avoid, avoid, but then forget the person that's sitting in front of you who has wishes and goals that might not always align with like completely avoiding hormones. And so I think a lot of the data that we have regarding vaginal estrogen, for example, for people who've had side effects from their therapy for hormone receptor-positive breast cancer and are miserable with vaginal dryness and maybe repeated urinary tract infections, is that it probably is going to be considered safe. We're getting, we don't have that data yet. The prospective data is still coming out, so we can't say that definitively. But I think we always have to come back to risk and a benefit discussion with patients and really make the best choice for someone and the best recommendations for the patient that's actually sitting in front of us.

Dr. Clancy: Yeah, makes good sense.

Dr. Huber-Keener: Yeah. And that data would show that we do have would show some safety. We always do try things that are not hormone first, right? Like in a matter of safety kind of for patients. But some of that observational data will also go and look at the fact that the women who use vaginal estrogen actually had decreased mortality from things. And we don't know if that's just because they were healthy enough to want vaginal estrogen. So was there other things that were already going on that were decreasing their mortality from that? But there's certainly so much more of a conversation about hormones with breast cancer survivors because of social media.

Dr. Fleege: Yeah, and I think, getting physical activity, the things that we talk about for preventing development of breast cancer are the same things we're talking about to reduce recurrence, right? Maintaining a healthy weight, being physically active, a balanced diet are the things that we'll talk about in our clinic as well, even after treatment.

Dr. Clancy: I can tell from both of you that you very much individually tailor these conversations depending on the patient risk. But is there any guidance to maybe the

primary care clinicians out there that when they're discussing breast cancer risk, how to put it all together in a almost in a priority way, what are the points that really need to be made to make sure that the patient can follow through with what's best for them as far as prevention? Kind of a hard question, but . . .

Dr. Huber-Keener: Yeah, I mean, it's what I tell people each time. It's an anti-inflammatory diet, controlling BMI, and we say a BMI less than 25 in the healthy range, but really a BMI of 30 or less is going to control it the most. getting that the recommended amount of exercise, that 150 minutes, not smoking, and then keeping alcohol to zero to three drinks per week. One thing that we haven't talked about that is kind of modifiable, but not modifiable is actually having pregnancies and delivering full term babies actually does decrease your risk depending on kind of age. And also lactation. The longer lactation happens, the more it decreases risk for women in the future. And so it's not that you should do any type of family planning based on your breast cancer risk, but if you do want to do things to reduce it, I think a lot of people actually think that pregnancy increases their risk overall. It's not to say that there aren't pregnancy associated breast cancers, but that overall in their lifetime that that could be protective for them.

Dr. Fleege: And I think one thing that Dr. Huber-Keener has alluded to is calculating someone's risk, right? Like calculating the risk of the patient that you're seeing. And so in primary care clinic is one of the best places I think that we can start individualizing what a person's risk is such that if it's not 12 to 14% that we quote the general population, but it's over 20%, then that does impact how we talk about risk factors, but also how we screen for breast cancers. And so there's several tools and calculators that will allow us to calculate an individual's risk based on their personal history and their family history.

Dr. Huber-Keener: And we're very lucky at the University of Iowa that for people who are already getting mammograms, their mammogram reports at least do a rough calculation using a model called the Tyrer-Cuzick model. If they come to us in genetics, we'll do a slightly different, more in-depth version of that. But that can give a lot of people, at least of mammogram age, that type of assessment. And if it's greater than 20%, many times they're coming to some of our high-risk clinics, or that's the indicator that they should be doing more of a risk assessment. I just think it's hard for a lot of our primary care colleagues that have so much to do to figure out how am I supposed to figure out who's at risk at age 25?

Dr. Clancy: Yeah, yeah. So with those, you know, the regular mammograms obviously is level one, but what other tools do you have for screening if those mammogram screens, maybe they don't identify a risky piece of tissue, but they do identify risk. What else is in your tool belt as far as options?

Dr. Huber-Keener: Yeah, so for the patients who have not been, so if we do a risk assessment or their mammogram doesn't show that they're greater than a 20% lifetime risk and they have dense breast tissue, that's when that is part of that law to talk, or at least the mammogram report has to say that supplemental imaging is something that should be discussed with their provider. And so what we have here available at the University of Iowa is automated whole breast ultrasound, which is not just like one part of the breast, but it's a machine that kind of goes across all of the breast tissue. And that can look at the breast tissue better. I would say now that we have 3D mammograms, that those are doing a pretty good job of that. But especially if you wanted to stagger it by six months and have more frequent breast imaging, you have that option. And then for people who do qualify for high-risk breast screening, breast MRI is going to be almost three times as good as mammogram at finding things. And then there's some, depending on what guidelines that you're looking at, breast MRI may be recommended even for extremely dense breast tissue. And then there is evidence for that heterogeneously dense breast tissue as well. We sometimes have an insurance issue with those things.

Dr. Clancy: So, you know, you're having more and more screening options, more and more knowledge on what are the risk factors. As we look to the future regarding breast cancer risk, what do you see on the horizon? Do you see a even better set of tools on the horizon as far as being able to diagnose or see risk earlier and be able to act? What's on the horizon for us?

Dr. Huber-Keener: I mean, in terms of genetics, we certainly have a—you know, we think about 10, maybe even up to 15% of breast cancers may have a true genetic mutation that we could identify. But there are also these familial breast cancers where there's more than should be happening in a family, but we couldn't find the gene that was responsible for it. So you already see companies like Myriad that are giving some of these risk scores or polygenic risk scores, and they're looking at little changes in many different genes that when you add them together, so it's like maybe blue versus brown eyes, but if you add enough of those changes together, does that cause proteins to come together differently such that it affects risk? And so I think from a genetic standpoint, that's going to come down the pipeline and be something that gets used. And then I do think that, you know, one of the things that we're trying at the university, and other places are, is to get more of these calculators built into a better way into our electronic medical record, like Epic here, and have it be part of templates that it just kind of pops out. What is, you know, as I say, when people come for risk assessments, the Tyrer-Cuzick is not perfect for mammogram, but I'd rather you have something than nothing. And that's the same thing from that, because I think for a long time, our primary care colleagues were using something like the Gail method model, which will look at it, but that's the whole reason that Dr. Fleege was saying

people don't think about second- or third-degree relatives because it wasn't including it on that calculator.

Dr. Clancy: Got it. Got it. Nicole, what do you see out on the horizon for us?

Dr. Fleege: I'm a little bit biased because patients see me at the time of breast cancer. I can tell you all about the horizon of breast cancer treatment, which if you have an hour, I could do. But I guess for me, what I'm hoping on a personal note is that in Iowa, we continue to expand services to reach patients that maybe are individuals that aren't thinking about breast cancer or having breast cancer risk assessed. And so how do we engage patients in rural communities that have to drive really far to see a genetic counselor? How do we get these services that we offer so beneficially with Dr. Huber-Keener and her colleagues at the university? How do we reach patients that don't have that access that we do here? And so I don't know that I can say we have that plan set on the horizon, but I'm hoping that's something we're continuing to work on in the next few years.

Dr. Huber-Keener: And at least through like the Iowa Cancer Consortium has resources for patients that, you know, if they don't have health insurance, they can get free mammograms, things like pap smears and those kinds of things as well, that we just kind of get the news out about what some of those resources are to more of our communities that don't want to drive three to four hours to the university.

Dr. Clancy: Yeah, you know, we're just at the start of this grant process, but the state of Iowa will receive a significant amount of money for the Rural Health Transformation Program. And the state of Iowa has put forward cancer prevention and early detection as one of their top priorities, so maybe some of your guidance will be called upon very soon as far as this. Great, great. Well, I want to thank both of you for making a really complex set of factors and subject much clearer on how it all fits together. As we close, what are some of the take-home points you'd like to leave with our listeners? And let's start with Katie.

Dr. Huber-Keener: Well, I'd just like to point out a healthy lifestyle can reduce your breast cancer risk by about 20 to 30%, so almost a third. So we can't change what we've been born with. I do say that everybody should have some sort of risk assessment for breast cancer by the age of 25, because there's so many things that we can do that affect mortality from breast cancer and also affect your ability to have to have some of these more treatments like those chemotherapies.

Dr. Clancy: Nicole, how about you?

Dr. Fleege: Yeah, I just, I appreciate advocating for yourself, and so never being told, you know, if you feel something within your breast, at least talking about that. It doesn't always

require breast imaging or meeting with some of us, but I think just being aware that breast cancer can occur at all ages, and we are seeing it occur in younger populations, trying to be active about the things you can modify, like Dr. Huber-Keener mentioned, and then, you know, bringing up any concerns you have with your medical team.

Dr. Huber-Keener: And starting mammograms at age 40, regardless of risk, if not before, but not at age 50.

Dr. Fleege: Yeah.

Dr. Clancy: Great, great, great. Well, you've both been great, and I really want to thank you for joining us today, but also for the great work that you do on women's health and breast cancer prevention and early detection. You just do great work.

[Upbeat theme music plays]

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